Prevalence and management of intrathecal morphine induced pruritus in the New Zealand Māori population

Jennifer Boudreau

2012

A Research Portfolio in fulfilment of the requirements for the degree of
Master of Heath Sciences in Advanced Nursing, at University of Auckland, New Zealand

Abstract

Background: The use of intrathecal morphine for patients undergoing total hip and knee joint replacements and for lower segment caesarean sections (LSCS) has gained popularity worldwide since its introduction in 1979 (Gehling & Tryba, 2009). Several studies show that morphine delivered via the intrathecal route is an effective and safe method of pain relief (Dahl, Jeppesen, Jorgensen, Wetterslev, & Moiniche, 1999; Sites et al., 2004). However, while the beneficial effects of intrathecal morphine have been clearly documented in many studies, so also have the adverse effects e.g., nausea and vomiting, pruritus, and respiratory depression (Gehling & Tryba, 2009; Gwirtz et al., 1999). Pruritus is described as one of the most common adverse effects, with a reported incidence of 30% to 100% (Szarvas, Harmon, & Murphy, 2003).

Aims: The aims of this research portfolio were to determine if the incidence of intrathecal morphine induced pruritus (ITMI) was influenced by ethnicity, age, or gender, and to explore how this pruritus was managed by health care professionals.

Methods: A two-phased approach was undertaken. A retrospective audit was conducted to determine the incidence of intrathecal morphine induced pruritus among certain patient groups and what treatment was received. A health care professional survey was then performed to explore the current awareness, observations, and management of intrathecal morphine induced pruritus.

Findings: The findings revealed significant ethnic disparities in patient responses to intrathecal morphine. Results of the health care professional survey show variances in their knowledge base, which has led to development of a framework for improvement in the management of intrathecal morphine induced pruritus.

Conclusions: Management of these outcomes can be enhanced by the implementation of the strategies and frameworks outlined. Utilisation of these research portfolio recommendations could enable earlier post-operative recovery and improved patient outcomes. These recommendations could ensure health care professionals maintain competency and awareness in the provision of diligent management of patients receiving intrathecal morphine.

Acknowledgements

These past few years of study and research have been both informative and exciting.
I would like to thank the following people:

Anecita Gigi Lim RN, MHSc, PGDipSciPharm, FCNA(NZ), PhDC and

Senior Lecturer School of Nursing

Faculty of Medical and Health Science

University of Auckland, and

Francesca Storr RGON, BHSc, MN (Hons), PGCert HSc

Clinical Nurse Specialist – Pain Management

Honorary Professional Teaching fellow University of Auckland, School of Nursing, for their continued support as supervisors,

Dr. Chris Frampton and Dr. Marion Blumenstein for their advice in statistical analysis,

Lorraine Nielsen (RLIANZA), Subject Librarian, The University of Auckland, for her assistance and enthusiasm,

Ngati Awa, BOPDHB, and NZNO for their scholarships awarded to me on this journey,

Julia Braid RN, Clinical Nurse Manager, ICU, Tauranga, for her support, and

To all the health care professionals who participated in this research project.

Most importantly I would like to thank my husband Pat. Without his support and encouragement over the years I may never have embarked upon, or completed this educational journey.

I would also like to thank my daughters Raquel and Sophia for inspiring me.

Thank you to Fred, Anne, and my whanau for their continued motivation and understanding when I couldn't attend family functions.

Preface

Pēpeha ō Jennifer Boudreau

Tēna koutou katoa
Ko Mataatua te waka
Ko Putauaki te maunga
Ko Ohinemataroa te awa
Ko Ngāti Awa te iwi
Ko Ngāti Pukeko te hapū
Ko Pūkeko te marae
Ko Te Ratapahi Mate raua ko Nellie ōku tīpuna ki te taha o tōku matua
Ko Bobby Woods raua ko Margaret Seamark ōku mātua.
Ko Heni (Jenny) taku ingoa
No Poroporo ahau
No reira, tēna koutou, tēna koutou, otira tēna tatou katoa.

Recently, my 15-year old nephew Sam, who is of Māori descent, was scheduled for the second and most complex surgery in a series of operations required for the correction of a congenital malformation of his right foot. His only parent Mere, my sister, was extremely anxious prior to the surgery knowing that Sam who suffers with Asperger's syndrome, experiences intense morphine induced pruritus post-operatively. During Sam's previous admission Mere had to spend countless hours with him, trying to calm him in the prevention of self-harm as he relentlessly tried to soothe his itching skin.

I visited Sam immediately post-operatively and he was using a morphine patient controlled analgesic (PCA) pump. During the course of my visit, Sam became increasingly itchy and extremely irritable. I gave him cool washcloths to soothe his skin and suggested that Mere inform Sam's nurse—which she did. Unfortunately, Sam's condition did not appear to be a priority for his nurse; it seemed there was very little acknowledgement of Sam's discomfort and no immediate assistance was received.

As feared, Sam became focused on one thing only and that was to relieve the pruritic effects. He began scratching so hard that he caused deep, red welts to appear across his chest and face. He was oblivious to the fact that he was causing himself to bleed. We asked the nurse for help and when she saw the blood all over the sheets she was visibly alarmed. Not waiting for further acceleration of Sam's anxiety, I encouraged Mere to call Sam's surgeon for assistance. He quickly prescribed the appropriate dosage of intravenous naloxone for administration and consequently had the intravenous morphine changed to intravenous fentanyl via the PCA.

After receiving two doses of naloxone, the pruritus quickly subsided and an exhausted Sam was finally able to settle down for the night. Mere, who had been there for hours, then had to go and pick up her other child from the sitter and eventually made it home just before midnight. It was a confusing and unpleasant evening for all involved. For Sam, who had to suffer through the pruritus experiencing an exaggerated delay in treatment; for Mere, dealing with the frustration and helplessness she endured as her son became more and more agitated; and for the nurse, who appeared overwhelmed and anxious.

This experience prompted me to pursue this topic of research.

(Note: All names have been changed to protect the identity of those portrayed).

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction

1.1 BACKGROUND TO THE ARGUMENT

A recent initiative from the New Zealand Government has been focused on achieving its health target to improve access to elective surgery. Technological and medicinal advancements combined with the fact that people are living longer, are placing demand on our public health system to increase the number of elective surgeries performed each year (Ministry of Health, 2011). Elective surgeries such as hip or knee joint replacements improve quality of life, by aiding in the reduction or elimination of pain, promoting independence, and therefore allowing the patient to resume participation in social and physical events (Ministry of Health, 2011). Ministry of Health (2010) statistics show a 5.2% increase in caesarean section procedures performed in New Zealand from 1999 to 2007, and also reflect that patients who opted for this procedure were over 35 years of age.

Worldwide, an estimated 234.2 million major surgeries are performed annually (Weiser et al., 2008). With the numbers of surgical patients evidently on the rise, most will require some form of pain management (Lee et al., 2010). Poorly managed pain and post-operative adverse effects are a major concern for a high percentage of patients, and combined with the 'stress response' to surgery, many undesirable consequences may develop (Macintyre & Ready, 2001). Subsequently, the demand is greater than ever for health care professionals to demonstrate professional diligence and comprehensive management of their patient's pain. Successful pain management leads to a shortened length of stay and ultimately reduced hospital costs (Kodali & Oberoi, 2011).

Traditionally, moderate to severe pain was managed with intermittent doses of intramuscular analgesics which were timed around the clock. The use of the PCA with self-administration of small, frequent, on demand intravenous analgesia was later introduced (Ferrante, Orav,

Rocco, & Gallo, 1988). Increasing emphasis has been placed on the importance of improved pain management, and the introduction of acute pain teams occurred in the early 1980s (McQuay, 2009). In the 1990s, many government bodies worldwide published recommendations and guidelines acknowledging that "a patient has the right to expect adequate treatment of acute pain and that all members of the health care team have an obligation to provide it" (Macintyre & Ready, 2001, p. 2).

Intrathecal morphine (ITM) has fast become a popular and effective post-operative analgesic for many different surgical procedures (Gehling & Tryba, 2009). A single dose of morphine injected into the cerebrospinal fluid (CSF) provides excellent analgesia for up to 18 to 24 hours after administration (Rathmell, Lair, & Nauman, 2005). Expected side effects of morphine include analgesia, sedation, respiratory depression, nausea, and constipation (Macintyre & Ready, 2001; Wallace & Staats, 2005). When administered intrathecally, the patient can frequently be subjected to adverse effects such as nausea and vomiting, pruritus, and urinary retention (Gehling & Tryba, 2009).

Pruritus is the most commonly documented adverse effect of intrathecal morphine and appears to be dose related. As noted in the obstetric population, between 8% and 72% of patients can be expected to need some form of pharmacological intervention to treat pruritus when intrathecal morphine is given in the dose range of 100 to 200 mcgs (Lockington & Fa'aea, 2007). Pruritus can be extremely troublesome for the patient, and sometimes more unpleasant than the pain itself (Szarvas et al., 2003).

Practicing registered nurses and midwives have many responsibilities in their daily activities. For those caring for post-operative patients, evaluating the effectiveness and managing the adverse effects of analgesia is a large part of their role. Adverse effects of opioid analgesia are experienced by many patients—to the point where some patients prefer to suffer through

the pain than try to cope with the distressing adverse effects (Apfelbaum, Chen, Mehta, & Gan, 2003).

The researcher embarked into this research portfolio resulting from anecdotal evidence collated while working in her role as a Clinical Nurse Specialist within the Acute Pain Service in a New Zealand facility. Intrathecal morphine was utilised for many procedures, and the adverse effect of intrathecal morphine induced pruritus was noted to be present in many post-operative patients. During "pain rounds" it became evident that intrathecal morphine induced pruritus was a significant obstacle in the patients' recovery, and appeared to occur with higher incidence in certain patient populations.

1.2 RESEARCH QUESTION

Is intrathecal morphine induced pruritus influenced by ethnicity, age, or gender, and how well is it managed by health care professionals?

1.3 PURPOSE OF THIS RESEARCH PORTFOLIO

The purpose of this research portfolio is to address two issues:

1. To explore the association of intrathecal morphine induced pruritus with ethnicity, age, and gender.

2. To report the outcomes of a health care professional survey showing their observations of the adverse effects of intrathecal morphine and their management of these adverse effects.

1.4 STRUCTURE OF RESEARCH PORTFOLIO

This research portfolio is divided into five chapters: introduction, review of literature, retrospective audit, health care professional survey, and the conclusion with implications for practice. It will be set out as follows:

Chapter 1: Introduction

Chapter 1 provides the background of the study and an outline of the structure of this research portfolio.

Chapter 2: Literature Review

A review of selected relevant literature is presented. The literature review is divided into six main sections, and will explore pain and the mechanisms involved, inclusive of pain pathways, and the pruritic response. The use of the analgesic morphine will be discussed regarding its use as an intrathecally administered analgesic, and its effectiveness in the management of post-operative pain.

An in-depth discussion in relation to the adverse effects experienced by patients after receiving intrathecal morphine with much focus on pruritus will be provided. Intrathecal morphine induced pruritus will then be explored and the concept of the incidence of the pruritus and its relationship with ethnicity introduced. This review will also explore the health care professional's comprehension, awareness, barriers, and overall management of opiate administration. In final consideration, the patients' satisfaction with this intervention will be examined.

Chapter 3: Findings of a Retrospective Audit

This chapter presents results of a retrospective audit conducted in an endeavour to answer the question: *"Is intrathecal morphine induced pruritus influenced by ethnicity, age, or gender?"*

Statistical analyses will be completed on patient records that were collected over a period of 21 months to examine the incidence of the adverse effect of intrathecal morphine induced pruritus. This chapter will explore its association with ethnicity, age, gender, and the treatment received. The significant findings are then presented.

Chapter 4: Findings of a Health Care Professional Survey

This chapter will present the findings of a survey, which explores the question: *"Health care professional management of intrathecal morphine induced adverse effects, are we scratching the surface?"*

A quantitative survey investigating health care professional's knowledge, observations, and management of intrathecal morphine induced pruritus will be presented. The results of this survey will be collated, discussed, and summarised highlighting the primary findings.

Chapter 5: Conclusions and Implications for Practice

This final chapter amalgamates and summarises the main results of the two studies performed. Conclusions will be presented discussing implications and recommendations for practice. Each aspect of the portfolio will be discussed and with the evidence that was obtained during the research. Theories and recommendations will be presented based on the findings.

Chapter 2: Literature Review

2.1 INTRODUCTION

This chapter reviews selected literature related to the use of intrathecal morphine, its adverse effects, and the management of surgical patients after they have received intrathecal morphine as their post-operative analgesic management. A comprehensive review of the available literature has been performed to identify and discuss the issues relevant to intrathecal morphine induced pruritus and its association with ethnicity. Six themes have been identified relevant to this literature review and have been separated into sections—Sections 2.2 through Section 2.7. Each section will be further separated into subsections to encompass the different aspects of each theme as they are being reviewed.

In this Chapter, Section 2.1 is comprised of an introduction, literature review definition and purpose, and the literature search strategy.

Section 2.2 will introduce the basic principles and understanding of the pathophysiology of pain and nociception.

Section 2.3 will introduce morphine and discuss the mechanism of action of morphine and its kinetics.

Section 2.4: Opiates and pruritus in ethnic populations. Genetic polymorphism literature will be reviewed and critically analysed in reference to pain, pruritus, and ethnicity. Pruritus and the ‘pruritic response’ will be explored, and the concept of the incidence of pruritus and its relationship with ethnicity introduced.

Section 2.5 will explore intrathecal morphine as a post-operative analgesia. A background of intrathecal morphine and its use will be discussed. Analysis of contemporary theories in

relation to the adverse effects experienced by patients after receiving intrathecal morphine with much focus on the adverse effect of pruritus will be carried out.

Section 2.6 will explore health care professionals and opiate management. Current knowledge and rationale of health care professionals in their medication management of opiates and intrathecal morphine induced pruritus will be explored. Review of the literature related to the health care professional's comprehension, awareness, barriers, and management of opiate administration will be performed.

Section 2.7 will describe patient satisfaction with intrathecal morphine. Literature is reviewed and discussed regarding patient overall satisfaction with their post-operative pain management when receiving intrathecal morphine. The review concludes in Section 2.8.

2.1.1 Literature review definition and purpose

A literature review is defined as a systematic and critical analysis of publications from different sources in a topic of interest in any discipline (Elliott, 2007). Manalo and Trafford (2004) add that a literature review also considers any gaps in the literature and possibilities of future research.

Elliott (2007) defines the purpose of a literature review as: "Examining the knowledge base to inform a defined area of clinical practice or theoretical perspective, or guide original research" (p. 42). The purpose of this literature review is to explore current evidence and scientific research related to acute post-operative pain management with the opiate morphine via the intrathecal route and its adverse effects. This review will also investigate the incidence of intrathecal morphineinduced pruritus and its association with ethnicity, age, and gender. It will explore the interventions and pharmacological management received by the patient for this pruritus and overall patient satisfaction.

2.1.2 Literature review search strategy and identified themes

The literature search was conducted by actively searching through Medline, Medline (OvidSp), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Pub Med, Up-To-Date, and EMBASE databases. The Internet search engine Advanced Google Scholar was also accessed. New Zealand literature, publications, and policies were accessed through the New Zealand Ministry of Health and the New Zealand Nursing Organisation. The original search had a date restriction from 2000 to current, however needed to be widened due to the lack of literature covering 'a propos' pain, ethnicity, and New Zealand interests, to obtain relevant literature for this review.

The search keywords using Boolean logic included 'morphine', 'intrathecal', 'intrathecal morphine, 'opiates', 'ethnicity', 'race', 'pruritus', 'post-operative analgesia', 'opioid-induced', 'side effects', 'adverse effects', 'genotyping', 'pharmacokinetics', 'pharmacogenetics', 'polymorphism', 'medicine administration', 'nurse', 'medication management', and 'patient satisfaction'. The search was limited to the English language, human research studies, and only those available as full text publications. The combined results collated 150 publications which were retrieved.

These articles were then organised into six categories, and those that were relevant to these topics were included. These categories included: post-operative pain (17 articles), morphine (15 articles), genetics, polymorphism, ethnicity, and pruritus (37 articles), risks and adverse effects of intrathecal morphine (34 articles), health care professional's attitudes towards opiates (11 articles), and patient satisfaction with their post-operative care (10 articles). Those articles that did not fit into these categories were excluded. Any publication that referred to epidural morphine was also excluded, along with those that were not specific to either total hip or knee arthroplasty or caesarean section procedures.

The reviewed literature contained many different research methods inclusive of meta-analyses, prospective, observational, randomised double-blind studies, randomised controlled studies, systemic reviews, cross-sectional surveys, respective cohort studies, prospective and retrospective audits, and some of qualitative descriptive design.

2.1.3 Summary

Within this introduction, specific topics for review have been identified and the format of this chapter has been presented. Details of the search for literature have been described and are inclusive of where the literature was retrieved and how it was organised. The use of intrathecal morphine, its adverse effects, and association with certain ethnic groups will be reviewed in this chapter. The identified themes will be discussed in greater detail as subsequent sections of this chapter to determine what, if any, factors are responsible for certain populations experiencing intrathecal morphine induced pruritus more-so than others, its management, and overall patient satisfaction. The following sections will present the themes identified in this introduction.

2.2 PATHOPHYSIOLOGY OF PAIN

This section will discuss the pathophysiology of pain and nociception. Fundamental understanding of the mechanism of pain is paramount for any health care professional before opiate medication administration. A brief history of pain, acute pain, literature related to nociception, gate control theory, and biopsychosocial aspects of pain will be reviewed.

2.2.1 History of pain

Historically, early mankind related pain with evil humours, spirits, and demons. Throughout the ages, pain was thought of as punishment from the Gods. The word ‘pain’ originates from the Latin word *poena* denoting punishment (Lai, 2002). Lai (2002) indicates that it wasn’t until many years later that Galen (A.D. 130 to A.D. 200) hypothesised the brain to be the centre of sensation and pain. In the 1600s, Descartes concurred and announced the concept of

pain pathways. This theory was then reinforced 300 years later by Melzack and Wall in their renowned publication 'Pain Mechanisms: A new theory' in 1965 (Lai, 2002).

2.2.2 Acute pain

Acute pain results from tissue injury and cellular damage following traumatic, surgical, or disease related injuries. It has a limited duration and usually exhibits an incremental reduction in intensity (Vadivelu, Whitney, & Sinatra, 2009). Sternbach (1963) states: "…religious, philosophical and other connotations have been ascribed to acute pain. However, it is clear that pain usually signals impending or actual tissue damage and thus permits the individual to avoid harm." The International Association for the Study of Pain (IASP) describes pain as: "…an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Lai, 2002, p. 6). This definition was first stated in 1979 and then reiterated in 1994 (IASP, 2011). Pain is individual, and the patient's response to pain and reporting of pain can be varied by a number of behavioural, psychological, and social factors (Macintyre & Ready, 2001).

2.2.3 Nociception

Nociception is described as the normal processing of noxious stimuli from tissue damage (McCaffery & Pasero, 1999). Also described as *inflammatory* pain due to inflammatory mediator involvement, nociception is either somatic or visceral in character. Somatic nociceptive pain is dermatomal in origin and well localised with a sharp, crushing, or tearing sensation. Visceral nociceptive pain is poorly localised with cramping, colicky, non-dermatomal characteristics (Vadivelu et al., 2009).

Pasero and McCaffery (2011) describe nociception as involving four processes: transduction, transmission, perception, and modulation. In the transduction phase, cell damage from noxious stimuli causes peripheral nociceptors to release a number of compounds known as excitatory substances (e.g., prostaglandins, bradykinin, substance P, serotonin, and

histamine). These substances support further activation of nociceptors, consequently generating the pain impulse (Marchand, 2008; Pasero & McCaffery, 2011; Vadivelu et al., 2009). Injured tissue may release substances such as potassium, which can invoke an immune response thereby sensitising the nociceptive receptors (Marchand, 2008).

Afferent information is transferred from the periphery through the dorsal root ganglia to the spinal cord via A-delta fibres and C fibres, or nerve axons (Pasero & McCaffery, 2011). The unmyelinated C fibres which transmit slowly are activated by chemical, thermal, mechanical, and cold noxious stimulation mediating a burning response (Dahl & Moiniche, 2004). The myelinated A-delta fibres are activated by mechanical and thermal noxious stimuli and transmit to the central nervous system (CNS) quickly, with the ability to define the exact location of the injury (Suchdev, 2002). This neuronal activity synapses in the dorsal horn and in the presence of norepinephrine, glutamate, and substance P, the stimulus is continued from the spinal cord to the brainstem and higher cortical levels via multiple ascending pathways. Glutamate specifically, binds to the N-methyl-D-aspartate (NMDA) receptors in the dorsal horn and promotes pain transmission (Pasero & McCaffery, 2011). Activated when noxious stimuli intensity and duration exceeds a certain level, the NMDA receptor is responsible for wind-up pain (Dickenson, 2002).

Perception occurs as the neural activity of pain transmission terminates in conscious awareness in the thalamus of the cerebral cortex. A network of cortical and sub-cortical matter is generated, which includes processes that influence movement, emotions, and drives responses related to pain (Pasero & McCaffery, 2011).

Modulation then occurs as the neural activity in the brain stem descends to the dorsal horn of the spinal cord, initiating survival actions of ‘fight and flight’ and the production of endogenous opioids (e.g., serotonin and nor epinephrine). These endogenous opioids in turn

produce analgesic effects (McCaffery & Pasero, 1999). Constant and amplified pain impulses from peripheral nociceptors may lead to central sensitisation, which may outlast the stimuli that initiated the pain sensation, forming a 'pain memory' (Dahl & Moiniche, 2004).

2.2.4 Gate control theory

Many early hypotheses of pain were widely discredited after the introduction of Melzack and Wall's gate control theory in 1965. Melzack and Wall (1965) proposed that the pain response is determined by interaction between the cells in the substantia gelatinosa of the dorsal horn, the dorsal column fibres that extend to the brain, and the first central transmission (T) cells in the dorsal horn. Melzack and Wall (1965) theorised that the following three processes are significant features of afferent input which hold the gate open thereby maintaining pain activity: on-going small fibre activity which precedes the stimulus, the stimulus evoked activity, and the balance of activity in large versus small fibres.

In the absence of noxious stimuli, a disproportionate increase in large over small fibre activity is produced which prevents signal transmission to the brain, thereby closing the gate and reducing the perception of pain (Dickenson, 2002). In his discussion of the gate control theory, Dickenson (2002) concludes with: "…the transmission of pain from the periphery to the spinal cord was subject to modulation by both intrinsic neurons and controls emanating from the brain" (p. 755). This gate control theory has revolutionised our understanding of the mechanism of pain, and is still frequently referenced today.

2.2.5 Biopsychosocial aspects of pain

Everyone experiences pain differently and much evidence is present in the belief that: "…central nervous systems sub-serving attention, emotion, and memories of prior experience exert control over the sensory input" (Melzack & Wall, 1965, p. 976). A study by Maclaren and Kain (2007) on the biopsychosocial model of pain, encourages clinicians to adopt this: "…highly innovative conceptual framework" (p. 411). This model advocates that the

biological, psychological, and social aspects of a person collaboratively affect both health and illness. This framework has received a substantially increased awareness over the past 20 years (Maclaren & Kain, 2007).

The biopsychosocial model was explained in greater detail by Hansen (2010). The biological component relates to the physiological and anatomical aspects of pain. The psychological aspect refers to three elements of pain: emotional, behavioural, and cognitive. The emotional element encompasses emotions that accompany pain e.g., fear, anxiety, depression, anger, guilt, and irritability. The behavioural element includes the actions taken in response to pain and consequences of pain in one's life. The cognitive elements are associated with awareness, memories, expectations of pain, and the ability to cope with it (Hansen, 2010). The social aspect of this model is influenced by a patient's cultural background and support system, such as family and friends (Maclaren & Kain, 2007).

2.2.6 Summary

In summary, pain interpretation has proven to be most complex, individual, and perceptual. Awareness and understanding of all aspects involved in the manifestations of pain can be beneficial for improvement in overall pain management. Patients who have undergone any of the three surgical procedures identified as focal points in this portfolio: a total hip joint arthroplasty, a total knee joint arthroplasty, or caesarean section would be expected to have experienced some degree of nociceptive pain.

2.3 MORPHINE

This section will explore the origins and profile of morphine and discuss its kinetics and actions, side effects, and use in the management of acute pain.

2.3.1 Origins and profile of morphine

Morphine is derived from the opium poppy 'papaverum somniferon', which was first isolated in 1806 by German pharmacologist Friedrich Sertürner. Sertürner named this compound 'morphium' after the Greek god of dreams 'Morpheus' (Rachinger-Adam, Conzen, & Azad, 2011). By 1817, morphine use had become widespread and was first commercially sold in 1827 (Rachinger-Adam et al., 2011). The development of the hypodermic needle in 1853 by Alexander Wood later accelerated its use (Yaksh, 1999). During the American Civil War, morphine was administered freely to soldiers for injuries and illness. After the war ended, over 100,000 soldiers were recognised as suffering from "soldiers disease" or morphine addiction (Trescot, Datta, Lee, & Hansen, 2008). Morphine, an opioid agonist, has been recognised as the 'gold standard' since its discovery for treating severe pain (Eckhardt et al., 2000; McCaffery & Pasero, 1999; Morrow, 2012).

2.3.2 Morphine kinetics and actions

Opioid drugs manifest their analgesic effects by binding to, and activating the opioid receptors (e.g., mu, kappa, delta, and sigma: symbolised as μ, ƙ, δ, and Σ). These receptors are located in the central nervous system and the peripheral nervous system (PNS) (Macintyre, Rowbotham, & Walker, 2008). Morphine acts as an agonist at mu-1 and mu-2 opioid receptors throughout the body, thereby mimicking the effects of endogenous opioids. Analgesia is an opioid agonist effect, which results from complex interactions involving both mu-1 and mu-2 opioid receptors at designated areas in the brain, spinal cord, and even in peripheral tissue (Coda, 2006). Barash, Cullen, Stoelting, Cahalan, and Stock (2009) state that: "…supra-spinal opioid analgesia originates in the peri-aqueductal grey matter, the locus ceruleus, and nuclei within the medulla and primarily involves mu opioid receptors" (p. 273).

Barash et al. (2009) propose that morphine decreases the release of substance P by presynaptically acting on primary afferent nociceptors at the spinal level. At this point,

morphine also decreases afferent transmission of nociceptive impulses by hyperpolarising interneurons in the substantia gelatinosa of the dorsal spinal cord. Macintyre et al. (2008) further explain that this resulting hyperpolarisation inhibits neuronal activity, which decreases signal transmission from the peripheral nervous system to the CNS, resulting in reduced pain stimuli processing. Morphine actuated peripheral analgesia is more of a presumption currently, but can be attributed to activation of the opioid receptors on primary afferent neurons, occurring only when there is inflammation at the injury site (Barash et al., 2009).

Morphine undergoes glucuronidation in the liver to produce morphine-3-glucuronide (MG3) and morphine-6-glucuronide (MG6) at a ratio of 2 to 1 (Tran, 2002). Mazoit, Butscher, and Samii (2007) performed a study of morphine use in post-operative patients and concluded with their statement: "M-6-G is a potent opioid agonist and M-3-G is a mild opioid antagonist" (p. 70). Mazoit et al. (2007) also indicated that MG3 and MG6 are poorly excreted in patients with renal failure. Impaired kidney function leads to accumulation of morphine metabolites, which may precipitate a more prolonged effect, respiratory depression, and possibly obtundation (Tran, 2002).

Morphine is known for its low lipid solubility, or hydrophilic properties (McCaffery & Pasero, 1999). This hydrophilic property makes morphine more soluble in aqueous solutions, subsequently contributing to the slow onset and long duration of action (Pasero & McCaffery, 2011). Sinatra (2009) cites Way, Fields, and Schumaker (2004) in stating this hydrophilic property of morphine is also associated with difficulty in penetrating the blood brain barrier. The significance of this property is realised when administering morphine as an intermittent intravenous bolus or via the intrathecal route. Pasero and McCaffery (2011) explain that adequate time must be allowed after administering morphine via these routes to assess patient response to the first dose before administration of another. Opioids with a slow

transfer between plasma and the site of action are less than suitable in achieving immediate pain control (Lotsch, Dudziak, Freynhagen, Marschner, & Geisslinger, 2006).

Morphine can be administered via many routes such as the oral route, sub-lingual, intranasal, nebulised, intrapulmonary, intravenously, intramuscularly, subcutaneously, rectal, vaginal, intra articular, topical, epidural, and the intrathecal route (Macintyre & Ready, 2001; Pasero & McCaffery, 2011; Sinatra, 2009).

2.3.3 Side effects of morphine

The stimulation and activation of opioid receptors leads to analgesia but also potentiates side effects (Tollison, Satterthwaite, & Tollison, 2002). These side effects are mediated by activation of the opioid receptors in the CNS (Tollison et al., 2002). Tollison et al. (2002) propose that these adverse events are also controlled through opioid receptors located outside the CNS. Tollison et al. (2002) add that these side effects may be actuated by non-opioid mechanisms, e.g., they may be the consequence of drug interactions with other medications such as sedatives or hypnotics.

Morphine acts on most systems in the body (Barash et al., 2009; Ho & Gan, 2009; Macintyre & Ready, 2001; Pasero & McCaffery, 2011; Sinatra, 2009; Tran, 2002). Eckhardt et al. (2000) support this in their statement, "the use of opioids is limited by its side effects" (p. 185). The side effects of morphine can be influenced by multiple variables including the dose, the route and speed of administration, genetic variability, drug interaction, levels of pain, patient co-morbidities, and emotional status of the patient (Tran, 2002).

Respiratory depression is a predictable side effect of morphine. Dose dependent ventilatory depression is produced due to morphine decreasing medullary respiratory centre response to carbon dioxide (Barash et al., 2009). Oxygen desaturation, obstructive apnoea, paradoxical

breathing, and bradypnoea can occur when sleeping or if continuous infusions are being received by the patient (Barash et al., 2009).

Central nervous system effects such as sedation, euphoria, dysphoria, nausea and vomiting, miosis, muscle rigidity, and cognitive or fine motor impairment may occur (Macintyre & Ready, 2001). Prolonged or profound sedation can occur with morphine administration especially if the patient has comorbidities and/or sedative medications (benzodiazepines, antihistamines) have been administered. Reduction in this side effect of sedation is managed by assessing the patient's comorbidities, limiting sedative medications, opioid rotation, opioid plus adjuvant analgesic, or administration via the spinal (intrathecal) route (McNicol et al., 2003).

Barash et al. (2009) emphasise miosis is indicative of opioid administration and also appears to correlate with opioid ventilatory depression. Morphine also depresses the cough reflex by exerting a direct effect on the medullary cough centre (Coda, 2006). Nausea and vomiting are caused by direct stimulation of the chemoreceptor trigger zone, enhanced by vestibular stimulation (Macintyre & Ready, 2001).

Cardiovascular effects are usually minimal however vasodilation, bradycardia, and myocardial depression may occur. Hypotension after morphine administration in the post-operative period may indicate the patient is hypovolaemic (Macintyre & Ready, 2001). Effects on the genitourinary system are caused by failure of sphincter relaxation, which results in dyssynergia or poor coordination between the urethral sphincter and bladder detrusor muscle, leading to urinary retention (Coda, 2006). Gastrointestinal system effects include delayed gastric emptying and constipation (Macintyre & Ready, 2001). Coda (2006) adds that morphine also causes symptoms of gastro-oesophageal reflux by reducing oesophageal sphincter tone.

Fukuda (2005) states that opioids increase smooth muscle tone in the biliary tract resulting in a rise in bile duct pressure, and may cause spasm of the sphincter of Oddi. Integumentary system effects include pruritus, which may at times be pronounced, relentless, and debilitating. This opioid related adverse effect of pruritus typically occurs around the face, neck, and upper thorax (Ho & Gan, 2009). The release of histamine from mast cells and circulating basophils may result in localised or general pruritus. Allergy due to a histamine reaction may occur, although a true allergic reaction is uncommon (Macintyre & Ready, 2001).

2.3.4 Morphine use in acute pain

Morphine provides powerful dose-dependent pain relief for those enduring moderate to severe acute pain. It remains the standard of comparison of all opiates, and its use in pain management has been vast and widespread (Sinatra, 2009). Morphine has a variety of uses inclusive of post-operative analgesia despite its association with significant dose-dependent adverse effects (Sinatra, 2009). Documentation and patient education are required in acute pain management inclusive of recording pain scales, titration of the intervention, and monitoring the efficacy of the morphine. Documentation is also a legal requirement for substance control purposes (Pasero & McCaffery, 2011).

Continuous and regular exposure to opioids may lead to the development of tolerance and physical dependence. Both these clinical manifestations however, are frequently mistaken for opioid addiction (Smith, 2008). Most patients have concerns about addiction to morphine and require considerable patient education to alleviate these fears. However, morphine use for purposes other than pain relief has led to restrictions to minimise the risk of addiction and abuse (Pasero & McCaffery, 2011). Okie (2010) argues that in recent years there has been an unprecedented rise in deaths caused by unintentional drug overdoses of opioid medications. This attestation has led to the release of a report from the Centre for Disease Control and

Prevention in the United States of America emphasising the importance of training physicians in the appropriate prescribing of morphine, and in the use of patient education materials.

2.3.5 Summary

Morphine has been utilised as a powerful analgesic in the Western world for almost 200 years and can be administered in a number of different ways. Many side effects are expected, but these side effects still do not outweigh morphine's efficacy in combating pain. Future research may lead us to being able to predict certain patient groups that are susceptible to these side effects. The potential of predicting who is susceptible to these side effects can enable us to then titrate the analgesia accordingly, resulting in improved pain management regimes. This will ultimately benefit patients in all areas of pain management, acute or chronic.

2.4 OPIATES AND PRURITUS IN ETHNIC POPULATIONS

Numerous publications are now supporting the hypothesis that genetic background influences morphine response. This section will discuss genetic variations and polymorphism and their implications with opioid induced pruritus and ethnic populations. This section is separated into four subsections: genetics and opiates, mechanism of genetic polymorphism and ethnicity, pathogenesis of pruritus and opioid induced pruritus, and pruritus and ethnicity.

2.4.1 Genetics and opiates

With advances in technology there is increasing evidence that a number of gene polymorphisms can contribute to variability in pain experienced in humans (Somogyi, Barratt, & Coller, 2007). Somogyi et al. (2007) undertook a study on the pharmacogenetics of the opioid receptor. The authors identified 100 variants in the mu opioid receptor gene OPRM1, which is the primary binding site target for opiates. A study by Bond et al. (1998) on the single-nucleotide polymorphism in the human mu opioid receptor gene showed similar

findings and the authors stated: “significant differences were observed amongst ethnic populations regarding allele distribution” (p. 9608). The A118G (allele) is the most commonly identified single nucleotide polymorphism (Bond et al., 1998). A linear trend was determined by Somogyi et al. (2007) highlighting that patients with the G variant required higher doses of morphine. The allele has been described as: “one of two or more versions of a genetic sequence at a particular location in the genome” (Feero, Guttmacher, & Collins, 2010, p. 2004).

A study by Bianchi et al. (2008) on morphine pharmacogenetics concluded with the authors reinforcing that the effects of morphine may be influenced by non-genetic factors such as patient age and organ function, concomitant therapy, drug interaction, or actual disease process. However, Bianchi et al. (2008) later added: “…there are now several examples in which inter-individual differences in drug response are due to sequence variants in genes encoding drug targets, drug metabolising enzymes, or drug transporters” (p. e10).

These inherited determinants remain stable throughout a person’s lifetime, unlike the other factors aforementioned that influence the drug response (Bianchi et al., 2008).

2.4.2 Mechanism of genetic polymorphism and ethnicity

Roden and George (2002) discuss the advent of pharmacogenetics, pharmacogenomics, and pharmacokinetics. These relatively new fields of science have achieved an increased awareness and perception of the molecular, cellular, and genetic determinants of drug actions, and the appreciation that variants in many genes might contribute to variability in drug action and response (Roden & George, 2002).

An example of gene variability discussed by Roden and George (2002) is well known to pain service areas in nursing and medicine as cytochrome P450 2D6, or CYP2D6. Cytochrome P450 are a group of metabolising enzymes in the liver responsible for drug metabolism

(Podgoreanu & Mathew, 2006). There are over 70 variants of the CYP450, but mainly the CYP2D6 enzyme subfamily have been described; some leading to 'loss of function' or poor metabolising. This loss-of-function is exhibited by homozygotes, which comprise 7% of the Caucasian and African-American populations who are rendered so-called 'poor metabolisers' (Roden & George, 2002). The main characteristic of these poor metabolisers is their inability to eliminate drugs appropriately, which can lead to a lack of therapeutic response or an increase in the risk of adverse reactions (Zanger, Raimundo, & Eichelbaum, 2004). These loss-of-function enzymes are very uncommon in the Asian population (Roden & George, 2002; Zanger et al., 2004).

At the opposite end of the spectrum are the 'hyper-extensive' or 'ultra-rapid metabolisers'. These individuals with multiple functional copies of the gene constitute up to 20% of the African population (Roden & George, 2002). Up to 25% of drugs are metabolised by CYP2D6, an enzyme which can now be identified in genetic testing for poor metaboliser phenotype prediction (Zanger et al., 2004). Between 5% and 10% of the analgesic codeine is converted to morphine in the liver, catalysed by the cytochrome P450 enzyme (Coller, Christrup, & Somogyi, 2009). Genetic variability of the CYP2D6 metabolising enzyme does exist. Roden and George (2002) explain: "…variability in the frequency and the types of allelic variant among ethnic populations is a common theme in contemporary genetics that could well under-lie ethnic specific beneficial and adverse drug responses" (p. 38).

Cepeda et al. (2001) performed a cohort study to evaluate ethnic differences in the morphine response and whether they were pharmacokinectically based. This study supports the existence of ethnic differences in response to opioids. This study showed that although Caucasians have higher serum morphine-3-glucuronide levels than Native American Indians, Native American Indians are more susceptible to morphine depression of the ventilatory response.

Tan et al. (2009) performed a prospective cohort study on ethnicity and the OPRM variant. The authors showed similar findings in their statement: "Ethnicity and OPRM 118A>G genotypes are independent and significant contributors to variation in pain perception and post-operative morphine requirements in patients undergoing caesarean section delivery" (p. 1). Tan et al. (2009) reported that ethnic Indian patients reported higher pain scores and used more morphine compared to the Chinese or Malays, noting that the frequency of OPRM 118G allele was higher in Indians compared to other Asian populations. The authors explained that being able to identify these predictors could eventually mean patients will get the appropriate post-operative analgesic titration requirement with the minimisation of side effects experienced.

2.4.3 Pathogenesis of pruritus and opioid induced pruritus

More recently, pruritus has been described as "localized or diffuse, and classified as pruritoceptive, neuropathic, neurogenic and psychogenic" (Sharma, Chugh, Kastury, & Kapoor, 2009, p. 119). Ganesh and Maxwell (2007) describe pruritus as a sensation that provokes a desire to scratch and can be aroused by a variety of mechanical, electrical, and chemical stimuli. Pasero and McCaffery (2011) explain: "pruritus, like pain, is transmitted via unmyelinated C-fibre nociceptors from the periphery (skin) to the CNS (dorsal horn of the spinal cord) where they synapse with pruritic-specific secondary neurons" (p. 499).

Waxler, Dadabhoy, Stojiljkovic, and Rabito (2005) concur that a sub-class of C-nociceptors originating in the skin transmit the pruritic impulse to the ipsilateral dorsal horn of the spinal cord. These C-fibres synapse with pruritic-specific secondary neurons which travel via the spinothalamic tract to the thalamus (Waxler et al., 2005). Tertiary neurons then relay this pruritic sensation to the level of conscious perception in the cerebral cortex (Sharma et al., 2009). Waxler et al. (2005) support this theory, stating the pruritic signals are then relayed to the somatosensory cortex of the post-central gyrus.

Ho and Gan (2009) proposed that the tonic inhibition of this 'pruritic-specific' pathway is reduced by opioids, which allow spontaneous activity of central pruritic neurons. Pruritus is an adverse effect, not an allergic reaction to opiates (Ho & Gan, 2009). A study by Waxler et al. (2005) on post-operative pruritus concluded that pruritus is transmitted by a subset of C-fibres that are different from those that transmit pain. The authors claim the two sensations seem interrelated, and emphasise that while painful stimuli can inhibit pruritus, inhibition of pain processing may enhance pruritus.

Pruritus caused by histamine release such as insect bites, urticaria, and allergic reactions can be treated with antihistamines (e.g., promethazine or diphenhydramine) however, there is no strong evidence to prove that antihistamines can relieve opioid induced pruritus (Grape & Shug, 2008). Some patients with opioid induced pruritus may report being less bothered by the pruritus after antihistamine treatment. However, this may likely be the result of the sedative effects of the antihistamine, a choice that is not recommended in combination with the already sedative effects of the opiate (Ho & Gan, 2009).

A study by Cevikbas, Steinhoff, and Ikoma (2010) explores spinal neurotransmitter receptors and pruritus. The authors propose that new receptors have been identified which shed light on the complexities of peripheral and central pruritus and the pruritic sensation. These receptors are the kappa opioid receptors and bombesin receptor-2. Pruritus is regulated by neuronal and non-neuronal cells and pruritus can be modulated and pharmacologically manipulated in areas such as the skin, spinal cord, dorsal root ganglion neurons, and selective areas of the brain (Cevikbas et al., 2010). This theory is still in its infancy and is yet to be proven in humans (Cevikbas et al., 2010).

2.4.4 Pruritus and ethnicity

Numerous researchers have proven that morphine response varies from person-to-person for pain (Pasero & McCaffery, 2011; Suchdev, 2002; Wellington & Chia, 2009). It is now

accepted that the prevalence of pruritus can be considerably varied across different ethnic populations (Tey & Yosipovitch, 2010). An example of this was highlighted in a study by Tey and Yosipovitch (2010) on the prevalence of pruritus in ethnic populations. The authors showed that African patients are the only ethnic group that suffer with pruritus after being treated with chloroquine for malaria. The authors also confirmed that biliary cirrhosis associated pruritus is more common in African-Americans and Hispanics—compared with Caucasians. Tey and Yosipovitch (2010) indicated certain types of pruritic dermatitis conditions to be common in Asians, but rare in African-Americans and Caucasians, claiming this may possibly be related to genetic polymorphism of the interleuken-31 receptor. The interleukin-31 expression is a newly discovered T-cell cytokine that has been implicated with pruritic conditions such as atopic dermatitis (Bilsborough et al., 2006).

2.4.5 Summary

There is now a noticeable amount of research emerging on the topic of ethnicity influencing the morphine response. There is an evident relationship between the pain and pruritic pathways. One may extrapolate that the incidence and severity of pruritus in certain situations may also be ethnicity related. The reviewed literature appears to support the concept that certain pruritic entities are specific to certain ethnic populations.

Understanding the significance of genetic polymorphisms and the role this may play in the morphine response in relation to pain may inspire further research to corroborate theories that the incidence of the adverse effect of pruritus is also related to ethnicity and genotype variants.

2.5 INTRATHECAL MORPHINE AS POST-OPERATIVE ANALGESIA

This section will introduce intrathecal morphine and issues associated with its use. Pruritus as an adverse effect of morphine when it is administered via the intrathecal route will be discussed. This section is divided into subsections that will introduce intrathecal morphine,

and then explore the use of intrathecal morphine, the adverse effects and their incidence, intrathecal morphine induced pruritus, intrathecal morphine induced pruritus related to ethnicity and gender, and finally its use in relation to dose and types of surgery.

2.5.1 The introduction of intrathecal morphine

Sometimes referred to as neuraxial analgesia, there have been numerous studies supporting the use of intrathecal morphine, its efficacy and safety profile, and its use in post-operative surgery (Dahl et al., 1999; Gehling & Tryba, 2009; Gwirtz et al., 1999; Sites et al., 2004).

A study by Chestnut (2005) on the efficacy and safety of intrathecal morphine and its usefulness in post-operative analgesia, describes the climate that existed before its use became widespread. The author explained that few anaesthesiologists played a role in post-operative pain management and surgeons typically prescribed intramuscular opioids for post-operative pain. Chestnut (2005) depicts an era where pain relief was inadequate and adverse effects occurred frequently. A study by Marks and Sachar (1973) reported that despite the use of intramuscular opioids, 73% of post-operative patients experienced distressing pain, implying that most physicians at that time prescribed inadequate doses of analgesics at infrequent intervals. Consequently, most patients feared surgery because of the risk of severe post-operative pain (Chestnut, 2005).

Since its introduction in 1979, intrathecal morphine has been utilised for anaesthetic and post-operative analgesia (Bailey et al., 1993; Gehling & Tryba, 2009; Wang, Nauss, & Thomas, 1979). Over the years, it has proven to be very effective and many studies have been conducted worldwide on the efficacy, dosage, and adverse effects experienced when morphine is administered via this route (Wang et al., 1979).

2.5.2 Morphine use via the intrathecal route

When administered via the intrathecal route, morphine is delivered directly into the (CSF), initially avoiding absorption by epidural fat and blood vessels where rostral migration occurs (Macintyre & Ready, 2001). Following intrathecal administration, the distribution of the opiate is complex. Within the spinal cord, morphine is rapidly distributed within the CSF. Here it binds to non-specific sites within the white matter, as well as specific receptors of the dorsal horn and eventually reaches the plasma compartment via venous uptake. The opiate then slowly traverses the dura to the epidural space, where it binds with the epidural fat and enters plasma slowly due to its hydrophilic properties. This slow transfer of morphine from the CSF allows large concentrations to continue circulating within the CSF, which leads to a delayed onset, extensive and prolonged cephalic infiltration, and a resultant lengthy analgesic duration (Fournier, Van Gessel, Weber, & Gamulin, 2000; Goodarzi, 1999; Rathmell et al., 2005).

Barash et al. (2009) explain that morphine injected intrathecally hyperpolarises interneurons in the dorsal spinal cord substantia gelatinosa, causing decreased afferent nociceptive transmission. Morphine also acts presynaptically on primary afferent nociceptors, thereby decreasing substance P release. Barash et al. (2009) propose that spinal morphine analgesia is mediated by mu-2 receptors.

This route of analgesia takes effect in approximately 47 to 75 minutes with a duration of up to 18 to 24 hours (Rathmell et al., 2005). When administered in combination with a local anaesthetic intrathecally (as a surgical anaesthetic with, for example, hyperbaric bupivacaine), the patient will sense the onset of spinal block within a few minutes (Bernards, 2006). The advantage of this method of administration and its lengthy duration of analgesic effect unfortunately, is associated with the risk of more serious unwanted side effects of delayed respiratory depression and sedation (Fournier et al., 2000).

When administered via the intrathecal route, the slow onset time combined with the dose-related duration of the analgesia, and the side-effect profile (in particular delayed onset respiratory depression and sedation) renders morphine as unsuitable for day-case surgery (Hindle, 2008). However, this route may be advantageous in elderly patients, or for those who are intolerant to frequent and high doses of morphine, and those who may exhibit difficulty in using a patient analgesic controlled device (Dabu-bondoc, Franco, & Sinatra, 2009).

2.5.3 Adverse effects of intrathecal morphine and their incidence

Gehling and Tryba (2009) performed a meta-analysis on the risks and adverse effects of intrathecal morphine and obtained significant information. The authors reported that the adverse effects of intrathecal morphine include nausea and vomiting, pruritus, urinary retention, and respiratory depression.

Within this meta-analysis, a study performed by Gwirtz et al. (1999) involved 5696 adult patients over a period of seven years. Thirty-seven percent of reported cases experienced intrathecal morphine induced pruritus. The authors concluded that respiratory depression was the least common at 3%, which apparently was easily detected by nursing staff. The authors reinforced that this respiratory depression was never life-threatening and always responsive to treatment with naloxone. In this study, the authors further explain that the incidence of nausea and vomiting however was about 25% and urinary retention was 1.8%. The low percentage of urinary retention in this study was supported by the fact that many patients receiving intrathecal morphine were also receiving indwelling catheters (Gwirtz et al., 1999).

A study by Rathmell et al. (2005) on intrathecal opiates, reported that the incidence of pruritus occurring after intrathecal morphine was administered varied from 30% to 100%. Nausea and vomiting occurred approximately 30% of the time, and the incidence of true respiratory depression of clinical significance is unknown, yet confirmed as ‘infrequent’. The

incidence of urinary retention in this study was approximately 35%. Rathmell et al. (2005) explain that urinary retention is a predictable side effect of morphine when administered intrathecally. The authors explain further, via this route, morphine interacts with the neuraxial section of the opioid receptors of the sacral spinal cord causing inhibition of sacral parasympathetic nervous system outflow. This leads to marked detrusor muscle relaxation and an increase in maximal bladder capacity. As a result, parasympathetic tone and a central analgesic action are affected, which modifies the bladder pain threshold (Rathmell et al., 2005).

A study by Bailey et al. (1993) showed that intrathecal morphine has been known to produce "…statistically significant dose-related increases in sedation and decreases in pupil size" (p. 49). The author concluded that, however these changes were small and reportedly did not coincide with hypoxemia.

2.5.3.1 Intrathecal morphine induced pruritus

When morphine is administered intrathecally, pruritus is the most common adverse effect and although not life threatening, may be unduly uncomfortable for patients decreasing their overall satisfaction (Ganesh & Maxwell, 2007). Pruritus can be so severe for some patients that opioid therapy must be modified or abandoned (Dunteman, Karanikolas, & Filos, 1996).

The exact mechanism of intrathecal morphine induced pruritus is unclear (Ganesh & Maxwell, 2007; Grant, Hepner, & Barss, 2010; Hindle, 2008; Szarvas et al., 2003). Szarvas et al. (2003) undertook a study on intrathecal morphine induced pruritus. These authors argue that this pruritic sensation arises from the superficial layers of the skin, mucous membranes, and conjunctivae. The sub-epidermal layer of the skin has nerve endings that cluster densely around 'pruritic points'. These points correspond to areas which are very sensitive to pruritogenic stimuli (Szarvas et al., 2003).

Colbert, O'hanlen, Galvin, Chambers, and Moriarty (1999) explored the theory that mediators such as serotonin and prostaglandins (PGE_1 and PGE_2) play a role in the pruritic sensation. Colbert et al. (1999) state that PGE_1 and PGE_2 enhance C fibre transmission to the CNS and release histamine which causes pruritus. Grant et al. (2010) argue that even though the aetiology of intrathecal morphine induced pruritus is unclear, it is not caused by a histamine release.

Waxler et al. (2005) proposed that the central mechanism of intrathecal morphine induced pruritus is related to the cephalic spread of the drug in the CSF, and its action on the medullary dorsal horn and the trigeminal nucleus in the medulla. Toomey and Biddle (2006) claim that pruritus has a 10% to 90% incidence in occurrence after a patient receives intrathecal morphine. Areas of the face, including the distribution of the trigeminal nerves (especially its maxillary and ophthalmic divisions) are particularly vulnerable to the effects of the intrathecal morphine (Toomey & Biddle, 2006; Waxler et al., 2005). Waxler et al. (2005) hypothesise that the pruritic receptors reside in an arrangement of cells called the 'subnucleus caudalis'. The subnucleus caudalis is an anatomical region of the trigeminal nucleus, which is an elongated structure spanning down into the cervical region of the brainstem (Waxler et al., 2005).

Ganesh and Maxwell (2007) studied the pathophysiology and management of intrathecal morphine induced pruritus and concluded that the incidence was 20% to 100%. The authors proposed that the possible mechanisms contributing to intrathecal morphine induced pruritus included mu opioid receptors, the brain, spinal cord, dopamine D_2 receptors, serotonin 5-HT_3 receptors, the prostaglandin system, and GABA and glycine receptors (Ganesh & Maxwell, 2007).

2.5.4 Intrathecal morphine induced pruritus related to ethnicity, age, and gender

This section was designated to review articles related to the association of intrathecal morphine induced pruritus, ethnicity, age, and gender. All the search engines that have been listed within the introduction of this chapter have been utilised and exhausted in an effort to find literature in relation to these topics. This search has been conducted by the researcher of this research portfolio over a period of two years from 2010 through 2012. To date, little evidence has been procured but the following.

Szarvas et al. (2003) performed a study on the pathophysiology of intrathecal morphine induced pruritus. The wide range in the reported incidence of intrathecal morphine induced pruritus suggests there may be individual patient differences that influence the pruritic perception. The authors concluded by hypothesising that individual allele structure and genetic polymorphisms are partly but not totally responsible. Tey and Yosipovitch (2010) support this view, by claiming pruritic receptors and response to anti-pruritic treatments are significantly affected by genetics.

There was no literature procured in relation to intrathecal morphine induced pruritus, age, or gender.

2.5.5 Intrathecal morphine in relation to dose and type of surgery

In a study by Gehling and Tryba (2009), the association with intrathecal morphine dosage and side effects were also explored. The authors clustered the participants into three separate groups according to the dose of intrathecal morphine administered by the anaesthetist prior to surgery. The first group received a morphine dose of less than 300 mcgs, the next group received greater than or equal to 300 mcgs of morphine intrathecally, and the third group received a placebo (all groups were supplemented with spinal anaesthesia). Gehling and Tryba (2009) indicated that the combination of spinal anaesthesia and intrathecal morphine was associated with an increase in nausea and vomiting, and pruritus.

Gehling and Tryba (2009) claim their results strongly indicated that those patients receiving a dose above 300 mcgs of intrathecal morphine exhibited a significant increase in the risk of pruritus, more noteworthy than those who received a dose lower than 300 mcgs of morphine.

The lower doses of intrathecal morphine were associated with a reduced risk of respiratory depression. The higher doses of intrathecal morphine reflected association with more episodes of respiratory depression compared with the lower dose. Gehling and Tryba (2009), therefore concluded that there is no evidence to confirm there is an effective dose of intrathecal morphine that is associated with no risk of respiratory depression. The authors added that the risk of nausea and vomiting increased in patients receiving less than 300 mcgs of morphine.

Gehling and Tryba (2009) surmised that: "the moderate incidence of side effects seems justified by the quality and duration of the analgesia" (p. 649). Like systemic opioid therapy, intrathecal morphine requires measures for prophylaxis and the treatment of its adverse effects, along with continuous observation of the patient's respiratory function. The use of intrathecal morphine is associated with longer analgesic duration, a decrease in additional intravenous opioids, and an unexplained reduced blood loss during surgery (Gehling & Tryba, 2009).

Rathmell et al. (2005) undertook a study on the role of intrathecal drugs in the treatment of acute pain. The authors explained that early trials of intrathecal morphine where doses varied between 500 mcgs and 1000 mcgs resulted in profound sedation and respiratory depression. Rathmell et al. (2005) concluded that there is a ceiling analgesic effect of intrathecal morphine, whereas the efficacy of doses above a certain range are often limited by side effects. Rathmell et al. (2005) have listed specific recommended dose ranges per surgical procedure within their study.

Rathmell, Pino, Taylor, Patrin, and Viani (2003) performed a randomised controlled study to determine appropriate dose ranges for intrathecal morphine. The authors concluded that the optimal dose of intrathecal morphine for pain control after total hip arthroplasty is 200 mcgs of morphine. At a dose of 200 mcgs, the analgesic effect is maximised and the side effects are minimised (Hindle, 2008; Rathmell et al., 2003). A study by Fischer and Simanski (2005) on recommendations for analgesia after total hip replacement showed similar findings. The authors stated the study showed significant benefit for the patient receiving 100 mcgs to 200 mcgs of morphine intrathecally. These patients exhibited reduced post-operative pain scores and a reduction in additional analgesic consumption (Fischer & Simanski, 2005).

A study by Girgin, Gurbet, Turker, Aksu, and Gulhan (2008) demonstrated significant dose dependent variability relating to adverse effects of intrathecal morphine when utilised for caesarean section patients. The authors indicated that a dose of 100 mcgs of intrathecal morphine produces comparable analgesic coverage to doses up to 400 mcgs, with a significantly decreased incidence of intrathecal morphine induced pruritus (when combined with low-dose bupivacaine). In a study by Sarvela, Halonen, Soikkeli, and Korttila (2002), the authors agreed that a dose of 100 mcgs of intrathecal morphine provided long lasting analgesia for caesarean section patients. The authors did report that the incidence of pruritus in this study was frequent.

Adverse effects of intrathecal morphine in relation to the type of surgery is discussed in many articles, and most concur that intrathecal morphine induced pruritus is very common in the obstetric population (Lockington & Fa'aea, 2007; Siddik-Sayyid et al., 2010; Szarvas et al., 2003). Siddik-Sayyid et al. (2010) indicated that intrathecal morphine induced pruritus in this population could be related to the interaction of oestrogen, with opioid receptors in the spinal cord and the increased cephalic spread of the medication administered.

2.5.6 Summary

Whether a patient receives opiates intravenously or intrathecally, astute health care professional observation is required. Morphine administered via the intrathecal route appears to be a safe form of post-operative analgesic, however pruritus has been identified as a very common adverse effect.

Despite the research that has been carried out to explore intrathecal morphine induced pruritus, its mechanisms and treatment, we are far from breaking barriers and fully understanding this physiological manifestation. Although the actual percentages in the occurrence of intrathecal morphine induced pruritus varied, it is evident that these statistics are high. There was a discernible lack of literature surrounding this topic of pruritus and its association with ethnicity, age, and gender. These evident gaps in the available literature reinforce that further research is required to enrich our understanding of these subjects.

2.6 HEALTH CARE PROFESSIONALS AND OPIATE THERAPY

This section of the literature review will be focused on the management provided by health care professionals for opiate therapy. It will be separated into subsections discussing opioid management by health care professionals, ethnic and cultural disparities in opioid management, and the management of intrathecal morphine induced pruritus. Despite extensive searches for relevant literature, there was a distinct paucity of information available.

2.6.1 Opioid management by health care professionals

Skills of pharmacovigilance are required in opiate administration. A study by Eisenhauer, Hurley, and Dolan (2007) on gaining insight into nurses' reported thinking during medication administration, concludes that the key element in medication administration is the constant professional vigilance of nurses. Eisenhauer et al. (2007) discuss this current concept and

have identified 10 descriptive categories that may influence a health care professional's thought process during opiate administration.

These categories are: thinking, dose-timing, checking, assessment, evaluation, teaching, side effects, 'work arounds', 'anticipated problem solving', and drug administration. Nurses' thinking processes extend beyond rules and procedures when administering medications, and they utilise critical thinking and clinical judgment based on patient data and interdisciplinary professional knowledge to provide safe and effective care (Eisenhauer et al., 2007). Eisenhauer et al. (2007) explain 'work arounds' as circumstances where nurses bypassed hospital protocols or procedures to expedite the patient receiving the medication, or to use their time more efficiently. 'Anticipated problem solving' is described by Eisenhauer et al. (2007) as nurses utilising their judgment skills and anticipating patient needs, for example, the timing of analgesia before physical therapy.

Murnion, Gnjidic, and Hilmer (2010) performed a cross-sectional survey of inpatients requiring opioid analgesia in an Australian hospital. The authors of this study concluded that maximum prescribed doses of opioids were not administered therefore the majority of their participants (65%) did not receive adequate analgesia. The authors added that this incomplete analgesia was associated with the presence of side effects. Murnion et al. (2010) surveyed both the nursing staff and the medical staff who had identified similar barriers to opiate administration. The authors listed these reported and identified barriers as follows: time constraints, poor knowledge of opioid preparations and titrations, and inability to assess pain accurately.

Manias (2003) performed a prospective audit on 100 patients in an Australian facility to explore nursing administration and their documentation practices regarding analgesia. This study was limited by its restricted access to documentation. Manias (2003) concluded that

keen clinical judgment (which is individualised to patient's needs) is essential in balancing the patient's needs for managing pain in the post-operative period. However, Manias (2003) identified that further research is required.

Nurses must improve their understanding of the validity of pain measurement, morphine pharmacokinetics and pharmacodynamics, and their institutional recommendations for pain management (Van Hulle Vincent & Gaddy, 2009). A study by Van Hulle Vincent and Gaddy (2009) on nurses' reported thinking when administering analgesics stated that nurses exhibited misconceptions about morphine pharmacokinetics. The authors added nurses' also demonstrated unwarranted concerns about the adverse effects of morphine. Manias, Aitken, and Dunning (2004) however, argue that nurses are required to make complex decisions during medication management to ensure the provision of high quality and individualised patient care.

2.6.2 Ethnic and cultural disparities in opioid management

Jimenez, Seidel, Martin, Rivara, and Lynn (2010) performed a retrospective cohort study in the United States of America where they explored perioperative analgesic treatment in Latino and non-Latino paediatric patients. Findings of this study suggest the amount of analgesia received by patients were correlated with the patient's ethnicity. Latino subjects received 30% less opioids than Caucasians—the cause was unknown and further studies are recommended to elucidate the reasons (Jimenez et al., 2010).

Disparities have emerged between genders where females are reported to be receiving less analgesia than men in pre-hospital settings (Michael, Sporer, & Youngblood, 2007). Michael et al. (2007) performed a retrospective study where 953 cases were analysed to examine socioeconomic factors such as ethnicity, age, gender, and income in relation to analgesic administration. Michael et al. (2007) concluded by stating their study did not identify any

possible cause or explanation and recommended further research to establish why females received less analgesia than males.

A study by McDonald (1994) investigated differences in administration of analgesia for male versus female patients, and white versus ethnic minority patients. Conclusions of this study included male patients received significantly larger doses of analgesia than female, and white (Caucasian) patients received significantly more post-operative analgesia than ethnic minority patients (McDonald, 1994). The authors indicated that the rationale offered for the outcome where males received more analgesia than females included the following: nurses responded more accurately to the male patient's visual cues and males were more vocal than females in expressing their pain. Additionally, McDonald (1994) proposed that physicians may have prescribed larger and more frequent doses for the male patient, reflecting a degree of gender stereotyping.

McDonald (1994) comments further, that the rationale for the statistically significant difference in analgesia received by Caucasian's compared to Asians, African-Americans, and Hispanic-Americans remains unclear. The author identified themes to explain this outcome which included: minority patients may have been less likely to express their pain, were more reluctant to receive opiates, their complaints were given less credibility, or a language barrier existed. McDonald (1994) explains the language barrier concept that was initially introduced, was later discredited as the majority of the ethnic minorities in the study were African-Americans, who use American-English as their first language.

2.6.3 Management of intrathecal morphine induced pruritus

As already mentioned, the aetiology of intrathecal morphine induced pruritus remains unclear yet its incidence remains statistically elevated. Ganesh and Maxwell (2007) propose that management of this adverse effect can be achieved by running a continuous infusion of naloxone at doses of 0.25 mcg to 1 mcg/kg/hour. The author adds, it is recommended that

this infusion should be 'piggy-backed' with maintenance intravenous fluids. However, with this administration of naloxone, the upper threshold at which it may begin to antagonise the analgesia is unknown (Ganesh & Maxwell, 2007). Intravenous boluses of naloxone at a dose of 40 mcgs are useful in treating moderate to severe pruritus without reversing the analgesic effect of morphine (Dabu-bondoc et al., 2009).

A study by Siddik-Sayyid et al. (2010) showed similar findings that naloxone infusions were required to maintain pruritic relief. In this prospective, randomised, double-blinded study Siddik-Sayyid et al. (2010) explore ondansetron, a selective 5-hydro-xytryptamine type 3 (5-HT_3) being utilised as an effective treatment in morphine induced pruritus. The authors concluded that ondansetron was effective for relieving pruritus caused by intrathecal morphine in patients undergoing caesarean sections, however up to 50% of patients required further treatment of naloxone for either primary failure of ondansetron, or recurrence of pruritus.

Ganesh and Maxwell (2007) agreed that the prophylactic administration of ondansetron reduced the risk of pruritus in one trial. Rathmell et al. (2005) and Pirat, Tuncay, Torgay, Candan, and Arslan (2005) concur that ondansetron has demonstrated efficacy in both prevention and treatment of neuraxial opioid induced pruritus. A study by Charuluxananan, Somboonviboon, Kyokong, and Nimcharoendee (2000), showed similar findings highlighting that the treatment success rate was higher in the ondansetron group than in the placebo group (80% *vs* 36%, $p < .001$) for patients who had intrathecal morphine induced pruritus following caesarean sections.

In a study by Colbert et al. (1999), the authors postulated that prostaglandins (PGE_1 and PGE_2) are involved in the aetiology of pruritus. The authors argue that the use of non-steroidal anti-inflammatory drugs (NSAIDS) inhibit cyclo-oxygenases and decrease the

formation of prostaglandins. Colbert et al. (1999) performed a randomised blind study on 105 patients who were administered with 100 mgs of diclofenac rectally, immediately post-induction. The results of this study indicated that in the group of patients who received intrathecal morphine in combination with diclofenac per rectum, there was a significant reduction in the severity of pruritus. Colbert et al. (1999) reported: "the reduction in pruritus scores varied from 25% at 30 minutes to 98% at 24 hours" (p. 950).

Studies have been performed on the use of propofol as management for pruritus (Charuluxananan et al., 2001; Toomey & Biddle, 2006; Törn, Tuominen, Tarkkila, & Lindgren, 1994). As an anaesthetic agent, the use of propofol requires vigilant monitoring to prevent catastrophic outcomes related to respiratory and cardiovascular depression (Toomey & Biddle, 2006). In most circumstances, an anaesthetist would be required for administration of propofol. Consequently, this intervention would not be appropriate or realistic for the post-operative ward setting. However, Toomey and Biddle (2006) argue that several studies have demonstrated that sub-hypnotic doses can depress the sensation of pruritus. A study by Törn et al. (1994) on the effects of sub-hypnotic doses of propofol on the side effects of intrathecal morphine showed similar findings. Törn et al. (1994) described a 40% decrease in intrathecal morphine induced pruritus after the patient received a 10 mg bolus of propofol followed by a sub-hypnotic infusion.

A recent study by (Sheen et al., 2008) proposes that a premedication of the antidepressant mirtazapine (30 mgs) prevents intrathecal morphine induced pruritus in patients undergoing lower limb surgery. The authors performed a randomised, double-blinded, placebo-controlled study with 110 patients and indicated a resultant $p = 0.0245$ significance where the placebo group experienced ITMI (Intrathecal Morphine Induced) pruritus more-so than the group receiving mirtazapine. Mirtazapine decreased the incidence and severity, delayed the onset

time, and shortened the duration of ITMI pruritus. However, around 70% of the patients who took mirtazapine displayed sedation and somnolence (Sheen et al., 2008).

2.6.4 Summary

A search into the understanding of health care professional's awareness, attitudes, and actions in regard to opiate therapy yielded little success, therefore the search dates were widened as some literature dates back to 1994.

It is evident and yet quite disturbing to acknowledge that disparities in patients receiving analgesic therapy may exist. Ensuring the patient receives the optimum post-operative analgesia, with the minimum of adverse effects being observed, and treated adequately, is the goal of any health care professional.

There are many alternatives available to treat intrathecal morphine induced pruritus. Nurses and midwives utilise all the skills and knowledge at their disposal to provide the best care possible for their patient. The significance and value of nursing and midwifery observation and medication management is invaluable, however real barriers such as time restraints continue to impede these efforts.

2.7 PATIENT SATISFACTION WITH INTRATHECAL MORPHINE

This section will discuss patient satisfaction with intrathecal morphine administration for their post-operative analgesia. Discussion will include comparisons with patients who have received intrathecal morphine, and patients who have received alternative post-operative analgesia.

2.7.1 Patient satisfaction

As mentioned earlier in this chapter, a study by Sarvela et al. (2002) established that intrathecal morphine at a dose of 100 mcgs was far superior to epidural morphine for post-operative analgesia in parturients after caesarean delivery in women that were receiving

ketoprofen. Sarvela et al. (2002) explain neuraxial analgesia is an effective and long lasting analgesic following caesarean section, with the added bonus of minimal exposure to opioids for lactating mothers. The authors state that those parturients who received the intrathecal morphine at 100 mcgs reported high satisfaction levels despite the incidence of pruritus being frequent. Only 2.7% of these patients reported they would not be willing to receive intrathecal morphine again if they required another caesarean delivery (Sarvela et al., 2002).

A study by Essving et al. (2011) argued that intrathecal morphine is no longer the 'gold standard' for post-operative analgesia. Essving et al. (2011) performed a double-blinded study with 47 patients to assess post-operative management and patient satisfaction for patients undergoing total knee joint arthroplasty. The authors indicated that patients received better post-operative analgesia from local infiltration analgesia (LIA) than those patients who received intrathecal morphine. The intrathecal morphine recipients (Group M), however received only 100 mcgs of intrathecal morphine. The LIA was a combination of local anaesthetic (ropivicaine 300 mgs), NSAIDS (ketorolac 30 mgs), and epinephrine (0.5 mgs), injected peri-articularly during surgery (Group L). An intra-articular catheter was left in situ in all patients of this study so follow up analgesia with the LIA (for Group L) or a placebo (for Group M) could be administered. These follow up preparations were administered at 24 hours and 45 hours, after which the catheter was removed. Both groups received additional morphine via PCA pump post-operatively. In this study, the participants reported better pain control in the LIA group on post-operative day one, but post-operative days two through seven were the same. Overall however, the patients in the LIA group reported better analgesia and an earlier mobilisation, leading to an earlier home readiness and a reduced hospital stay (Essving et al., 2011).

While this study appears to favour the local infiltration anaesthetic technique, further results highlighted that the incidence of respiratory depression was higher in the LIA group,

although none required naloxone. There were seven positive cultures from the catheter tips (coagulase-negative staphylococcus) however antibiotics were not administered. Essving et al. (2011) added there was no evidential difference in the statistics of pruritus, urinary retention, or nausea and vomiting from either group. The intrathecal morphine dose of 100 mcgs in this study is much lower than the recommended dose of 200 mcgs for total hip arthroplasty (Rathmell et al., 2003). Patients undergoing total knee arthroplasty have higher post-operative analgesic requirements in comparison with patients undergoing total hip arthroplasty. An intrathecal dose of 300 mcg is now recommended for patients undergoing total knee arthroplasty, a dose which reflects a reduction in additional analgesia, and minimisation of side-effects (Hindle, 2008).

Another study by Sites et al. (2004) states that when undergoing a total knee arthroplasty, patients reported superior post-operative analgesia with fewer side effects and a more favourable experience after receiving a femoral nerve block with intrathecal bupivacaine. This was compared with patients who received intrathecal morphine as their post-operative analgesia. This prospective randomised clinical study involved 41 participants who were randomly divided into two groups. The first group received intrathecal morphine 250 mcgs plus hyperbaric bupivacaine 15 mgs. The second group received a spinal anaesthetic of hyperbaric bupivacaine 15 mgs, plus a single injection femoral nerve block containing ropivicaine 0.5% (40 mls), clonidine (75 mcgs), and epinephrine (5 mcgs). All participants received post-operative ketorolac and a patient controlled analgesic device.

Sites et al. (2004) reported both groups received equal analgesic management, but the femoral nerve block group reported less opioid induced side effects, resulting in an increased patient satisfaction over the intrathecal morphine group. In the follow up satisfaction survey, 20% of the intrathecal morphine group rated their experience as “unsatisfactory”. This 20% represented four participants, all of whom were female, and all claimed severe nausea to be

the source of their non-satisfaction. This study was limited by its short duration of 24 hours post-operatively.

Toomey and Biddle (2006) indicate patient satisfaction studies have placed pruritus amongst the most distressing, non-life threatening sensations that are experienced during neuraxial analgesia. Toomey and Biddle (2006) emphasise even though research is now being geared towards the study of pruritus, much is still unclear and propose: "pruritus may be the most recently appreciated 'little' big problem that anaesthetist's face" (p. 383).

2.7.2 Summary

Intrathecal morphine has been compared with other types of post-operative analgesic management, however it was difficult to find studies that measured actual patient satisfaction with intrathecal morphine alone. The studies that have measured patient satisfaction are small in participants and design. Analysis has determined that even though most patients are satisfied with the analgesic action of intrathecal morphine, the adverse effects do influence their overall comfort levels.

2.8 CONCLUSION

Intrathecal morphine has been utilised as a post-operative analgesic for over 30 years. It has proven to be an effective analgesic, however does carry with it a number of adverse effects, some of which can be quite debilitating for the patient. Intrathecal morphine requires management and observation for many hours post-administration and additional analgesia is often required. The incidence of pruritus as an adverse effect has proven to be statistically high and influential in patient overall satisfaction, therefore the importance of adequate management must not be undervalued. Literature concurs that the pain and pruritic pathways are related, however further research is required in this area to enable a better understanding of the opiate induced pruritic mechanism.

Adequate management of pain leads to many achievable goals such as reduced suffering and post-operative complications, which enable earlier mobilisation and rehabilitation. Effective and adequate management of a patient's post-operative pain may also contribute toward reducing the risk of chronic pain developing. Clinical experience however, confirms opiate administration is influenced by time constraints and fear of side effects being exacerbated or complicated with patient comorbidities. Literature did expose some disparities that exist in opiate medication administration and most of them were for reasons unknown. Institutional information and protocols for the medication management of opiate induced side effects are available but their implementation is varied. Further research is required to study health care professional barriers to, and understanding of, the administration and follow-up of opiate therapy, and management of these adverse effects.

The concept of intrathecal morphine induced pruritus being related to ethnicity has been explored but there was a noticeable dearth of literature surrounding this subject. Further exploration of this theory may lead to health care professionals being able to titrate the most appropriate opiate dose for each individual in relation to ethnic and genetic indicators. This could lead to the provision of maximum analgesia with the minimum of adverse effects being experienced. By identifying patients who may be susceptible to intrathecal morphine induced pruritus, we may also be able to minimise the adverse effects experienced through the titration phase with different interventions such as offering a combination of, or alternative opioid therapy.

Intrathecal morphine can be beneficial for the inpatient but not in the day stay setting as this area cannot accommodate the required lengthy post-operative observations for side effects. Continued education, the employment of, and adherence to policies surrounding prolonged monitoring for these side effects in patients who have received intrathecal morphine will not reduce the incidence of these side effects, but may promote patient comfort and safety.

It is clear that emphasis on education and the continued utilisation of acute pain services are a necessity for improved pain management. It will be through continued health care professional education and patient education that will see the dissolution of existing disparities. The patient who is medically informed is less afraid to ask for analgesia. The patient who is aware of their rights, and understands that the responsibilities of the 'health care professional' are inclusive of the promotion of comfort, is empowered. As patients and health care professionals become better educated and more invested in their overall care, a bond and mutual trust and respect can pave the way to superior management of pain and the side effects incurred.

The identified gaps in this literature review have led to the inspiration of the following two chapters: a retrospective audit to determine if intrathecal morphine is influenced by ethnicity, age, or gender, and a health care professional survey to evaluate their observations and management of intrathecal morphine adverse effects.

Chapter 3: Retrospective Audit

3.1 INTRODUCTION

Current understanding of ITMI pruritus and its association with ethnicity is still in its infancy. Review of the literature in Chapter 2 indicates there are few studies that have been undertaken which discuss the topic of certain patient groups being more susceptible to the adverse effects of intrathecal morphine than others (Szarvas et al., 2003; Tey & Yosipovitch, 2010). As there is a paucity of research on intrathecal morphine induced pruritus amongst patient groups, an audit was undertaken in a hospital in New Zealand on patients receiving intrathecal morphine, to determine the incidence of intrathecal morphine induced pruritus among certain populations.

This chapter presents the background in Section 3.2, introducing intrathecal morphine and its use in post-operative analgesia. This section will also briefly discuss the adverse effect of intrathecal morphine induced pruritus in relation to ethnicity. Section 3.3 explores the purpose of this audit, and Section 3.4 shows the methods section of this audit and presents the framework of analysis that was followed throughout the audit. Section 3.5 will present the results, Section 3.6 discusses the results, and Section 3.7 concludes the chapter.

3.2 BACKGROUND

As previously mentioned in Chapter 2, intrathecal morphine has been utilised for postoperative analgesia after surgery since 1979 (Bailey et al., 1993; Gehling & Tryba, 2009; Wang et al., 1979). Named appropriate to the route in which the morphine is administered, intrathecal morphine is injected into the CSF at any level of the cerebrospinal axis (U.S. Department of Health and Human Services, 2012). Since its introduction, anaesthetists throughout the world now offer this route of analgesia, and in combination with a spinal anaesthetic e.g., heavy marcaine or hyperbaric bupivacaine, intrathecal morphine has proven

to be a safe analgesic for a number of surgeries including orthopaedic and caesarean section procedures (Kalso, 1983; Karaman, Kocabas, Uyar, Hayzaran, & Firat, 2006).

In any acute care facility, many post-operative patients will experience adverse effects from opiates to some degree. Review of the literature has shown that many adverse effects are expected with this intervention. Specific to the intrathecal route, patients may suffer pruritus, urinary retention, nausea and vomiting, or respiratory depression (Rathmell et al., 2005). Research reveals a 30% to 100% incidence of pruritus being experienced after receiving intrathecal morphine (Jenkins, Spencer, Weissgerber, Osborne, & Pellegrini, 2009; Rathmell et al., 2005; Szarvas et al., 2003). The incidence of urinary retention has been reported at approximately 35%, while nausea and vomiting has been reported at approximately 30% (Gehling & Tryba, 2009). A study by Gehling and Tryba (2009) indicates a 3% incidence of respiratory depression occurring in patients receiving intrathecal morphine, however the true incidence of significant respiratory depression is unknown.

As indicated above, the incidence of intrathecal morphine induced pruritus is significant, yet the exact mechanism remains unclear (Ganesh & Maxwell, 2007; Grant et al., 2010; Hindle, 2008; Szarvas et al., 2003). Klepstad, Dale, Skorpen, Borchgrevink, and Kaasa (2005) proposed that a patient's genetic predisposition may influence their response to opioids. The authors observed that there were variations amongst responses on the clinical efficacy of morphine related to genetic influences. This study also demonstrated genetic variability associated with intrathecal morphine. This finding suggests that the adverse effect of pruritus may also be influenced by genetic variation. Variations in response to morphine have also been observed in relation to gender influences (Cepeda et al., 2001; Pleym, Spigset, Kharasch, & Dale, 2003).

Despite the efforts of health care professionals to enhance patient recovery, 80% of patients experience acute pain after surgery and 86% experience pain greater than “moderate”, suffering either severe or extreme pain (Apfelbaum et al., 2003). Adverse effects of opioid analgesia are experienced by many patients to the point where some prefer to suffer through the pain rather than try to cope with the distressing adverse effects (Apfelbaum et al., 2003). With the adverse effect of pruritus being so prevalent, an unfortunate consequence has been realised: the desire to scratch this opiate-induced pruritus may be more unpleasant than the actual pain itself (Szarvas et al., 2003).

3.3 PURPOSE

A retrospective audit is generally based on a review of records of discharged patients (European Union, 2012). Retrospective audits may make use of computer databases and link present outcomes to past events, and may also be referred to as an ‘ex-post facto’ design (Elliott & Thompson, 2007). The purpose of this retrospective audit is to identify patients receiving post-operative intrathecal morphine who experienced intrathecal morphine induced pruritus during the course of the treatment period. These results are taken from the medical records of patients undergoing caesarean sections and orthopaedic surgeries (total hip and knee joint replacements), who had received intrathecal morphine as their post-operative analgesic management. The incidence of intrathecal morphine induced pruritus has been explored and the two types of surgeries investigated.

This study was conducted in a publicly funded facility in New Zealand, where it was common practice to utilise intrathecal morphine as post-operative analgesia for orthopaedic surgeries such as total hip and knee arthroplasty, and caesarean section procedures. Patients were monitored by the acute pain team in this facility for 24 hours following administration of intrathecal morphine, and certain variants in patient responses became apparent. An

interesting theme was identified, and this audit was conducted to determine if intrathecal morphine induced pruritus is influenced by ethnicity, age, or gender.

3.4 METHOD

This audit was performed on data that was collected over a period of 21 months. Records of patients admitted to the facility from 2009 to 2011 for surgical procedures were explored. A retrospective review of the medical notes of 992 surgical patients referred to the acute pain service for management of their pain was undertaken.

Procedure: Ethics approval for this review was obtained from Northern Y Regional Ethics Committee (Appendix A). Approval from the departmental head was received to review these files (Appendix B). A letter of support was received from the Regional Māori Health Services (Appendix C). Patient consent was not required for this audit as the data is not identifiable. The data collected included information from records that had been maintained on each patient for 18 hours post-operatively, assessing their pain status, adverse reactions, and the severity of these reactions experienced. Also recorded was the treatment (if any) they received. Further data collected which will also be briefly discussed includes adverse effects such as nausea and vomiting, respiratory depression, hypotension, and patient satisfaction scores with intrathecal morphine being utilised for their post-operative analgesia.

Selection criteria: Inclusions of this audit were all patients who received intrathecal morphine as their post-operative pain management. Those patients of New Zealand Māori and New Zealand European descent only were included. Patients who had undergone total hip arthroplasty, total knee arthroplasty, or caesarean section procedures were selected. These groups were later organised into two groups: *orthopaedic* and *caesarean* groups. The range of ages from the data was between 15 and 87 years and included both genders.

Exclusions from this study included patients with allergies to morphine, and those with a history of skin conditions and associated pruritus. Also excluded were records that did not belong to either of the identified surgery groups.

The New Zealand Māori and New Zealand European ethnic groups were focused on as they generated the majority of data. This information was recorded from the demographic profile as documented in their medical record history. The initial criteria of the inclusion of data with an age of less than 75 years and those with less than two comorbidities, was later revoked to widen the scope of this audit.

An 'audit tool' was developed to identify participants suitable for this audit, and the data was entered into a Microsoft Excel spread sheet and organised (Appendix D). This audit tool was developed to capture certain information required to track and record discernible evidence for this audit (Annells & Whitehead, 2007). This data was later imported into the Statistical Programme for Social Sciences (SPSS). Information was collected and evaluated for the presence of pruritus in relation to ethnicity, age, gender, type of surgery, actual dose of intrathecal morphine, and the presence and intensity of pruritus on a scale of 'zero to ten'.

This scale is known as the Verbal Numeric Rating Scale (VNRS) (Jenkins et al., 2009). Zero pruritus is descriptive of having no pruritus. Pruritus measuring 10 out of 10 is described as the most intense itching ever, or severe pruritus. Jenkins et al. (2009) also describes another scale that can be utilised to measure pruritus, the Verbal Rating Scale (VRS). This scale measures pruritus from zero to three. Zero being no pruritus, one indicates mild pruritus, two indicates moderate pruritus, and three indicates severe pruritus. The VNRS was chosen to simplify patient responses as pain scales were also measured on a scale of zero to ten.

The dosage of intrathecal morphine varied from 50 mcgs through 400 mcgs. This dose was determined by the anaesthetist who administered the intrathecal analgesic depending on the weight and age of the patient, and the type of surgical procedure they were undergoing.

From all of the 992 patient records reviewed, a total of 129 patients received intrathecal morphine for their post-operative analgesic management. Of these 129 patients, four were excluded from this study as their surgeries did not fall into one of the three surgical categories identified for this audit. A further 16 records were excluded as they did not fall into the two ethnic categories. A total of 109 records were suitable for this study.

Of the 109 records found suitable, 13 records had no documentation regarding the incidence of intrathecal morphine induced pruritus occurring during the intervention—therefore these 13 records were also omitted from the audit. There were a remaining total of 96 records deemed appropriate for this audit.

Statistical analysis was performed and data reflecting the incidence of the adverse effect of intrathecal morphine induced pruritus was measured by cross tabulation in relation to a number of variables. All the associated information and data was crosschecked by an independent source and transcribers who all completed confidentiality agreements (Appendix E).

3.5 RESULTS

The results of the audit will be presented in four sections. First, the breakdown of the total demographic data of all records will be presented in Section 3.5.1. Analysis of data for the audit is then grouped according to the incidence of intrathecal morphine induced pruritus in Section 3.5.2. Section 3.5.3 shows the treatment received for the ITMI pruritus and recorded pruritic scores. Section 3.5.4 presents data reflecting the incidence of other adverse effects that were recorded, and Section 3.5.5 presents patient satisfaction scores as recorded.

3.5.1 Demographic data

The demographic data of all the records where patients had received intrathecal morphine has been organised into ethnicity, gender, and type of surgery as set out below.

3.5.1.1 Intrathecal morphine and ethnicity

Of the total 96 records reviewed 42% (*n* = 40) of the patients were New Zealand Māori and 58% (*n* = 56) were of New Zealand European descent (Refer to Figure 1 below).

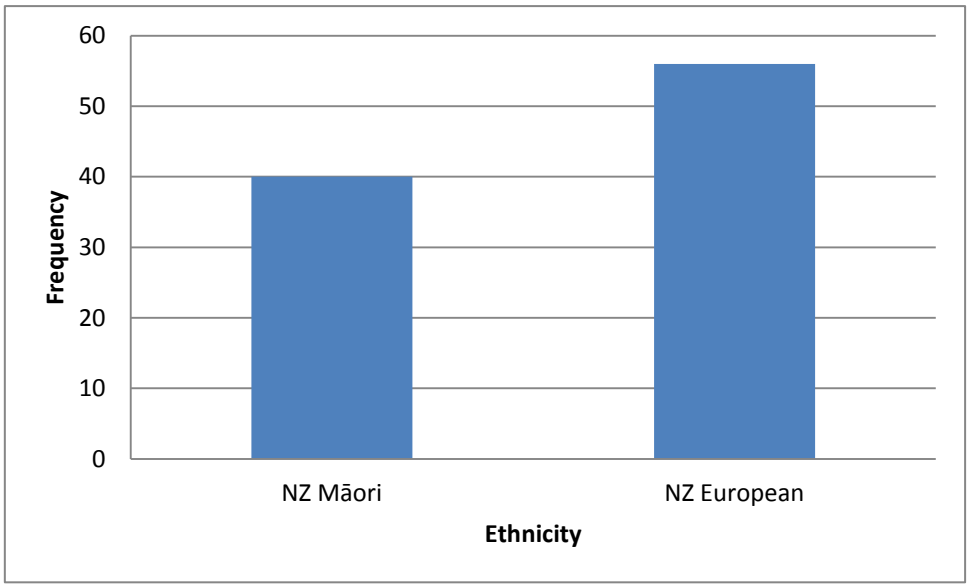

Figure 1. Ethnicity demographics (*n* = 96)

3.5.1.2 Intrathecal morphine, ethnicity, and gender

Of the New Zealand Māori, 82.5% (*n* = 33) were female and 17.5% (*n* = 7) were male. Of the New Zealand Europeans, 68% (*n* = 38) were female and 32% (*n* = 18) were male (Refer to Table 1).

Table 1
Demographics of all records included in audit (n = 96)

Participants	%	*n*
NZ Māori	42	40
Female	82.5	33
Male	17.5	7
NZ European	58	56
Female	68	38
Male	32	18

3.5.1.3 Intrathecal morphine, type of surgery, ethnicity, and gender

Of the 96 records reviewed, 74% were females (*n* = 71). Of these, 71 females, 66% (*n* = 47) underwent caesarean sections and 34% (*n* = 24) of the females underwent orthopaedic surgery. In the caesarean group, 64% (*n* = 30) were New Zealand Māori and 36% (*n* = 17) were New Zealand European females.

Of the 96 records, 26% (*n* = 25) were male patients, all of whom only underwent orthopaedic surgery. Of the 25 male patients, 28% (*n* = 7) were New Zealand Māori and 72% (*n* = 18) were New Zealand European.

In the orthopaedic group, 14% were New Zealand Māori males and 37% were New Zealand European males. New Zealand Māori females made up 6% of the sample, and New Zealand European females made up 43% of the orthopaedic group (Refer to Table 2).

Table 2
Demographics of surgeries, ethnicity, and gender (n = 96)

	Caesarean		Orthopaedic	
Participants	*n*	%	*n*	%
NZ Māori				
Female	30	64	3	6
Male			7	14
NZ European				
Female	17	36	21	43
Male			18	37

3.5.2 Incidence of ITMI pruritus

Results of the records indicating the presence of intrathecal morphine induced pruritus have been set out below. Recorded ITMI pruritus and its association with ethnicity, gender, age, dose, type of surgery, treatment received for ITMI, and ITMI pruritis scores have been presented.

3.5.2.1 ITMI pruritus and ethnicity

To determine if intrathecal morphine induced pruritus is correlated with ethnicity, the data was divided to identify in which ethnic groups the incidence of intrathecal morphine induced pruritus was more prevalent. The incidence of intrathecal morphine induced pruritus was calculated in relation to ethnicity from the 96 records reviewed. In total, 30 of the 96 total records (31%) had indicated the patient experienced ITMI pruritus. Nineteen (47.5%) of the 40 New Zealand Māori in total, experienced intrathecal morphine induced pruritus. Eleven (19.6%) of the 56 New Zealand European group experienced intrathecal morphine induced pruritus. This reveals a statistical significance of (p = 0.004) (Refer to Figure 2).

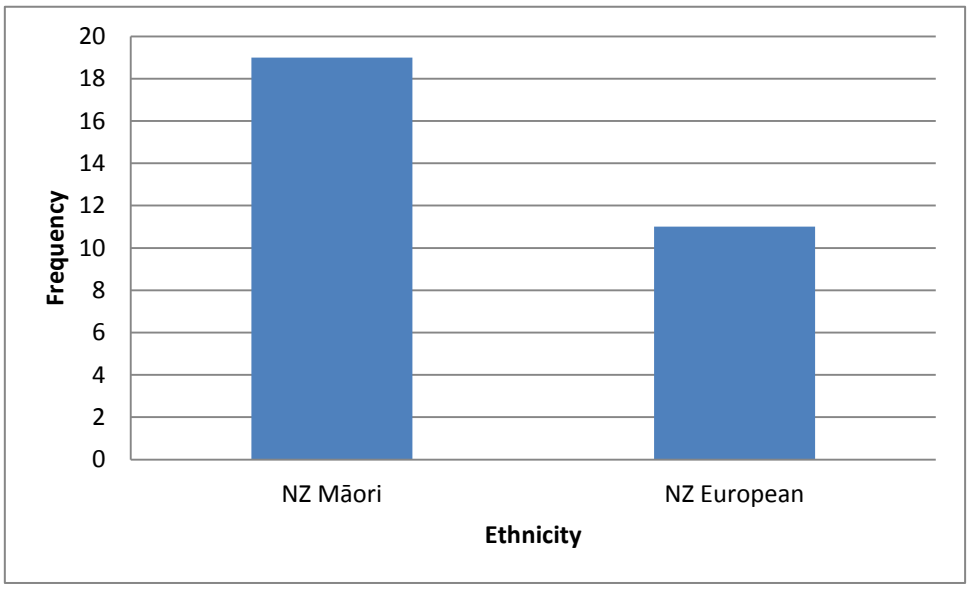

Figure 2. Ethnicity and ITMI pruritus (p = 0.004)

3.5.2.2 ITMI pruritus, ethnicity, and gender

As shown in Table 1, of the 96 records reviewed in this audit 26% (n = 25) of the patients were male, while 74% (n = 71) were females. Of the 25 males, 24% (n = 6) experienced intrathecal morphine induced pruritus, four were New Zealand Māori and two were New Zealand European. From the total of 71 females, 34% (n = 24) experienced ITMI pruritus, 62.5% (n = 15) were New Zealand Māori, and 37.5% (n = 9) were New Zealand Europeans (Refer to Table 3 overleaf).

Table 3
ITMI pruritus associated with ethnicity and gender (n = 30)

Participants	*n*
NZ Māori	19
Female	15
Male	4
NZ European	11
Female	9
Male	2

3.5.2.3 ITMI pruritus, ethnicity, gender, and type of surgery

Intrathecal morphine induced pruritus and its incidence was then determined in association with ethnicity, gender, and type of surgery, and will be presented in Table 4. Of the 47.5% of New Zealand Māori that experienced ITMI pruritus, 15 were female (79%) and four were male (21%). Of the 15 New Zealand Māori females experiencing ITMI pruritus, 13% (n = 2) underwent orthopaedic surgeries, and 87% (n = 13) underwent caesarean sections. Of the four New Zealand Māori males that experienced ITMI pruritus, 100% were males that underwent orthopaedic surgery.

Of the 19.6% New Zealand Europeans that experienced ITMI pruritus, nine were female (82%) and two (18%) were male. Of the nine New Zealand European females that experienced ITMI pruritus, 67% (n = 6) had caesarean sections and 33% (n = 3) underwent orthopaedic surgery. The two males in the New Zealand European group that experienced ITMI pruritus underwent orthopaedic surgery (Refer to Table 4 overleaf).

Table 4
Incidence of ITMI with ethnicity, gender, and type of surgery (n = 30)

Participants	*n*	Caesarean (*n*)	Orthopaedic (*n*)
NZ Māori	19		
Female	15	13	2
Male	4		4
NZ European	11		
Female	9	6	3
Male	2		2

3.5.2.4 ITMI pruritus, age, gender, and ethnicity

From the total of 30 records where intrathecal morphine induced pruritus was documented, 18 patients (60%) were aged between 15 and 35 years of age. Of these 18, 12 (67%) were New Zealand Māori and six (33%) were New Zealand European, and all were female. Only one record (3%) indicated an age between 36 and 55 years and that was a New Zealand Māori female. There were nine records (30%) between 56 and 75 years of age that experienced intrathecal morphine induced pruritus. Of these nine, three (33%) were female and of these three, one was New Zealand Māori and two were New Zealand European. Also, of these nine records aged between 56 and 75 years of age, six (67%) were males. Of these six males, four were New Zealand Māori and two were New Zealand European. There were two females (7%) of the total 30 that experienced intrathecal morphine induced pruritus aged between 76 and 95 years, one New Zealand Māori, and one New Zealand European (Refer to Table 5 overleaf).

Table 5
ITMI pruritus and age (n = 30)

	Age Group			
Participants	15–35	36–55	56–75	76–95
NZ Māori				
Female	12	1	1	1
Male			4	
NZ European				
Female	6		2	1
Male			2	
Total	18	1	9	2

3.5.2.5 ITMI pruritus and dose of intrathecal morphine with ethnicity

From the total number of records (*n* = 30) where intrathecal morphine induced pruritus was documented, the actual dose administered was analysed in relation to ethnicity. Between 50 mcgs and 100 mcgs of morphine administered, there were 13 records (43%) that indicated ITMI pruritus. Nine were New Zealand Māori and four were New Zealand European. Between 101 mcgs and 200 mcgs of morphine administered, 15 records (50%) indicated ITMI pruritus. Of those, 10 were New Zealand Māori and five were New Zealand European. A dose between 201 mcgs and 300 mcgs administered had no records indicating ITMI pruritus, and from a dose between 301 mcgs and 400 mcgs administered there were two (7%) documented incidences of pruritus, both of New Zealand European descent (Refer to Table 6).

Table 6
ITMI pruritus associated with dose of intrathecal morphine and ethnicity (n =30)

		Dose (mcgs)			
Participants	*n*	50–100	101–200	201–300	301–400
NZ Māori	19	9	10	0	0
NZ European	11	4	5	0	2
Totals	30	13	15	0	2

3.5.2.6 ITMI pruritus and type of surgery with ethnicity

Data was also reviewed in relation to the type of surgery and the incidence of intrathecal morphine induced pruritus. Patients undergoing caesarean sections and orthopaedic surgeries had intrathecal morphine administration. There was a total of 47 patients who were given intrathecal morphine while having caesarean sections (Refer to Table 2) and 19 (40%) were reported to have had pruritus (Refer to Table 4). Thirteen (68%) of these patients who developed ITMI pruritus while undergoing caesarean section were New Zealand Māori and six (32%) were New Zealand Europeans (Refer to Table 7).

There was a total of 49 patients who received intrathecal morphine for orthopaedic surgery (Refer to Table 2) and 11 (22%) of these experienced intrathecal morphine induced pruritus (Refer to Table 4). Of these 11, six (55%) were New Zealand Māori and five (45%) were New Zealand European (Refer to Table 7).

Table 7
Association of ITMI pruritus with type of surgery and ethnicity (n = 30)

		Type of Surgery	
Ethnicity	*n*	Orthopaedic (*n*)	Caesarean (*n*)
NZ Māori	19	6	13
NZ European	11	5	6

3.5.3 Treatment received for ITMI pruritus

The data reviewed for the audit also included information about patients who received treatments for their intrathecal morphine induced pruritus. This was further classified based on the patients' ethnic background. As shown in Figure 2, of the 47.5% New Zealand Māori group that experienced ITMI pruritus after receiving intrathecal morphine, 21% (*n* = 4) were treated. Of the 19.6% New Zealand European patients who experienced intrathecal morphine induced pruritus, 36% (*n* = 4) received treatment (Refer to Table 8 overleaf).

Table 8
Records of ethnic groups who experienced ITMI pruritus and received treatment for it (n = 30)

	Pruritus/Treatment	
Participants	Experienced Pruritus (*n*)	Received treatment (*n*)
NZ Māori	19	4
NZ European	11	4

3.5.3.1 ITMI pruritic scores and ethnicity

This data shows the score of intrathecal morphine induced pruritus as it was recorded by ethnicity. There were 30 records with documented VNRS scores. The VNRS was used to measure the recorded pruritus score that was reported from patients who had received intrathecal morphine using a scale from zero to ten. As shown in Table 9 below, 16 of the records (53%) experienced minimal pruritus between one and three. In this scoring group, eight (50%) were New Zealand Māori and eight (50%) were New Zealand European. There were 11 records (37%) that scored between four and six. Nine (82%) were New Zealand Māori and two (18%) were New Zealand European. There were three records (10%) that scored between seven and ten; two (67%) were New Zealand Māori and one (33%) was New Zealand European.

Table 9
Patient ITMI pruritus scores (n = 30)

	Score		
Participants	1–3	4–6	7–10
NZ Māori	8	9	2
NZ European	8	2	1
Totals	16	11	3

3.5.4 Other ITMI adverse effects

3.5.4.1 ITMI nausea and vomiting

The following results are related to other documented side effects of intrathecal morphine. They have been collected from the data and are included in this audit. From the total of 96 records, the incidence of post-operative nausea and vomiting occurring was 18% (*n* = 17). Of

these 17 patients experiencing nausea and vomiting, two (12%) were of New Zealand Māori descent and 15 (88%) were New Zealand European. Thirteen (76%) incidences of nausea and vomiting occurred within the orthopaedic group, and four (24%) in the caesarean group.

Nine patients (53%) experienced nausea and vomiting with doses between 50 mcgs and 100 mcgs, six patients (35%) experienced nausea and vomiting with doses between 101 mcgs and 200 mcgs, and two patients (12%) experienced nausea and vomiting with doses between 301 mcgs and 400 mcgs. There were no records indicating nausea and vomiting occurred at doses between 201 mcgs and 300 mcgs. Referring to Table 10 below, the figures represent orthopaedic surgeries unless otherwise indicated.

Table 10
ITMI nausea / vomiting and ethnicity, dose, and surgery (n = 17)

	Dose (mcgs)		
Participants	50–100	101–200	7–10
NZ Māori	2*	0	0
NZ European	7	6**	2
Total	9	6	2

Notes. *Both were caesareans. ** Two of six were caesareans.

3.5.4.2 ITMI respiratory depression

Respiratory depression was explored. Of 96 patients receiving intrathecal morphine, there was one event of respiratory depression (1%) which occurred in a New Zealand Māori female patient undergoing a caesarean section receiving a dose of 101 to 200 mcgs of intrathecal morphine (Refer to Table 11).

Table 11
ITMI respiratory depression and ethnicity, dose, and surgery (n = 1)

	Dose
Participants	101–200
NZ Māori	1*
NZ European	0
Total	1

Note. *This was a caesarean.

3.5.4.3 ITMI hypotension

The incidence of post-operative hypotension after intrathecal morphine administration was also measured. Of the 96 records reviewed, nine events (9%) of post-operative hypotension occurred and eight of these occurred within the orthopaedic group. Records of patients receiving a dose of 50 to 100 mcgs of intrathecal morphine had five events (56%) of hypotension, one New Zealand Māori and four New Zealand Europeans. Of these five, only one (20%) New Zealand European was in the caesarean group, and the remaining four (80%) were in the orthopaedic group. Three records (33%) indicated hypotension occurring at doses of 101 to 200 mcgs of intrathecal morphine. These were all New Zealand Europeans in the orthopaedic group. No events of hypotension occurred with doses between 201 to 300 mcgs, and only one event (11%) occurred at doses between 301 to 400 mcgs of intrathecal morphine. This one record was a New Zealand European in the orthopaedic group. Referring to Table 12 below, the figures represent orthopaedic surgeries unless otherwise indicated.

Table 12
ITMI hypotension ethnicity, dose and surgery (n = 9)

	Dose		
Participants	50–100	101–200	7–10
NZ Māori	1	0	0
NZ European	4*	3	1
Totals	5	3	1

Note. *These were caesareans.

3.5.5 Patient satisfaction with intrathecal morphine

Patient satisfaction with intrathecal morphine used as their post-operative analgesia was also reviewed. The level of patient satisfaction was measured using a scale of zero to ten, where zero equals completely unsatisfied and ten equals extremely satisfied. From the 96 records, four records (4%) indicated they were not satisfied. One New Zealand Māori (25%) and three New Zealand Europeans (75%) rated their satisfaction between zero and three. Of the 96, 22% (*n* = 21) were moderately satisfied. Eight (38%) New Zealand Māori and 13 (62%) New

Zealand Europeans rated their satisfaction with intrathecal morphine between four and six. Finally, 74% (*n* = 71) of the records indicated the patients were very satisfied with intrathecal morphine as their post-operative analgesia. Thirty-one (44%) of these were New Zealand Māori and 40 (56%) New Zealand Europeans rated their level of satisfaction between seven and ten as shown in Table 13.

Table 13
Patient satisfaction scores with intrathecal morphine (n = 96)

	Score		
Participants	0–3	4–6	7–10
NZ Māori	1	8	31
NZ European	3	13	40
Total	4	21	71

3.6 DISCUSSION

This audit was undertaken to determine the incidence of pruritus in a population receiving intrathecal morphine. Numerous data has been presented and compared to determine the incidence of intrathecal morphine induced pruritus amongst different ethnic groups, gender, age, dosage, and types of surgery. The data was categorised according to specific ethnic groups as there was a paucity of other groups represented in the records reviewed for this audit, which would indicate that the population in this locality was predominantly New Zealand Māori and New Zealand Europeans.

Overall, 31% of the records indicated the occurrence of intrathecal morphine induced pruritus, which is consistent with current literature. Literature has shown that this incidence of intrathecal morphine induced pruritus occurring is between 30% and 100% (Jenkins et al., 2009; Rathmell et al., 2005; Szarvas et al., 2003).

When exploring the results to determine any association of intrathecal morphine induced pruritus with ethnicity, the results clearly show that New Zealand Māori exhibited intrathecal

morphine induced pruritus with a much higher incidence than New Zealand Europeans (p = 0.004).

An interesting concept that has emerged from these results indicates that although New Zealand Māori were more likely to experience intrathecal morphine induced pruritus, a considerably lower percentage of New Zealand Māori were treated for it than were New Zealand Europeans. This may be due to a number of factors, however it is evident that more New Zealand Europeans either sought treatment or they were more likely to get treatment, than those of New Zealand Māori ethnicity.

The impact of this concept reveals a possible disparity that has been identified in the literature in Chapter 2. While reviewing literature regarding health care professionals' attitudes and management of opiates and their side effects, certain disparities were identified indicating that treatments varied between different ethnic groups. This literature could not determine any reasons or rationale behind these disparities and recommended further research. This audit also cannot identify rationale for these statistics, as it is limited by its data. The concept that New Zealand Māori were more likely to not seek treatment or intervention for the intrathecal morphine induced pruritus has been postulated, however further research is required into this topic to ascertain more awareness and understanding.

Further exploration reveals that more than half the New Zealand Māori scored their pruritus as moderate to severe, whereas less than one-third of New Zealand Europeans scored their pruritus as moderate to severe. This signifies that not only do New Zealand Māori experience a higher incidence of intrathecal morphine induced pruritus, but they experience it with greater intensity than New Zealand Europeans.

The data reflected that more female than male experienced this adverse effect, however this is not significant because there were more females overall within this audit. The majority of

the records indicated intrathecal morphine induced pruritus was experienced by female patients who underwent caesarean sections, and the data indicated that these females who underwent caesareans were predominantly New Zealand Māori. These statistics may highlight a topic for future research to determine why more New Zealand Māori are having caesarean sections than New Zealand Europeans. The data also reflected that more New Zealand Europeans had orthopaedic surgery than New Zealand Māori, which is another topic for future research.

When comparing the association of intrathecal morphine induced pruritus with age, the patients were found to be predominantly younger, being either 35 years or younger. There was only one record of a patient that had experienced intrathecal morphine induced pruritus between the ages of 36 to 55 years. These results may be influenced by the fact that patients undergoing caesarean sections are generally younger than 35 years, and those undergoing orthopaedic joint replacements are predominantly older than 55 years of age.

Exploration of the association of intrathecal morphine induced pruritus with the type of surgery and dose of intrathecal morphine reveals a general trend that it occurs in both orthopaedic and caesarean surgery, and was more likely to be associated with doses between 50 mcgs to 200 mcgs of intrathecal morphine.

Investigation into other adverse effects of intrathecal morphine indicated that both nausea and vomiting, and post-operative hypotension were experienced predominantly by New Zealand Europeans in the orthopaedic group, and with intrathecal morphine doses of 200 mcgs or less. Current literature has not indicated post-operative hypotension as an adverse effect of intrathecal morphine, however this audit has revealed an incidence of 9%. The literature review in Chapter 2 discusses a meta-analysis by Gehling and Tryba (2009) where the authors indicate that intrathecal morphine was associated with an unexplained reduced blood

loss, but this does not explain the hypotension. This has highlighted a gap in literature and may also be a topic for further research and exploration.

The incidence of respiratory depression occurred with fewer incidences than current documented literature. Gwirtz et al. (1999) state this adverse reaction occurs in 3% of the patients after intrathecal morphine administration. Another significant outcome observed was the fact that most of the adverse effects experienced occurred at doses of 200 mcgs of intrathecal morphine or less. Doses administered between 201 mcgs and 300 mcgs had no documented reports of any adverse effects.

The incidence of these adverse effects will be elaborated on throughout Chapter 4, while discussing the results of a health care professional questionnaire.

Overall, results of this audit have identified a number of themes:

- ITMI pruritus is significantly higher in the New Zealand Māori group
- New Zealand Māori experience ITMI pruritus with more intensity
- New Zealand Māori are less likely to be treated for ITMI pruritus
- ITMI pruritus was associated with younger, and female patients
- No adverse effects of intrathecal morphine were reported at doses between 201 mcgs and 300 mcgs.

Despite these adverse effects being experienced, there was an extraordinarily good response to intrathecal morphine being utilised for these patients as their post-operative analgesic regime. The majority of both ethnic groups reported they were very satisfied.

3.7 CONCLUSION

For registered nurses and midwives providing care for post-operative patients, constant observation and assessment is vital. Managing the patient's post-operative pain adequately with the minimisation of adverse effects experienced is paramount for every health care professional involved their care. Understanding that certain patient groups may be more susceptible to certain side effects or adverse effects and require preventative medication, or medication management to treat these side effects, is gaining more and more recognition.

New Zealand Māori have a significantly increased incidence of intrathecal morphine induced pruritus occurring after receiving intrathecal morphine. They experience it with more intensity and are less likely to be treated for it. Doses between 201 mcgs and 300 mcgs of intrathecal morphine had no reported adverse effects. Increasing our knowledge and awareness of the diversities of cultures in response to opiate medications may lead to improved overall management. Nurses and midwives cannot control the amount of intrathecal morphine the patient receives, but they can be more vigilant in their assessment and management of these patients with the knowledge that certain doses may affect patients differently.

An increase in education for patients regarding the adverse effects of intrathecal morphine that may be experienced, and placing emphasis on the fact that there is treatment for these adverse effects is paramount. Ensuring that all patients are *informed* is their right, and a health care professional's duty. The outcome of this audit has led to a survey in the form of a questionnaire being performed in Chapter 4 to explore current knowledge of the health care professionals that were involved in the care of these patients.

Chapter 4: Health Care Professional Survey: Health care professional management of intrathecal morphine induced adverse effects— are we scratching the surface?

4.1 INTRODUCTION

For surgical nurses and midwives providing care for their post-operative patients, much of this care is focused in promoting the enhanced recovery after surgery (ERAS) protocol. The quicker the patient is ambulatory, the less likely the patient is to suffer adverse effects of an anaesthetic or bedbound complications (Fearon et al., 2005). Also receiving increased acknowledgement is the high importance of the management of the patient's post-operative pain. A staggering 10 to 50% of unrelieved post-operative pain has now been linked to the development of chronic pain (Kehlet, Troels, & Woolf, 2006). A study by Macrae (2001), indicates that 20% of patients presenting in chronic pain clinics identify surgery as one of the causes of their chronic pain, half of them claiming surgery was the sole cause. A study by Fearon et al. (2005), indicates that for the ERAS protocol to be effective, a multimodal approach is utilised combining identified elements that focus on stress reduction and the promotion of patient return to function.

Post-operative pain management is achieved by the use of opiates, which represent a class of analgesics providing powerful dose-dependent analgesia for those suffering moderate to severe pain (Sinatra, 2009). Offering versatility of administration, morphine preparations come in many forms. Intrathecal morphine has fast become a popular method of analgesia and whether administered alone or in combination with local anaesthetics (and occasionally clonidine) into the CSF, it provides a powerful and highly efficient analgesic for a variety of surgical procedures (Dabu-bondoc et al., 2009).

As discussed in Chapter 2, the many adverse effects of morphine have been documented and may affect multiple systems throughout the body (Macintyre & Ready, 2001). In specific to administration via the intrathecal route the following troublesome and sometimes serious adverse effects may occur: nausea and vomiting, pruritus, respiratory depression, and urinary retention (Dabu-bondoc et al., 2009; Gehling & Tryba, 2009; Gwirtz et al., 1999; Rathmell et al., 2005).

Chapter 2 identified that ITMI pruritus is a common adverse effect of intrathecal opioid administration (Grant et al., 2010). Occasionally, the intensity of the pruritus is so extreme that sleep patterns are interrupted (Dabu-bondoc et al., 2009). Although opioid induced pruritus aetiology is unclear, it is not caused by a histamine release. Dabu-bondoc et al. (2009) indicate this is apparent because peak effects are noted three to six hours following administration. Treatment for this adverse effect is varied, however much of the available literature concurs intravenous naloxone to be effective. Intravenous naloxone boluses administered in minute doses of 0.04 mgs intermittently will selectively reverse the opiate adverse effect of pruritus, without reversing the intrathecal opioid analgesia or affecting the analgesic status of the patient (Dabu-bondoc et al., 2009; Grant et al., 2010).

Chapter 3 explored the incidence of intrathecal morphine induced pruritus occurring within two different ethnic groups in a facility in New Zealand, and the treatment that these patients received. Also identified in Chapter 2, was the gap in available literature related to these topics. This survey was then undertaken to determine and discuss the observations made by the health care professionals that provided care for these patients, and their management of the opioid induced pruritus. This was facilitated by circulating a questionnaire for nurses and midwives working in post-surgical and maternity departments.

4.2 PURPOSE

The purpose of this study was to explore health care professional knowledge, observations, and management of intrathecal morphine induced pruritus. This includes discussion of the adverse effects that were most commonly observed within this patient population after receiving intrathecal morphine, and how well they were managed by these groups of health care professionals. It will also explore health care professional current level of knowledge and confidence in the management of intrathecal morphine.

4.3 METHOD

Nurses and midwives were invited to participate and contribute their expertise and knowledge in the management of patients who had received intrathecal morphine as their post-operative analgesia. Ethics approval was received from Northern Y Regional Ethics Committee to perform this survey (Appendix A). The questions in this survey were designed to reveal current knowledge and practice, and were piloted. The initial comments and feedback were received and taken into consideration during the course of the development of a five page questionnaire (Appendix F).

4.3.1 Design of the questionnaire

The technique utilised in this survey was closed-ended with a structured, fixed number of alternative responses which can vary in their format (Elliott & Schneider, 2007). Each question allowed for open-ended response formats and were interpreted by the 'content analysis' method (Elliott & Schneider, 2007).

The finalised questionnaire contained 22 questions and was distributed throughout the surgical orthopaedic and maternity departments where the patients received care for lower segment caesarean sections, and for total hip and knee joint replacements (arthroplasty).

Demographics of the participants were recorded, followed by questions related to health care professional observations of intrathecal morphine induced nausea and vomiting, respiratory depression, pruritus, urinary retention, and hypotension.

4.3.2 Selection of participants

Surgical RNs (nurses) and midwives at a district health board in New Zealand were invited to participate in this survey and a total of 30 health care professionals completed the questionnaire. Exclusions were those health care professionals that do not provide care for patients who have received intrathecal morphine.

All the health care professionals were given a participant information sheet (Appendix G) and signed a consent form before participation (Appendix H).

4.3.3 Analysis of data

The data collected from this survey was entered directly into SPSS. SPSS was then utilised to analyse the data. There is a random variability between 26 and 30 due to the fact that some of the participants did not respond to all questions. All questions allowed comments to be added by the participants of this survey. Ninety-one percent of the questions (n = 20) had comments, with exactly 106 comments in total received and recorded. Those comments were then tabulated and organised (Appendix I), and have been integrated throughout the results in Section 4.4.

A study by Gehling and Tryba (2009) on the risks and adverse effects of intrathecal morphine indicated that intrathecal morphine induced pruritus was associated with different doses of morphine. The authors indicated that patients receiving a dose of morphine that was greater than or equal to 300 mcgs as their post-operative analgesia experienced a significant increase in the risk of pruritus. During this research, the amount of morphine administered was

recorded, but due to the nature of this research focusing on pruritus and ethnicity, it will not be discussed in this chapter.

4.4 RESULTS

Results of this survey will be set out as follows. Firstly, in Section 4.4.1, the demographics of the participant's age, years of experience, and level of education will be presented. The frequency of the most commonly observed adverse effects associated with administration of intrathecal morphine will be discussed in Section 4.4.2. Section 4.4.3 will describe the adverse effects of intrathecal morphine that nursing and midwifery consider to be of most importance, with emphasis on the management of these adverse effects. Section 4.4.4 explores health care professional knowledge and understanding of the medications utilised in the management of ITMI nausea and vomiting and pruritus. Section 4.4.5 shows observed responses and incidence of these adverse effects amongst certain ethnicities. Section 4.4.6 shows health care professional knowledge of the facility protocol in the management of intrathecal morphine, and their overall confidence with their current level of knowledge. Section 4.4.7 shows health care professional responses to a number of statements included which are related to intrathecal morphine management. Section 4.4.8 shows final comments made by health care professionals in an open-ended format.

4.4.1 Demographics

As shown in Table 14 overleaf, 30 participants took part in this survey. Of the 30, 14 were nurses and 16 were midwives.

4.4.1.1 Age of participants

The majority of the participants were aged above 41 years of age (11 nurses and 6 midwives). The entire nursing group provided age demographics. 7% (n = 1) were aged between 20 and 30 years, 14% (n = 2) were aged between 31 and 40 years, and 79% (n = 11) were older than 41 years of age. Twelve of the 16 midwives provided responses and 17% (n = 2) were aged

between 20 and 30 years, 33% (*n* = 4) were aged between 30 and 40 years, and 50% (*n* = 6) were older than 41 years of age as shown in Table 14.

Table 14
Age groups of the health care professionals (n = 26)

Age	Nurses (*n*)	Midwives (*n*)
20–30 years	1	2
31–40 years	2	4
>41 years	11	6
Totals	14	12

Figure 3 below reflects these figures in a bar chart.

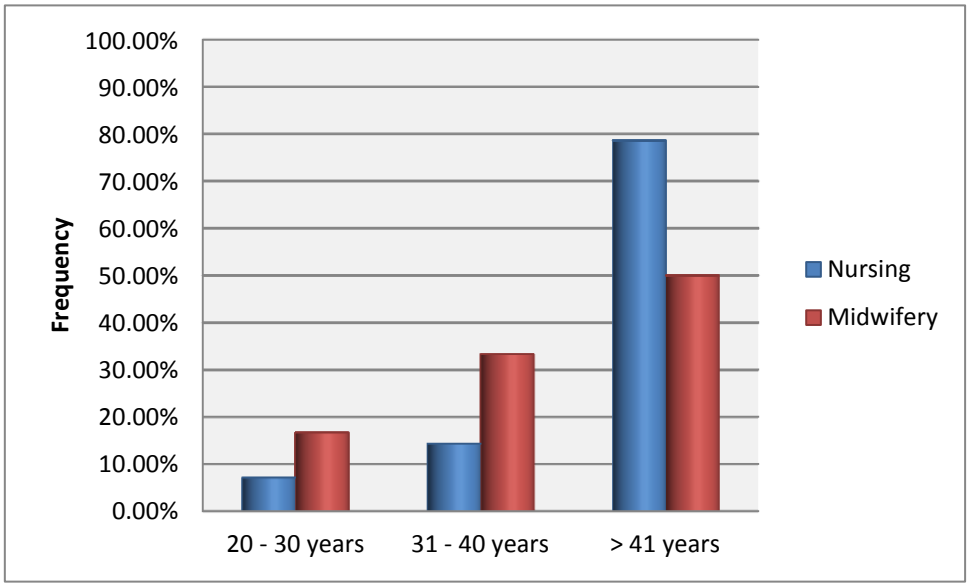

Figure 3. Nursing and midwifery ages in years

4.4.1.2 Participant years of experience

Both the nursing group and the midwifery group were asked to indicate their years of experience. As shown in Table 15 overleaf, the majority of nurses had more than 11 years' experience, whereas the majority of the midwives had between six to eleven years' experience. In the nursing group, 13 of the 14 respondents answered this question. Fifteen percent (*n* = 2) have less than five years' experience, 23% (*n* = 3) of nurses have six to ten years' experience, and 62% (*n* = 8) have more than eleven years' experience in their field. The entire midwifery group replied to this question, and 25% (*n* = 4) have less than five

years' experience, 44% of midwives (*n* = 7) have six to ten years' experience, and 31% (*n* = 5) have more than 11 years in their field.

Table 15
Health care professional's years of experience (n =29)

Years	Nurses (*n*)	Midwives (*n*)
0–5 years	2	4
6–10 years	3	7
>11 years	8	5
Total	13	16

Figure 4 reflects these figures in a bar chart.

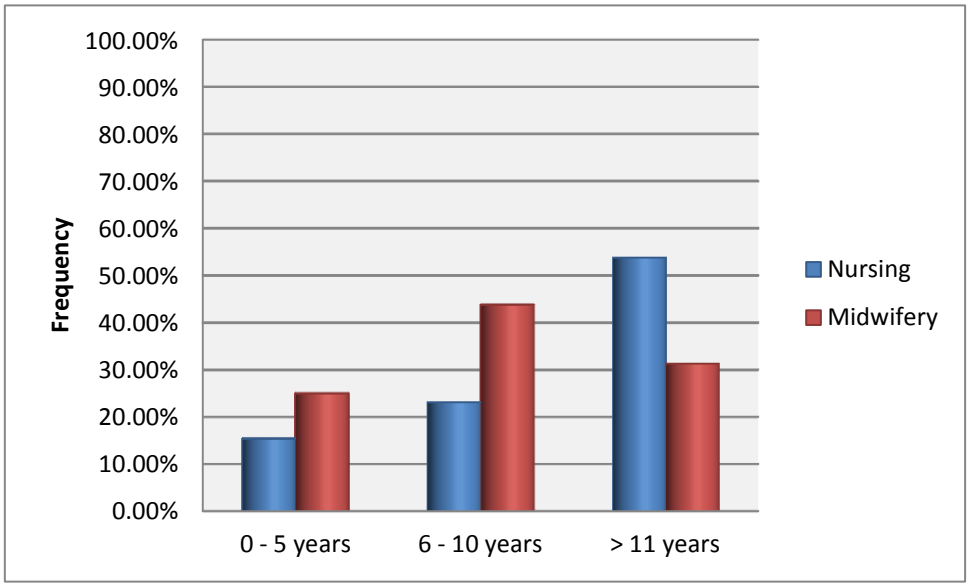

Figure 4. Nursing and midwifery years of experience

4.4.1.3 Participant level of education

As shown in Table 16 overleaf, the entire nursing group responded to the question asking of their level of education. The resultant figures indicate that 29% (*n* = 4) of nurses are hospital trained, 57% (*n* = 8) of nurses have a bachelor's degree, and 14% (*n* = 2) of nurses hold a degree higher than a bachelor's. Of the 16 midwives, 13 responded to this question and results show that 8% (*n* = 1) of midwives were hospital trained, 84% (*n* = 11) of midwives hold a bachelor's degree, and 8% (*n* = 1) of midwives hold a degree higher than a bachelor's or postgraduate qualifications.

Table 16
Health care professional's level of education (n = 27)

Level	Nurses (*n*)	Midwives (*n*)
Hospital trained	4	1
Bachelor's degree	8	11
Higher education/PG education	2	1
Total	14	13

Figure 5 below shows these results in a bar chart.

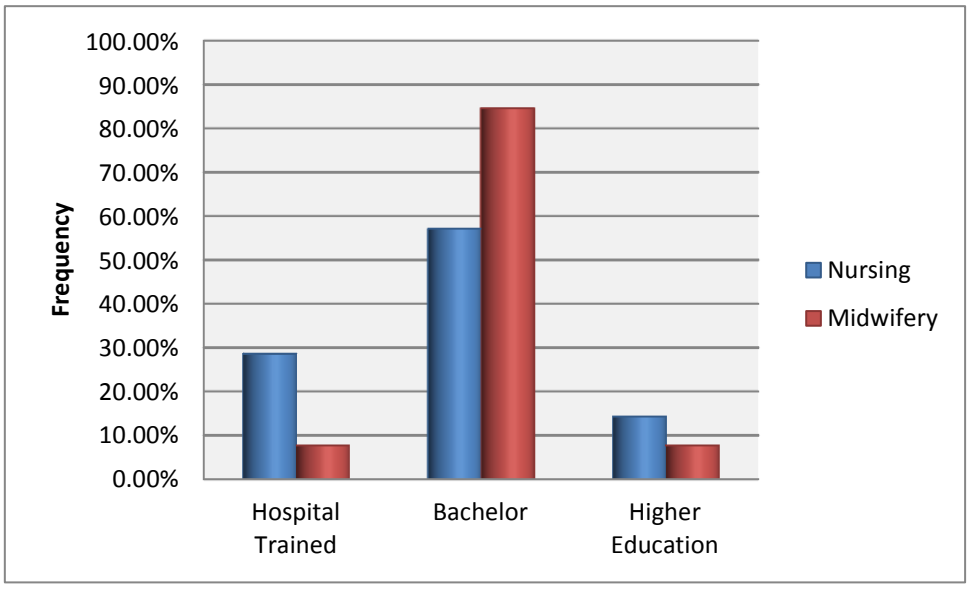

Figure 5. Level of education of nurses and midwives

4.4.2 Most commonly observed adverse effects of intrathecal morphine

The most commonly observed adverse effects seen in patients by health care professionals are presented below.

Pruritus, hypotension, and nausea and vomiting were the most commonly observed adverse effects reported by nurses, while pruritus and nausea and vomiting were more commonly seen by the midwives. Sixty-four percent (*n* = 9) of nurses and 69% (*n* = 11) of midwives reported nausea and vomiting as the most commonly observed adverse effects of intrathecal morphine. Urinary retention was reported mainly by nurses at 14% (*n* = 2), whereas no midwives reported they had observed urinary retention in these patients. Seventy-one percent

(*n* = 10) of nurses reported they had observed pruritus in these patients, and 94% (*n* = 15) of midwives reported observing pruritus. In response to the questions regarding respiratory depression, 50% (*n* = 7) of nursing and 25% (*n* = 4) of midwives reported they had observed respiratory depression in patients who had received intrathecal morphine. The adverse effect of hypotension was also observed, whereas 71% (*n* = 10) of nurses reported observing hypotension and 13% (*n* = 2) of midwives reported observing hypotension in their patients that had received intrathecal morphine (Refer to Table 17).

Table 17
Observed adverse effects of intrathecal morphine (n = 27)

Most commonly observed side effect	Nurses (*n*)	Midwives (*n*)
Nausea/vomiting	9	11
Urinary retention	2	0
Pruritus	10	15
Respiratory depression	7	4
Hypotension	10	2

Figure 6 below reflects these figures in a bar chart.

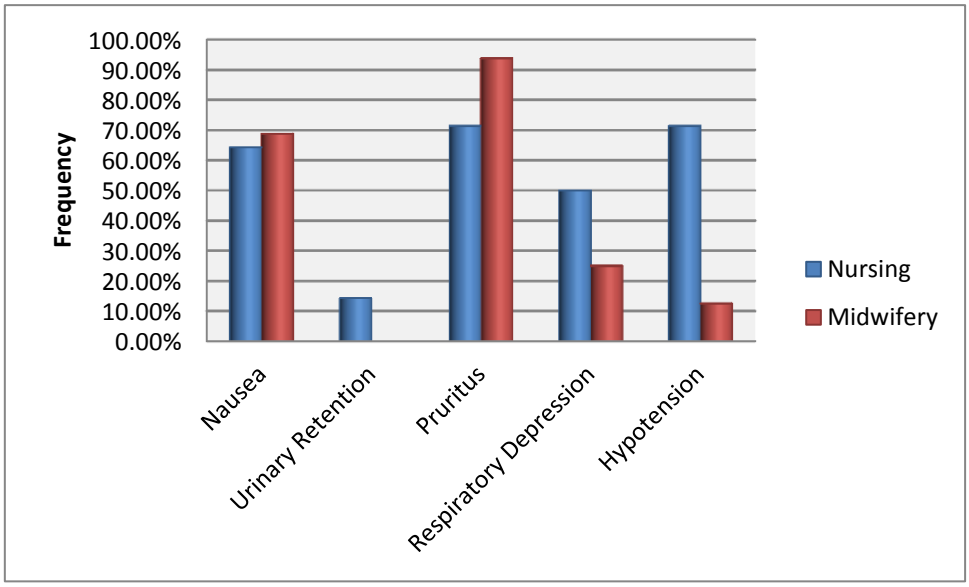

Figure 6. Observed adverse effects by nursing and midwifery after patients received intrathecal morphine

4.4.3 Important adverse effects of intrathecal morphine and management

Participants were then asked to rank these adverse effects considered as most important to observe for through to the least important to observe for. Respiratory depression was rated highest by both groups, followed by hypotension.

Seventy-nine percent (*n* = 11) of nursing and 87% (*n* = 14) of midwifery reported that respiratory depression was the most important side effect to observe for after a patient has received intrathecal morphine. Fourteen percent (*n* = 2) of nursing and 12.5% (*n* = 2) reported that hypotension was the next most important adverse effect to observe for. ITMI pruritus was rated equally with urinary retention and nausea and vomiting as the third most important (or least important) adverse effect to observe for, but only by the nursing group at 8% (*n* = 1) as shown in Table 18.

Table 18
The most important adverse effects to observe for in patients receiving ITM

Most important side effect to observe for	Nurses (*n*)	Midwives (*n*)
Respiratory depression	11	14
Hypotension	2	2
Nausea/vomiting	1	0
Urinary retention	1	0
Pruritus	1	0

Figure 7 below reflects these figures in a bar chart.

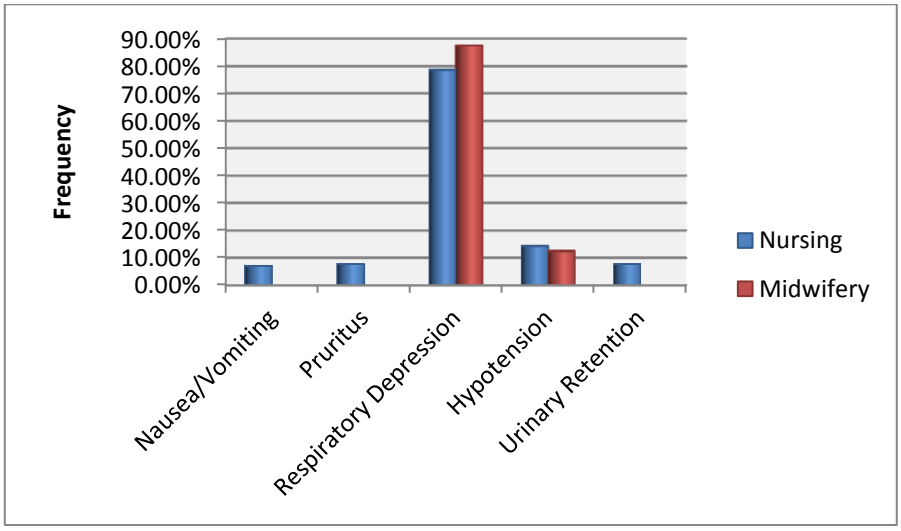

Figure 7. Most important adverse effects to observe for in patients receiving ITM

Open-ended comments received by nurses in support of their responses regarding urinary retention were as follows:

> *"Most times the patient has a urinary catheter." (p01)*
>
> *"Patient usually has an IDC." (p13)*

An open-ended comment received by a midwife responding to this question indicated a possible additional adverse effect:

> *"Haemorrhage—especially when concealed, can go unrecognised when the mother's pain level is so well controlled by intrathecal morphine." (p04)*

4.4.3.1 Importance of the management of ITMI nausea/vomiting and pruritus

As shown in Table 19, both groups have strongly indicated that management of intrathecal morphine induced pruritus and nausea and vomiting is considered important. Ninety-two percent (*n* = 12) of nurses and 94% of midwives (*n* = 15) felt it was important to treat nausea and vomiting. Of the nurses, 46% (*n* = 6) felt it was important to manage intrathecal morphine induced pruritus and 75% (*n* = 12) of the midwives thought it was important to treat ITMI pruritus.

Table 19
HCPs who think management of nausea/vomiting and ITMI pruritus important

Importance of managing these adverse effects	Nausea/vomiting (*n*)	Pruritus (*n*)
Nurses	12	6
Midwives	15	12

These results have also been presented in a bar chart as set out in Figure 8 (overleaf).

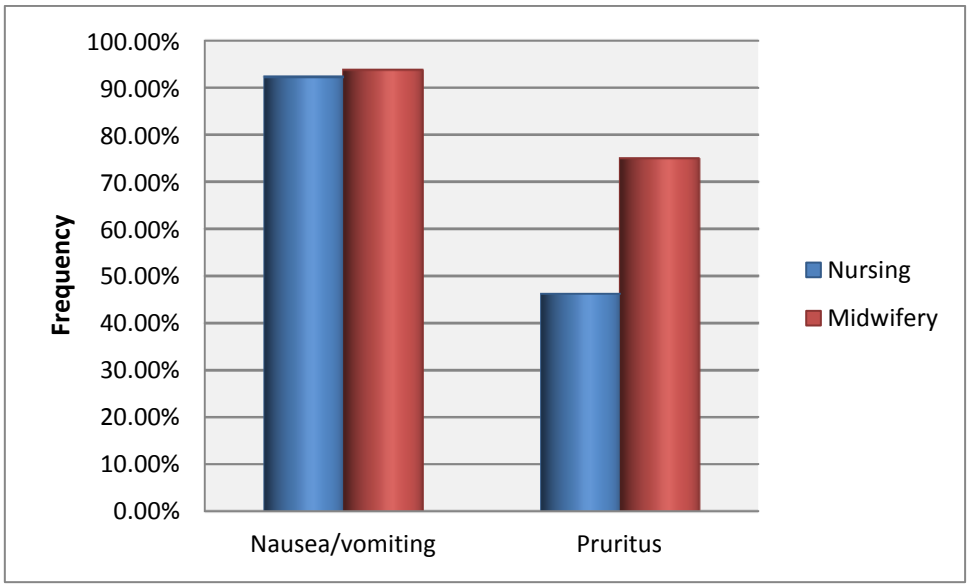

Figure 8. Nursing and midwifery who think management of nausea, vomiting, and pruritus is important

There were many open-ended comments from both nurses and midwives related to the importance of the management of nausea and vomiting and pruritus showing that these adverse effects are very unpleasant experiences for patients:

> *"Sometimes the patient hates the nausea and vomiting more than the pain itself." (p02)*

> *"Nausea can be worse than pain for the patient." (p13)*

In some situations, nausea and vomiting can lead to airway obstruction:

> *"Pain is first importance but airways very important if the patient vomits." (p18)*

> *"It can threaten the airway and reduce enjoyment of those first few hours with their new baby." (p05)*

Therefore, they perceive nausea and vomiting to be more significant in their management of patients receiving intrathecal morphine.

The 'mother-baby bonding' process is of great significance to midwives as they encourage the baby friendly hospital initiative (BFHI), a global effort to implement practices that protect, promote, and support breastfeeding (World Health Organization, 2012). Therefore, management of nausea and vomiting is of high priority while promoting this initiative:

> *"Interferes with bonding with mother and baby. Mother feels miserable." (p28)*

"Awful to be vomiting while trying to care for and feed a new-born." (p22)

The management of intrathecal morphine induced pruritus was also considered important to health care professionals. It appears to have been considered as important as nausea and vomiting in terms of patient care:

"Same as nausea and vomiting, pruritus can be intense and debilitating." (p04)

"Can be very distressing for clients and is often a priority for them." (p06)

"Can be very aggravating /irritating for patients: unable to sleep, rest, etc." (p16)

"Can be extremely uncomfortable for the patient." (p14)

"Irritating and disturbs sleep." (p21)

4.4.4 Medications utilised in the management of intrathecal morphine induced nausea, vomiting and pruritus

The facility protocol for intrathecal morphine indicates cyclizine as the first line medication to be administered for nausea and vomiting, and naloxone for pruritus (see Appendix J). It appears that this protocol may be routinely followed for the management of nausea and vomiting more so by the nursing group than the midwife group. Results show that 64% (n = 9) of nursing and 40% (n = 6) of midwifery reported they would administer intravenous cyclizine first for nausea and vomiting. A midwife commented on the use of ondansetron:

"Ondansetron first line. This is not first line if following the protocol, but most commonly used as effective." (p22)

Conversely, the majority of both the nursing group and the midwifery group responded that they would utilise naloxone as the first line medication to be administered for intrathecal morphine induced pruritus in accordance with the facility protocol. One hundred percent (n = 14) of nurses and 80% (n = 12) of midwives reported they would administer intravenous naloxone first.

4.4.5 Ethnicity related observations of intrathecal morphine induced nausea, vomiting, and pruritus

A number of the participants have reported observing intrathecal morphine induced nausea and vomiting and pruritus occurring within certain ethnicities.

4.4.5.1 Observed ITMI nausea and vomiting within ethnicities

Twenty-one percent (*n* = 3) of the 14 nurses, and 6% (*n* = 1) of the 16 midwives reported they had observed the incidence of intrathecal morphine induced nausea and vomiting to be higher in certain ethnic groups. New Zealand Europeans were identified by both groups to be more likely to experience nausea and vomiting compared to other ethnic groups. Results showed that 67% (*n* = 2) of nurses reported observing New Zealand Europeans experiencing ITMI nausea and vomiting, and 33% (*n* = 1) of nurses report observing New Zealand Māori experiencing ITMI nausea and vomiting. The entire group of midwives (*n* = 1) reported observing New Zealand Europeans experiencing ITMI nausea and vomiting more than any other ethnicity as shown in Table 20.

Table 20
Ethnicities observed with ITMI nausea and vomiting by nurses and midwives

Ethnicity	Nurses (*n*)	Midwives (*n*)
NZ Māori	1	0
NZ European	2	1

4.4.5.2 Observed ITMI pruritus within ethnicities

Twenty-one percent (*n* = 3) of nursing and 6% (*n* = 1) of midwives reported that they have observed different ethnicities experiencing intrathecal morphine induced pruritus after receiving intrathecal morphine. Of these 21% of nurses, 67% (*n* = 2) reported that they observed New Zealand Māori experiencing intrathecal morphine induced pruritus and 33% (*n* = 1) of nurses reported observing New Zealand Europeans experiencing intrathecal morphine induced pruritus.

In contrast, midwives differed in that although they had observed intrathecal morphine induced pruritus occurring, the entire midwife group indicated the ethnicity was neither New Zealand Māori nor New Zealand European as shown in Table 21.

Table 21
Ethnicities observed with ITMI pruritus by nurses and midwives

Ethnicity	Nurses (*n*)	Midwives (*n*)
NZ Māori	2	0
NZ European	1	0

Figure 9 below reflects these figures in a bar chart.

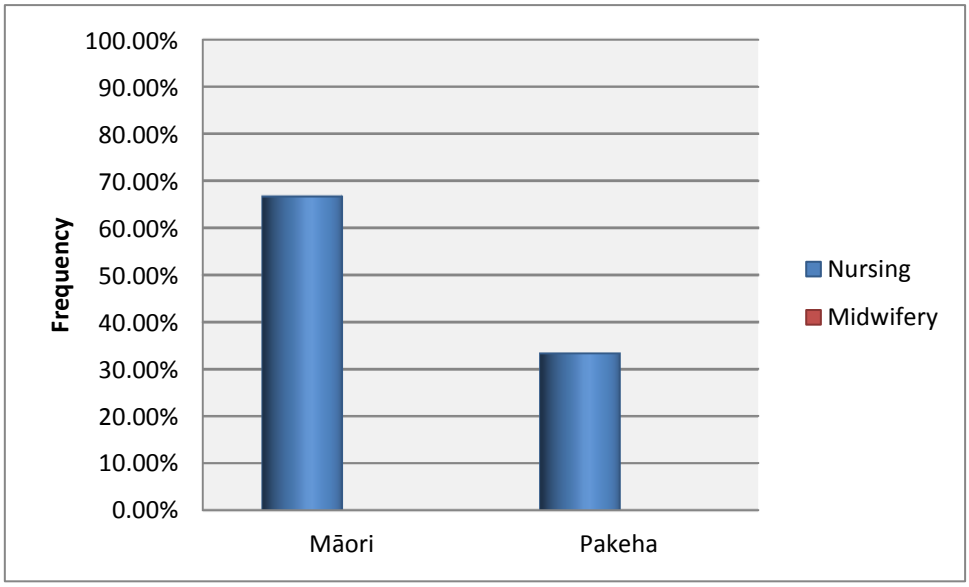

Figure 9. Ethnicities observed with ITMI pruritus by nurses and midwives

4.4.6 Facility protocols and health care professionals confidence in their current level of knowledge

Participants were then asked if the facility had a protocol for managing patients receiving intrathecal morphine for post-operative pain. Ninety-three percent (*n* = 13) of nurses reported their facility did have a protocol, and 7% (*n* = 1) were unsure.

The majority of the midwives at 80% (*n* = 12) were also aware that there is a protocol in their facility in relation to intrathecal morphine, however there were 20% (*n* = 3) who reported there was no protocol. Comments reflecting these figures included:

"There is a guidance document used but not DHB protocol." (p04)

Nurses and midwives level of knowledge and confidence was also explored in this survey. The purpose of the question was to determine individual knowledge and confidence in health care professional management of patients receiving intrathecal morphine. The majority of the nurses and midwives responded positively to this question. Eighty six percent (n = 12) of nurses and 75% (n = 12) of midwives responded that they were confident. Although they were confident in their knowledge and skills, more continuing education and training were considered important:

> *"Refreshers and updates are always appreciated (for new staff too) either by anaesthetist or pain team." (p16)*
>
> *"Moderately confident but could use more training." (p22)*
>
> *"I am confident but there is always room to learn." (p01)*

4.4.7 Responses to statements

Four statements were written in relation to patients who had received intrathecal morphine, and the nursing and midwifery groups were asked if they agreed with these statements. As shown in Figure 10 overleaf, both nurses and midwives had similar responses when asked if they agreed with the statement: "It is important to treat patients experiencing nausea and vomiting." Fourteen (100%) of the nurses and 94% (n = 15) of midwives agreed it is important to treat patients experiencing nausea and vomiting after having received intrathecal morphine.

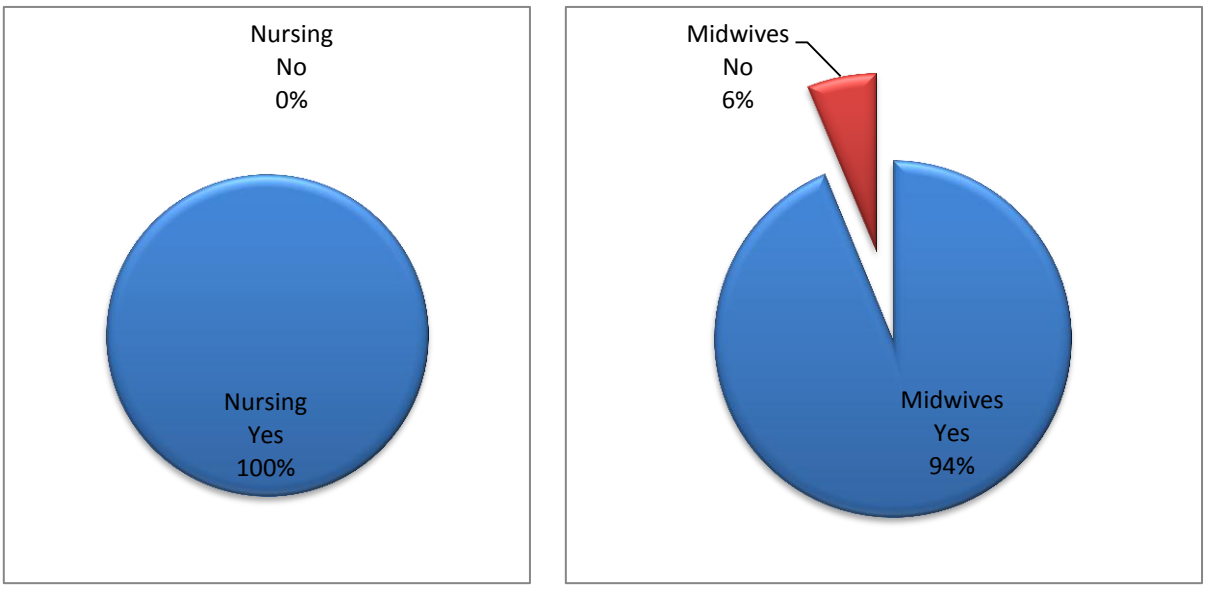

Figure 10. Total nursing and midwives agree it is important to treat nausea and vomiting

The participants were then asked if they agreed with the statement: "It is important to treat patients experiencing intrathecal morphine induced pruritus", and 100% (*n* = 14) of nursing and 87% (*n* = 14) of midwifery agreed it was important to treat intrathecal morphine induced pruritus as shown in Figure 11.

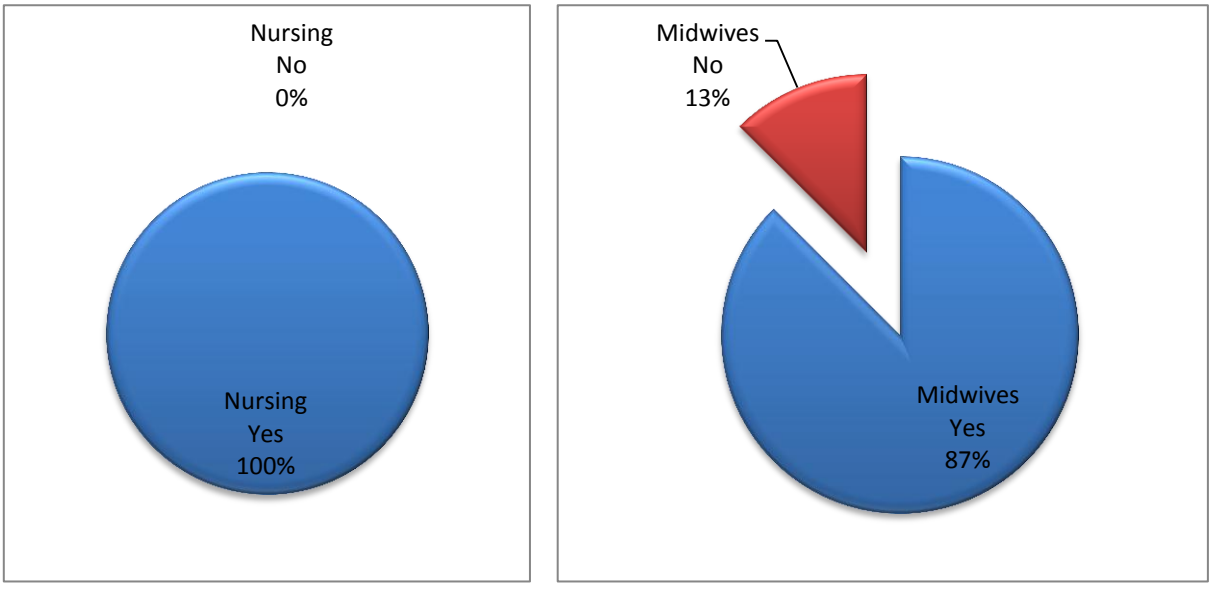

Figure 11. Total nursing and midwifery agree it is important to treat pruritus

All of the midwives (100%) and 93% (*n* = 13) of nurses that took part in this survey agreed intrathecal morphine was an effective post-operative analgesic. All of the nurses (100%) and

87% (n = 14) of the midwives felt they had a good understanding of the side effects of intrathecal morphine.

4.4.8 Final comments

The last question asked health care professionals to contribute additional comments in relation to their management of patients who had received intrathecal morphine. The nurses were concerned with the adverse effect of hypotension. Some felt it was very common after intrathecal morphine with comments such as:

> *"Hypotension can be the biggest, most time consuming problem after ITM for patients on the surgical ward. This typically occurs 4–10 hours post-op in my experience. It is occasionally required to transfer the patient to the ICU when BP stability is not achieved on the ward." (p09)*

> *"… often after arriving back from PACU BP drops, respiration rates drop, and takes 1:1 nursing, which is very hard when you have five other patients to care for as well." (p17)*

> *"The vast majority of our patients that have ITM invariably have low BP post-op." (p16)*

Midwives however seemed to feel their patients benefited from ITM with comments such as:

> *"In comparison with patients that have not received ITM undergoing C/S (caesarean section) my experience is that ITM patients have better pain control, fewer side effects than with PCA or IV/oral analgesia only; and also mobilise more quickly. Thank you for the opportunity to participate in this interesting research." (p05)*

> *"I have found that for many post C/S mothers ITM maintains them pain free for 16-18 hours without the need for any other medication. These mothers are then able to be more physically active (less risk of DVT) and more able to bond and care for their baby. If they are breast feeding (vast majority are) I believe the baby receives considerably less opiate than conventional methods of PCA or IV narcotics." (p04)*

Final comments in general were:

> *Small doses of ITM (100 mcgs to 150 mcgs) seems to have limited benefit as patients suffer from pain after the spinal (LA) has worn off. Some patients require fentanyl and tramadol." (p02)*

> *I think more in services on this topic are important to reinforce the knowledge we have and to ask questions in ITM post-op cares." (p19)*

4.5 DISCUSSION

This study has explored and examined the observations and management of health care professionals in dealing with the adverse effects of intrathecal morphine, focusing on pruritus. It has become apparent that different patient groups responded differently to the intrathecal morphine, and the two health care groups focused on different outcomes. One can interpret the expediency of intrathecal morphine as a post-operative pain management adjunct for many different surgical procedures from the responses received from this survey.

Within the nursing group most were older than 41 years of age, had greater than 11 years' experience and held a bachelor's degree. These demographic figures are fairly consistent with results of a report published in 2012 by the New Zealand Nursing Council. Statistics showed "forty percent of New Zealand-trained registered nurses had a Bachelor degree of some kind", and "twenty-one percent of all registered nurses received their qualification before 1980, rising to 24% amongst solely New Zealand-trained RNs" (Huntington, 2012, p. 35). Huntington (2012) also showed that the "…average age of registered nurses is 45.0" (p. 25).

Within the midwifery group most were older than 41 years' of age, had six to ten years' experience, and held a bachelor's degree. These figures are again consistent with results published in a midwives demographic report by the Midwifery Council of New Zealand. "The average age of practising midwives is 47.2 years" (Midwifery Council of New Zealand, 2011, p. 3). The Council also shows figures on page six reflecting the majority have been practicing for six to ten years, and the majority hold a Bachelor's degree (p. 22).

These demographics show the survey has received results from a body of very experienced professionals.

The data reveals variances between the adverse effects that were observed by health care professionals and the importance of which adverse effects to observe. When discussing their observations, both groups reported similar results. The majority of the nursing group and the midwifery group observed the adverse effects of nausea and vomiting in their patients after receiving intrathecal morphine. An even higher percentage observed the adverse effect of ITMI pruritus, and in this survey it is the most commonly observed adverse effect. In patients who received intrathecal morphine, 71% of nurses and 94% of midwives observed ITMI pruritus. Current literature claims the incidence of intrathecal morphine induced pruritus at 30 to 100% (Ganesh & Maxwell, 2007; Gwirtz et al., 1999; Rathmell et al., 2005).

Urinary retention was the least observed adverse effect with only 14% of the nursing group reporting its incidence. This may be due to the fact that as the health care professionals have commented, most of these patients receive urinary catheters post-operatively. This figure was however higher than documented in current literature. Gwirtz et al. (1999) claim that the incidence of urinary retention in their study is 1.8%. Respiratory depression was observed with a much higher incidence than indicated in current literature in these patients after receiving intrathecal morphine. Respiratory depression is generally treated when respiratory rates are less than 10 per minute and or evidence of diminished tidal volume is present (Dabu-bondoc et al., 2009). This questionnaire was not designed to measure the effect or degree of respiratory depression, so further research into this occurrence may be warranted.

Over 70% of the nurses group reported observing hypotension in their patients after receiving intrathecal morphine. This figure may be attributed to the fact that these patients had undergone orthopaedic surgery, were elderly, and may have had one or more comorbidities. Ho and Gan (2009) propose that morphine releases histamine and hypotension may occur indirectly, and that this hypotension may be attenuated by optimising intravascular volume.

Macintyre and Ready (2001) propose morphine induced hypotension indicates patient hypovolaemia.

Results reflecting the most important adverse effects to observe for shows at over 79%—both health care professional groups acknowledged that respiratory depression was the most important adverse effect to observe for in a patient that has received intrathecal morphine. Respiratory depression associated with opioids has the potential for major morbidity and even mortality (Fitzgibbon, 2009). The importance of observing for this opiate induced respiratory depression cannot be underestimated.

The adverse effect of hypotension was recorded as the next most important to observe for especially within the nursing group. There is a paucity of literature related to the topic of hypotension occurring in the orthopaedic patient after receiving intrathecal morphine. This has highlighted a gap in the current literature and a topic of further research, one that has not been investigated extensively, thus far.

Intrathecal morphine induced pruritus was recorded as one of the least important adverse effects to observe for, supported by 70% of nurses and none of the midwifery group. This may be attributed to the fact that health care professionals rely on the patient to inform them of the adverse effects they are experiencing, unless they become visually apparent and obvious.

Nausea and vomiting also were one of the least important adverse effects to observe for with again, 70% of the nursing group and none of the midwifery group acknowledging this as an important adverse effect to observe for. This may be due to the fact as mentioned that these health care professionals again, feel the patient will not hesitate to tell them they are suffering from nausea or vomiting or it will become visually evident.

Initial results from both groups related to the importance of treating nausea and vomiting increased from a vast majority, to almost complete agreement when the statement was reiterated near the end of the survey. Less than half the nurses and three quarters of the midwives initially reported they felt it was important to manage intrathecal morphine induced pruritus, and again these figures rose in the last section of the survey when the statement was reiterated. At this point, all nurses and most midwives agreed it was important to treat these patients with intrathecal morphine induced pruritus. The change in their perspective may be attributed to the continued questions in relation to intrathecal morphine induced pruritus and the emphasis placed upon it within this survey.

Although midwives observe ITMI pruritus more often than nursing, their reluctance to initiate treatment may be attributed to many factors including not wanting to administer more medications to a lactating mother, and their uncertainty of the role of low dose naloxone and its reversal effect on the opiate administered intrathecally.

Between both groups an average of 52% reported they would administer cyclizine as their first line medication for nausea and vomiting in a patient who had received intrathecal morphine. Cyclizine has been identified as the first line anti-emetic in the facility protocol for nausea and vomiting in a patient after receiving intrathecal morphine. This outcome has identified a possible area for further education. All of the nursing group and 80% of the midwifery group reported they would administer naloxone for intrathecal morphine induced pruritus. Naloxone was also indicated in the facility protocol as the first line anti-pruritic treatment. Further education may be indicated within the midwifery group.

The questions related to the incidence of nausea and vomiting in relation to ethnicity reflected that both the nursing group and the midwifery group reported having observed nausea and vomiting to occur more frequently in the New Zealand European group than in

the New Zealand Māori group. The questions related to the incidence of ITMI pruritus and ethnicity reflected that 67% of nursing reported they had observed ITMI pruritus in New Zealand Māori, more-so than in New Zealand Europeans.

Both the nursing group and the midwifery group had a very high percentage of those reporting that they are aware of their facility protocol for the management of intrathecal morphine and its adverse effects, yet there were a small number that did not know or stated that their facility did not have a protocol. This may be attributed to new employees not being orientated sufficiently to their area of practice and would indicate that on-going education is of importance when managing patients who have received intrathecal morphine.

Overall, the majority of both professions reported they felt confident with their current level of knowledge in the management of patients receiving intrathecal morphine. Many of the comments received from both of these health care professional groups indicated that on-going education would be well received and is essential in the provision of adequate management on intrathecal morphine.

4.6 CONCLUSION

The results of this survey show that both the nursing group and the midwifery group acknowledge that patients receiving intrathecal morphine experience intrathecal morphine induced pruritus, however, the emphasis on treating this adverse effect was not consistent. The nursing group has observed that New Zealand Māori experience intrathecal morphine induced pruritus with more incidence than New Zealand Europeans or any other ethnicity. Further education is required in some areas to ensure all professionals are aware of the facility protocol and treatments for adverse effects.

The comments received in the open-ended sections of each question emphasise that all health care professionals have definite views and opinions about the adverse effects of intrathecal

morphine. These views reveal general concern for the well-being of their clients and most important of all, their comfort and safety. The midwives appear to focus on accentuated ‘mother baby bonding’ and immediate care, with lesser amounts of opiates passing to the baby via breast milk. The surgical nurses were more likely to be diligent in their observations of post-operative hypotension. However, the statistics reveal the majority of both groups of health care professionals are both vigilant and decided in their observations and treatment of these adverse effects.

Overall, both professions feel confident and were comfortable with their care and knowledge of intrathecal morphine, its adverse effects, and its management. As educated professionals, both groups are open and willing to learn more to increase their knowledge base. This will ultimately lead to an improved patient post-operative pain management regime which promotes the ERAS protocol.

Chapter 5: Conclusion and Implications for Practice

5.1 INTRODUCTION

The purpose of this research portfolio was to explore two areas of post-operative pain management when intrathecal morphine has been utilised as post-operative analgesia. These two areas are whether intrathecal morphine induced pruritus is influenced by ethnicity, age, or gender, and how well it is managed by health care professionals.

5.2 SUMMARY

Adequate management of post-operative pain and the implementation of ERAS protocols have become significant components of a surgical patient's post-operative care plan (Fearon et al., 2005; Pasero & McCaffery, 2011). This includes adequate management of post-operative opioid adverse effects. When intrathecal morphine is utilised for post-operative pain management, adverse effects have been documented as pruritus, nausea and vomiting, respiratory depression, and urinary retention (Gehling & Tryba, 2009).

The management of intrathecal morphine induced pruritus was the focus of this research portfolio.

The following research question has provided direction for this research portfolio: *Is intrathecal morphine induced pruritus influenced by ethnicity, age, or gender, and how well is it managed by health care professionals?* In an effort to answer the question, this research portfolio was separated into three main sections:

- Chapter 2 explored published literature surrounding morphine and its administration via the intrathecal route, adverse effects and the association with ethnicity, and its

subsequent management by health care professionals. It also explored patient satisfaction after having received intrathecal morphine.

- Chapter 3 presented statistics revealing ethnic differences related to the incidence of certain patient groups experiencing intrathecal morphine induced pruritus, and the treatment received from health care professionals.

- Chapter 4 presented results from a survey that examined the observations and management of health care professionals in dealing with the adverse effects of intrathecal morphine, focusing on pruritus.

This concluding chapter has incorporated all the information and evidence that has been attained from the previous chapters to answer the research question, and provide recommendations for clinical practice and future research.

5.3 IMPLICATIONS FOR PRACTICE

Intrathecal morphine has been utilised for many decades and its safety and efficacy has been proven in many studies (Dahl et al., 1999; Gehling & Tryba, 2009; Gwirtz et al., 1999). Certain studies have established appropriate doses specific to the variety of surgeries undertaken where intrathecal morphine is utilised for post-operative analgesia (Rathmell et al., 2005).

Intrathecal morphine does have specific adverse effects and pruritus is by far the most common (Grant et al., 2010). It is an overwhelmingly disabling adverse effect that can interfere with a patient's sleeping patterns causing discontentment, irritation, and frustration—subsequently impeding post-operative recovery (Ganesh & Maxwell, 2007; Jenkins et al., 2009).

The advent of pharmacogenetics has increased our awareness to the genetic differences that may be responsible for certain ethnicities responding differently to opioid therapy (Bianchi et al., 2008). Roden and George (2002) have discussed pharmacogenetics and have pioneered research in the appreciation that genetic factors may contribute to variability in drug action and response. Tey and Yosipovitch (2010) have highlighted ethnic differences in response to certain pruritic conditions, yet there is a dearth of information available in the study of the association of ethnicity and intrathecal morphine induced pruritus. With further research and development in this area, we may gain more insight into the differences of ethnic responses. In doing so, in the future we may be able to titrate the opioids specific to certain ethnic groups, thereby maximising the outcome.

Many studies have proven that intrathecal morphine induced pruritus is manageable and treatable (Charuluxananan et al., 2001; Colbert et al., 1999; Pirat et al., 2005; Siddik-Sayyid et al., 2010). The use of ondansetron and pre-operative diclofenac, are medications that can be considered as first line to minimise the likelihood or intensity of intrathecal morphine induced pruritus. The follow-up regime of a naloxone infusion for those more at risk could also be implemented. These may be more suitable than alternatives that hold sedative properties such as cyclizine.

Further research is warranted to gain insight into the causality of why certain populations receive different care approaches. Studies have been performed, but were limited by their methodology and the outcomes were not conclusive (Jimenez et al., 2010; Michael et al., 2007).

There was a paucity of literature available and little evidence was retrieved in relation to intrathecal morphine induced pruritus and its association with ethnicity, age, or gender. Chapter 3 has addressed this identified gap in the literature.

Chapter 3 asked the question: *Is intrathecal morphine induced pruritus related to age, gender, or ethnicity?*

Statistics retrieved from an audit, discerning if certain ethnic populations were more at risk for developing intrathecal induced pruritus than others in a rural facility within New Zealand were discussed. The high percentage of the two ethnic groups identified within this audit reflects that this community population is predominantly New Zealand Māori and New Zealand European. Here, the incidence of intrathecal morphine induced pruritus was significantly higher in the New Zealand Māori population than the New Zealand European population, and New Zealand Māori experienced it with more intensity.

This audit was limited in its outcome of measuring whether intrathecal morphine induced pruritus is influenced by gender, due to the large amount of records viewed as being suitable for the audit that were female. It was also limited in its outcome of measuring whether intrathecal morphine induced pruritus is influenced by age, as records of the women undergoing caesarean section procedures were generally younger than 35 years, which is not consistent with current literature. Records of patients undergoing joint replacement surgery in this audit were generally older than 55 years of age. Further, more detailed research would be required to validate this theory.

Despite the fact that New Zealand Māori experienced the intrathecal morphine induced pruritus more-so than New Zealand Europeans, this group received less treatment or attention for this adverse effect. It would be highly recommended that patients being prepared for surgery at pre-assessment clinics were educated in the anaesthetic alternatives available to them.

The development of a leaflet or brochure explaining intrathecal morphine and the possible adverse effects experienced could be beneficial. This leaflet could contain information about

intrathecal morphine induced pruritus, and to who may be more susceptible to this adverse effect, while also informing patients that there is treatment readily available for this adverse effect. Emphasis can be placed on the fact that once this adverse effect is controlled, the benefits of intrathecal morphine are invaluable to those patients not suitable for general anaesthetics and the obstetric population. This brochure can be added to the patients' pre-operative information, giving them the opportunity to read at their leisure. They can be further empowered with this knowledge to make an informed decision regarding the care they receive whilst undergoing elective surgery.

Statistics from this audit also reflected that at doses between 201 mcgs and 300 mcgs, there were no adverse effects experienced in either population. Continued education in the health care profession can lead to an increased awareness regarding the doses received, and augment their vigilance in their care for patients who receive doses other than within these parameters.

In this District Health Board area, the audit showed that more New Zealand Māori women are having caesarean sections than New Zealand Europeans, and more New Zealand Europeans are having joint replacements than New Zealand Māori. These outcomes have highlighted gaps in the literature and may be topics for future research.

Despite these adverse effects, the majority of records indicated the patients were satisfied with intrathecal morphine being utilised as their post-operative analgesic regime.

Chapter 4 asked the question: *Health care professional management of intrathecal morphine induced adverse effects, are we scratching the surface?*

Two common themes or concerns emerged from this survey, as two separate groups of health care professionals reported their observations while providing care for patient groups after receiving intrathecal morphine for their post-operative analgesia. Both groups acknowledged that intrathecal morphine induced pruritus did occur, however they did not place a high

significance in the treatment of this adverse reaction. The nursing group was more concerned about observing for post-operative hypotension, and the midwifery group was more concerned about improving the "mother baby bonding" experience, and reducing the amount of opiate which the baby received from the lactating mother. An advantageous feature of intrathecal morphine in the obstetric population is the minimal amount of opiate that is passed on to the neonate, along with the prolonged analgesic effect for the mother. Both concerns that have been highlighted by the health care professionals are valid and place their patient's well-being in high regard.

The nursing group did observe that New Zealand Māori experienced intrathecal morphine induced pruritus more-so than New Zealand Europeans. One of the limitations of this survey was that there was a lack of documentation around the discussion of the treatment offered to these two population groups. This made it difficult to measure why certain populations received more or less care. Future research may be warranted in this area to discern clarification and develop a framework for improvement.

It is apparent that all health care professionals care about the well-being of their patient. They try to provide the best care they can within the time restraints bestowed upon them. They strive to be as well-educated and diligent as they can, focusing on maximising patient outcomes. Whether they are nurses or midwives, hospital trained or holding a bachelor's degree, young or old, they are open to continued education regarding intrathecal morphine. A recommendation would be to develop a framework inclusive of a model to assist in broadening health care professional clinical skills, to enable enhanced decision making when managing patients who have received intrathecal morphine as their post-operative analgesia.

This framework could include the issuing of a certificate of competence to health care professionals after receiving specific education related to intrathecal morphine and its

management. This could be provided by the facility Acute Pain Service, a team of professionals that play an essential role in the management of post-surgical patients. The Acute Pain Service can ensure new employees are being educated to the facility protocols, and current employees can be made aware of the protocol and receive regular updates. This will increase and maintain health care professional awareness of intrathecal morphine induced pruritus, and its effects on the post-operative patient. Ultimately, this will enable improved management.

5.4 CONCLUSION

Through the undertaking of a comprehensive literature review and two quantitative studies, this research portfolio has demonstrated that certain ethnic populations do respond differently to intrathecal morphine, and both health care professionals and patients would benefit from further education. Although there are relatively small sample sizes in both studies, the results could be representative of the New Zealand population. This appears to be the first audit of its kind in New Zealand to date.

Findings of this research portfolio have been utilised to suggest recommendations for more education, thereby empowering both patients and health care professionals.

Further, more extensive research may be indicated in other District Health Boards in New Zealand to gain further insight into these topics, and aid in planning the most effective way to provide for the needs of these patients.

This research portfolio has shown that:

- New Zealand Māori experience intrathecal morphine induced pruritus with more frequency and more intensity than New Zealand Europeans within this District Health Board of New Zealand.

– Health care professionals do have existing variances in their knowledge regarding the provision of care for these patients, and are receptive in receiving regular updates and in-services.

Appendices

APPENDIX D: AUDIT TOOL CATEGORIZING DATA

Ethnicity	Type of Surgery	Intrathecal morphine dose	Post-op Nausea	Post-op Pruritus	NALOXONE GIVEN	Post-op Respiratory Depression	Patient Satisfaction score	Hypotension BP
NZM	LSCS	150	0	0		0	8	
NZP	L THJR	100	2	0		0	5	
NZP	R THJR	100	0	0		0	3	
NZP	L THJR	100	1	0		0	8	
NZM	R TKJR	200	0	4		0	7	
NZP	LSCS	200	1	0		0	10	
NZP	L THJR	100	0	0		0	8	
AO EUR	LSCS	100	0	5		0	5	85/42
AO EUR	L THJR	200	0	0		0	8	Y
NZP	LSCS	100	0	8	Y	0	8	
TONGA	LSCS	200	0	0		0	10	
NZP	LSCS	200	1	0		0	10	
NZM	LSCS	200	0	0		0	8	
NZM	LSCS	200	0	3		Y	10	
NZP	LSCS	100						
NZP	L TKJR	100						
NZP	L THJR	100	0	0		0	10	
NZM	R THJR	100	0	0		0	7	70/40
NZM	LSCS	100	1	0		0	9	
NZP	LSCS	100	0	0		0	9	
NZP	L THJR	180	0	0		0	5	
NZM	L THJR	100	0	4		0	8	
NZP	L THJR	100	0	0		0	6	83/40
NZP	R TKJR	100	0	0		0	10	
NZP	L THJR	100						
NZM	LSCS	100						
NZP	L TKJR	100	0	0		0	10	
NZP	L TKJR	100	0	0		0	10	
NZM	LSCS	100						
AO EUR	LSCS	100						
NZP	L THJR	100						
NZM	LSCS	150	0	0		0	10	

APPENDIX F: HCP QUESTIONNAIRE

RN / RM Questionnaire

Intrathecal morphine has been utilised as post-operative analgesic pain management since the late 1970s. It has been utilised more frequently as an alternative to conventional anaesthetic and post-operative analgesic, especially in obstetrics for caesareans and in orthopaedics for joint replacement surgery. The following questions are in reference to a patient receiving intrathecal morphine for their post-operative analgesic management.

1. Demographics: Circle that which applies to you;

Area of Practice you currently work in	Surgical	Midwifery	(Other)
Level of education	Hospital trained	Bachelor	(Other)
Years of experience in this field	0-5 yrs.	6-10 yrs.	>11 yrs.
Age	20-30 yrs.	31-40 yrs.	>41 yrs.

2. Based on your clinical experience of caring for a patient with intrathecal morphine what are the most common side / adverse effects that you have observed?

Nausea and vomiting	
Urinary retention	
Pruritus	
Respiratory depression	
Hypotension	
Other	
(Please Comment)	

3. Of these side / adverse effects which one is more prevalent? (Rank from 1 [most prevalent] – 6 [least prevalent])

Nausea and vomiting	
Urinary retention	
Pruritus	
Respiratory depression	
Hypotension	
Other	
(Please Comment)	

4. Rank from 1 – 6 in order of importance, which side / adverse effects, you would routinely monitor for in these patients?

Nausea and vomiting	
Urinary retention	
Pruritus	
Respiratory depression	
Hypotension	
Other	
(Please Comment)	

Nausea, vomiting and pruritus are common and unpredictable side / adverse effects of intrathecal morphine. The next set of questions refers to these side effects:

5. What is the first line medication used in your facility for the treatment of nausea and vomiting, in a patient that has received intrathecal morphine? (tick only one box)

Naloxone	
Maxalon	
Cyclizine	
Ondansetron	
Other	
(Please Comment)	

6. What is the first line medication used in your facility for the treatment of pruritus, in a patient that has received intrathecal morphine? (tick only one box)

Phenergen	
Benadryl	
Ondansetron	
Naloxone	
Other	
(Please Comment)	

7. How important is the management of nausea and vomiting in a patient that has received intrathecal morphine? (Select one answer only)

Very important	
(Please comment)	
Not so important	
(Please comment)	

8. How important is the management of pruritus in a patient that has received intrathecal morphine? (Select one answer only)

Very important	
(Please comment)	
Not so important	
(Please comment)	

9. Have you observed certain patient ethnicities experiencing nausea and vomiting more so than others, after receiving intrathecal morphine?

Yes	
No	

10. If you selected yes in question 9, please tick which ethnicity(s)?

New Zealand Māori	
New Zealand Pakeha	
European	
Asian	
Other (Pease comment)	

11. Have you observed certain patient ethnicities experiencing pruritus more so than others, after receiving intrathecal morphine?

Yes	
No	

12. If you selected yes in question 11, please tick which ethnicity(s)?

New Zealand Māori	
New Zealand Pakeha	
European	
Asian	
Other (Pease comment)	

Intrathecal morphine is a medication that is frequently used for post-operative pain management. The questions that follow refer to your knowledge and skills in relation to intrathecal morphine administration and post-operative monitoring.

13. How frequently would you assess a patient's pain status after receiving intrathecal morphine? (Tick which box applies)

Every 1/2 hour for 2 hours, then 4 hourly	
Every 1 hour for 4 hours, then 4 hourly	
Every 2 hours for 8 hours then every 4 hours for 10 hours (total 18 hours)	
Every 4 hours for 8 hours then every 2 hours for 10 hours (total 18 hours)	
Only when your patient complains of pain	

14. What pain assessment tool do you utilise when assessing your patients pain? (Tick all that apply)

Wong-Baker face scale	
Numerical rating scale	
Verbal rating scale	
Other	
(Please comment)	

15. Does your facility have a protocol for managing patients receiving intrathecal morphine for post-operative pain management?

Yes	
No	
Don't know	
If no, how does your facility manage intrathecal morphine?	

16. If your patient continues to complain of pain after receiving intrathecal morphine, which medication would you offer your patient next? (rank from 1 – 5)

IV Morphine PCA	
Tramadol	
Paracetamol and NSAIDS	
IV Fentanyl PCA	
IV Tramadol	

17. Are you confident with your current level of knowledge in pain management in patients receiving intrathecal morphine for post-operative pain management?

Yes	
No	
(If no, please comment)	

A nurse/midwife's knowledge and understanding of intrathecal morphine and its associated side / adverse effects is essential. The following statements refer to patients that have received intrathecal morphine for post-operative pain management. Do you agree with these statements?

18. "It is important to treat patients who are experiencing nausea/vomiting"

Yes	
No	
(If no, please comment)	

19. "It is important to treat patients who are experiencing pruritus"

Yes	
No	
(If no, please comment)	

20. "Intrathecal morphine is an effective post-operative analgesic"

Yes	
No	
(If no, please comment)	

21. "I have a good understanding of the side effects of intrathecal morphine"

Yes	
No	
(If no, please comment)	

22. Please feel free to add any further comments:

Thank you for taking the time to complete this survey.

APPENDIX G: PARTICIPANT INFORMATION SHEET

SCHOOL OF NURSING

PARTICIPANT INFORMATION SHEET

Registered Nurse/Midwife

Researcher Introduction

My name is Jennifer Boudreau and I am a post graduate student at the University of Auckland conducting a Master in Health Science research portfolio. At the time of preparation for this research project I am / was employed by the Bay of Plenty District Health Board as Clinical Nurse Specialist at Whakatane hospital.

Project Description and Invitation

Is intrathecal morphine induced pruritus influenced by ethnicity, age or gender and how well is it managed by health care professionals?

This project will be inclusive of a questionnaire designed to ascertain the depth of the RN / RM current understanding about the adverse effects and medication management for intrathecal morphine. As many of your patients receive intrathecal morphine as an anaesthetic you have been deemed an appropriate participant of this survey. I would like to formally invite you to participate in this survey.

Project Procedures

In acceptance to participate in this audit, you will be asked some questions in relation to intrathecal morphine, the adverse effects, and the treatment (if any) you administered to your patients. The survey will consist of a series of questions which is expected to take up to thirty minutes in total. Your participation is voluntary and there is no physical, psychological, social discomfort or incapacity expected to occur during this survey. No funding has been requested or applied to this survey.

The data collected will be used for statistical evidence of adverse effects experienced and results can be made available upon request at completion of the project, December 2012.

Data storage / retention / destruction / future use

The data obtained during this audit will be collected in questionnaire form on documents that will be stored for ten years, and then be destroyed (shredded) upon completion.

Right to withdraw from Participation

As a participant you have the right to withdraw from this survey at any time. You have the right to withdraw your data from the research for a period of three months following collection.

Anonymity and confidentiality

Your rights to anonymity and confidentiality will be respected for the entirety of this audit. No names or personal, medical or other information will be released to any persons other than that of those who are assisting me in statistical representation of the information I collect during this survey (who will have also completed a confidentiality agreement).

Contact Details and Approval Wording

Researcher

Jennifer Boudreau, PG Dip Hsc

Tauranga
Bay of Plenty District Health Board
Email: jennifer.boudreau@bopdhb.govt.nz
Cell: 021 237 3091

Supervisors

Anecita Lim, MHSc, FCNA (NZ) RN, Senior Lecturer, University of Auckland

School of Nursing, Health and Science Building, 29 Park St, Grafton, Auckland
Ph: work (09) 923 3782
Email: g.lim@auckland.ac.nz

Francesca Storr, MN (Hons) Clinical Lecturer, University of Auckland, Nurse Specialist – Pain Management, National Women's Health, Auckland City Hospital

Auckland City Hospital, 1232 Grafton Rd, Auckland 1001
Ph: work (09) 307 4949
Email: francescas@adhb.govt.nz

Head of Department

Robyn Dixon, MA PhD, RN, Associate Professor, University of Auckland

School of Nursing, Health and Science Building, 29 Park St, Grafton, Auckland
Ph: (09) 923 7388
Email: r.dixon@auckland.ac.nz

Health and Disability Advocate Free Service

0800 112233
Level 10, Tower Centre, 45 Queen St, Auckland 1010.
Phone: 09 373-1060
Email: hdc@hdc.org.nz

APPROVED BY THE NORTHERN Y REGIONAL ETHICS COMMITTEE ON DECEMBER 05, 2011, Reference number NTY/11/EXP/073.

APPENDIX H: CONSENT FORM FOR RN RM

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

SCHOOL OF NURSING

CONSENT FORM

Registered Nurse/Midwife

THIS FORM WILL BE HELD FOR A PERIOD OF 10 YEARS

Project Title: Nursing and Midwifery Management for Intrathecal Opiates

Researcher: Jennifer Boudreau

I have read the participant Information Sheet. I understand the nature of the research and why I have been selected. I have had the opportunity to ask questions and have had them answered to my satisfaction.

- I agree to take part in this research.
- I understand that I am free to withdraw at any time, and can withdraw any data traceable to me up to three months from collection of said data.
- I wish / do not wish to receive a summary of the findings.
- I understand that a third party who has signed a confidentiality agreement may be employed to assist in statistical analysis of the data collected.
- I understand that the outcome of this research may be published.
- I understand that the data will be kept for a period of ten years, after which they will be destroyed.

Name _____

Signature _____

Date _____

Mailing Address: (If not prior collected)

J. Boudreau
333 Glue Pot Rd
RD 3
Oropi
Tauranga 3173

APPROVED BY THE NORTHERN Y REGIONAL ETHICS COMMITTEE ON DECEMBER 05, 2011, Reference number NTY/11/EXP/073.

APPENDIX I: ORGANISED COMMENTS FROM HEALTH CARE PROFESSIONALS

Health care professional comments on questions

Q.	Sb.	Pf.	Comment
1			
2	3	RM	Pruritus: occasional
	4	RM	Have not experienced hypotension as women stable and cared for in post natal long after the ITM given (usually)
3	3	RM	Pruritus most prevalent. Others never seen in maternity really
	4	RM	I have only cared for women post C/S – they already have an IDC so I cannot rank urinary retention
4	1	PRN	Re: urinary retention. Most times patient has a urinary catheter. Patient only in PACU a limited time
	3	RM	Respiratory depression and hypotension: 1 and 2: as per protocol
	4	RM	Other: haemorrhage – especially when concealed, can go unrecognised when mothers pain level so well controlled by ITM e.g. usual signs of hematoma development are masked
	11	RN	Block height, pain score
	13	PRN	Patient usually has IDC
5	6	RM	Depends on the anaesthetist
	10	RM	Droperidol, if ineffective Cyclizine then Zofran
	19	RN	Protocol states naloxone. Usually Cyclizine first
	22	RM	Ondansetron first line. This is not first line if following the protocol, but most commonly used as most effective
6	16	RN	A dry cloth usually assists (gentle massage of nose area or area itchy) initially
	18	RN	Dry cloth, massage
	21	RM	Cold dry cloth
	23	RM	Gentle rub with dry cloth
	26	RM	Other: piriton
7	1	PRN	Can't be mobilised, increases pain and discomfort, pt. can't eat: needs fluids and nutrition, pt. loses trust: therapeutic relationship
	2	RN	Sometimes patients hate n/v more than the pain itself
	3	RM	Rarely seen in maternity
	4	RM	It may not be a fleeting effect – ITM has a long duration and treatment is easy and effective
	5	RM	Because it can threaten the airway and also reduce enjoyment of those first few hours with their new baby
	6	RM	Very distressing for patient especially with a fresh section wound
	7	RN	Otherwise the patient feels terrible, unable to drink and eat therefore takes longer to mobilise
	8	RN	Provide comfort
	12	RN	It is miserable feeling nauseated
	13	PRN	Nausea can be worse than pain for the patient
	14	PRN	Can be long acting
	16	RN	If susceptible – many patients are not troubled by this, but if they are then it is usually quite disabling till "on top of"
	18	RN	Pain first importance but airways very important if patients vomit
	19	RN	Maintenance of airway as primary safety concern
	22	RM	Awful to be vomiting while trying to care for and feed a new-born
	24	RM	For patient comfort and pain management
	25	RM	Fluid balance, patient comfort
	27	RM	Initially patient feels better after they vomit and decline anti-emetic. If persists then they are happy to have medication
	28	RM	Interferes with bonding with mother and baby. Mother feels miserable
	29	RM	Compromises patient comfort
8	1	PRN	Allergic reactions, needs to be controlled, might get worse. Discomfort for patient scratching and impaired skin
	2	RN	Depending on how bad the itching is, a cloth may be all you need
	3	RM	Usually very mild symptoms, treated with cool flannel only
	4	RM	Same as n/v/ itching can be intense and debilitating

LEGEND: Q = question, Sb = participant number, P = profession, RN = registered nurse, RM = registered midwife, PRN = post anaesthetic care unit RN

APPENDIX J: POST INTRATHECAL MORPHINE PRESCRIPTION

X7411 7/06

Patient Label

BAY OF PLENTY DISTRICT HEALTH BOARD
HAUORA A TOI

CLINICAL PAIN SERVICE

POST INTRATHECAL MORPHINE PRESCRIPTION

The above patient has received intrathecal (spinal) opiate of

Morphine _____ mcg at _____ hours on _____

02 at _____ via nasal prongs /mask for _____ hrs

1.	**NO ADDITIONAL NARCOTICS OR SEDATIVES FOR 24 HOURS, unless SPECIFICALLY ORDERED by an anaesthetist.**	
2.	RESPIRATIONS	To be recorded at 4 and 8 hours post opiate insertion Then every 2 hours for the next 10 hours
	RESPIRATORY RATE < 8 /MINUTE	Administer Naloxone 100mcg I.V. every 2 minutes with a maximum of 400mcg or until respirations are 12 /min Notify the Clinical Pain Service or Anaesthetist
3.	NAUSEA AND /OR VOMITTING	Cyclizine 25 - 50mg I.V. PRN Q8H (slow push) If ineffective administer Zofran 4mg I.V. PRN Q6H If ineffective administer Naloxone 40 mcg I.V. PRN Q15 minutes with a maximum of 200mcg over 24 hours **N.B. 0.1ml in a 1ml syringe = 40mcg**
4.	PRURITIS	Gentle massage with dry facecloth Administer Naloxone 40mcg I.V. Q4H prn if massage ineffective Maximum total dose over 24 hours will be 200mcg **DO NOT ADMINISTER Benadryl or Phenergan**
5.	PAIN SCORES	To be recorded at the same time as respiration recordings
6.	I.V. ACCESS	Remain in for 6 hours post recordings
7.	WARD PLACEMENT	To be in the acute settings nearest to nurses station No curtains to be drawn except for washes etc Bed night light to be on overnight
8.	NON OPIOID ANALGESIA	Paracetamol and /or Nsaids may be administered as charted
9.	BREAK THROUGH PAIN	Administer Tramadol 50 - 100mg orally PRN Q6H to maximum of 400mg /24 hours or Tramadol 25mg I.V. PRN Q15 minutes to maximum of 600mg /24 hours See Tramadol protocol for administering

Comments _____

_____

Signed _____ Print _____

(Anaesthetist)

References

Annells, M., & Whitehead, D. (2007). Analysing data in qualitative research. In Z. Schneider, D. Whitehead, D. Elliot, G. Lobiondo-Wood & J. Haber (Eds.), *Nursing and midwifery research: Methods and appraisal for evidence-based practice* (3rd ed.). Sydney, Australia: Elsevier.

Apfelbaum, J. L., Chen, C., Mehta, S. S., & Gan, T. J. (2003). Postoperative pain experience: Results from a national survey suggest postoperative pain continues to be undermanaged. *Anesthesia & Analgesia, 97*(2), 534-540. doi: 10.1213/01.ANE.0000068822.10113.9E

Bailey, P. L., Rhondeau, S., Schafer, P. G., Lu, J. K., Timmins, B. S., Foster, W., . . . Stanley, T. H. (1993). Dose-response pharmacology of intrathecal morphine in human volunteers. *Anesthesiology, 79*(1), 49.

Barash, P. G., Cullen, B. F., Stoelting, R. K., Cahalan, M. K., & Stock, M. C. (2009). *Handbook of clinical anesthesia* (6th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Bernards, C. M. (2006). Epidural and spinal anesthesia. In P. G. Barash, B. F. Cullen & R. K. Stoelting (Eds.), *Clinical anesthesia* (5th ed., pp. 691-717). Philadelphia, PA: Lippincott Williams & Wilkins.

Bianchi, M., Fornasari, D., Antonini, R. A., Beretta-Piccoli, B. T., Nava, S., & Neuenschwander, H. (2008). The pharmacogenetics of morphine-induced analgesia: A case report. *Journal of Pain and Symptom Management, 36*(1), e10-e12. doi: 10.1016/j.jpainsymman.2008.02.002

Bilsborough, J., Leung, D. Y. M., Maurer, M., Howell, M., Boguniewcz, M., Yao, L., . . . Gross, J. A. (2006). IL-31 is associated with cutaneous lymphocyte antigen–positive skin homing T cells in patients with atopic dermatitis. *Journal of Allergy and Clinical Immunology, 117*(2), 418-425.

Bond, C., LaForge, K. S., Tian, M., Melia, D., Zhang, S., Borg, L., . . . Yu, L. (1998). Single-nucleotide polymorphism in the human mu opioid receptor gene alters β-endorphin

binding and activity: Possible implications for opiate addiction. *Proceedings of the National Academy of Sciences in the United States of America, 95*(16), 9608-9613.

Cepeda, M. S., Farrar, J. T., Roa, J. H., Boston, R., Meng, Q. C., Ruiz, F., . . . Strom, B. L. (2001). Ethnicity influences morphine pharmacokinetics and pharmacodynamics. *Clinical Pharmacology and Therapeutics, 70*(4), 351-361. doi: 10.1016/S0009-9236(01)51508-8

Cevikbas, F., Steinhoff, M., & Ikoma, A. (2010). Role of spinal neurotransmitter receptors in itch: New insights into therapies and drug development. *CNS Neuroscience and Therapeutics, 17*(6), 742-749. doi: 10.1111/j.1755-5949.2010.00201.x

Charuluxananan, S., Kyokong, O., Somboonviboon, W., Lertmaharit, S., Ngamprasertwong, P., & Nimcharoendee, K. (2001). Nalbuphine versus propofol for treatment of intrathecal morphine-induced pruritus after cesarean delivery. *Anesthesia & Analgesia, 93*(1), 162-165.

Charuluxananan, S., Somboonviboon, W., Kyokong, O., & Nimcharoendee, K. (2000). Ondansetron for treatment of intrathecal morphine-induced pruritus after cesarean delivery. *Regional Anesthesia and Pain Medicine 25*(5), 535-539. doi: org/10.1053/rapm.2000.7809

Chestnut, D. (2005). Efficacy and safety of epidural opioids for post-operative analgesia. *Anesthesiology, 102*(1), 221-223.

Coda, B. A. (2006). Opioids. In P. G. Barash, B. F. Cullen & R. K. Stoelting (Eds.), *Clinical anesthesia* (5th ed., pp. 353-383). Philadelphia, PA: Lippincott Williams & Wilkins.

Colbert, S., O'hanlen, D. M., Galvin, S., Chambers, F., & Moriarty, D. C. (1999). The effect of rectal diclofenac on pruritus in patients receiving intrathecal morphine. *Anaesthesia, 54*(10), 948-952. doi: 10.1046/j.1365-2044.1999.01066.x

Coller, J. K., Christrup, L. L., & Somogyi, A. A. (2009). Role of active metabolites in the use of opioids. *European Journal of Clinical Pharmacology, 65*(2), 121-139.

Dabu-bondoc, S., Franco, S. A., & Sinatra, R. S. (2009). Neuraxial analgesia with hydromorphone, morphine, and fentanyl: Dosing and safety guidelines. In R. S.

Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. 230-244). New York, NY: Cambridge University Press.

Dahl, J. B., Jeppesen, I. S., Jorgensen, H., Wetterslev, J., & Moiniche, S. (1999). Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing caesarean section with spinal anesthesia: A qualitative and quantitative systemic review of randomized controlled trials. *Anesthesiology, 91*(6), 1919-1927.

Dahl, J. B., & Moiniche, S. (2004). Pre-emptive analgesia. *British Medical Bulletin, 71*(1), 13-27.

Dickenson, A. H. (2002). Gate control theory of pain stands the test of time. *British Journal of Anaesthesia, 86*(6), 755-757. doi: 10.1093/bja/88.6.755

Dunteman, E., Karanikolas, M., & Filos, K. S. (1996). Transnasal butorphanol for the treatment of opioid-induced pruritus unresponsiveness to antihistamines. *Journal of Pain and Symptom Management, 12*(4), 255-260. doi: 10.1016/0885-3924(96)00154-6

Eckhardt, K., Ammon, S., Hofmann, U., Riebe, A., Gugeler, N., & Mikus, G. (2000). Gabapentin enhances the analgesic effect of morphine in healthy volunteers. *Anesthesia & Analgesia, 91*(1), 185-191.

Eisenhauer, L. A., Hurley, A. C., & Dolan, N. (2007). Nurses' reported thinking during medication administration. *Journal of Nursing Scholarship, 39*(1), 82-87. doi: 10.1111/j.1547-5069.2007.00148.x

Elliott, D. (2007). Reviewing the literature. In Z. Schneider, D. Whitehead, D. Elliott, G. Lobiondo-Wood & J. Haber (Eds.), *Nursing and midwifery research: Methods and appraisal for evidence-based practice* (3rd ed., pp. 46-60). Sydney, Australia: Elsevier.

Elliott, D., & Schneider, Z. (2007). Quantitative data collection and study validity. In Z. Schneider, D. Whitehead, D. Elliott, G. Lobiondo-Wood & J. Haber (Eds.), *Nursing and midwifery research: Methods and appraisal for evidence-based practice* (3rd ed., pp. 191-205). Sydney, Australia: Elsevier.

Elliott, D., & Thompson, D. (2007). Common quantitative methods. In Z. Schneider, D. Whitehead, D. Elliott, G. Lobiondo-Wood & J. Haber (Eds.), *Nursing and midwifery Research: Methods and appraisal for evidence-based practice* (3rd ed., pp. 156-174). Sydney, Australia: Elsevier.

Essving, P., Axelsson, K., Åberg, E., Spännar, H., Gupta, A., & Lundin, A. (2011). Local infiltration analgesia versus intrathecal morphine for postoperative pain management after total knee arthroplasty: A randomized controlled trial. *Anesthesia & Analgesia, 113*(4), 926-933. doi: 10.1213/ANE.0b013e3182288deb

European Union. (2012). Planning and setting up the clinical audit. Retrieved September 27, 2012, from http://www.optimalblooduse.eu/audit/planningandsettingup.ashx

Fearon, K. C. H., Ljunkgvist, O., Von Meyenfeldt, M., Revhaug, A., Dejong, C. H. C., Lassen, K., . . . Kehlet, H. (2005). Enhanced recovery after surgery: A consensus review of clinical care for patients undergoing colonic surgery. *Clinical Nutriton*(24), 466-477. doi: 10.1016/j.clnu.2005.02.002

Feero, W. G., Guttmacher, A. E., & Collins, F. S. (2010). Genomic medicine - An updated primer. *The New England Journal of Medicine, 362* (21), 2001-2011. doi: 10.1056/NEJMra0907175

Ferrante, F. M., Orav, E. J., Rocco, A. G., & Gallo, J. (1988). A statistical model for pain in patient-controlled analgesia and conventional intramuscular opioid regimens. *Anesthesia & Analgesia, 67*(5), 457-461.

Fischer, H. B. J., & Simanski, C. J. P. (2005). A procedure-specific systematic review and consensus recommendations for analgesia after total hip replacement. *Anaesthesia, 2005, 60, pages 1189–1202 doi:, 60*(12), 1189-1202. doi: 10.1111/j.1365-2044.2005.04382.x

Fitzgibbon, D. R. (2009). Respiratory depression: Incidence, diagnosis, and treatment. In R. S. Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. 416-432). New York, NY: Cambridge University Press.

Fournier, R., Van Gessel, E., Weber, A., & Gamulin, Z. (2000). A comparison of intrathecal analgesia with fentanyl or sufentanil after total hip replacement. *Anesthesia & Analgesia, 90*(4), 918-922.

Fukuda, K. (2005). Intravenous opioid anesthetics. In R. D. Miller (Ed.), *Miller's anesthesia* (6th ed., pp. 379-437). St. Louis, MO: Churchill Livingstone.

Ganesh, A., & Maxwell, L. G. (2007). Pathophysiology and management of opioid-induced pruritus. *Drugs, 67*(6), 2323-2333.

Gehling, M., & Tryba, M. (2009). Risks and side-effects of intrathecal morphine combined with spinal anaesthesia: A meta-analysis. *Journal of the Association of Anaesthetists of Great Britain and Ireland, 64*, 643-651. doi: 10.1111/j.1365-2044.05817.x

Girgin, N. K., Gurbet, A., Turker, G., Aksu, H., & Gulhan, N. (2008). Intrathecal morphine in anesthesia for cesarean delivery: Dose-response relationship for combinations of low-dose intrathecal morphine and spinal bupivacaine. *Journal of Clinical Anesthesia, 20*(3), 180-185. doi: 10.1016/j.jclinane.2007.07.010

Goodarzi, M. (1999). Comparison of epidural morphine, hydromorphone and fentanyl for postoperative pain control in children undergoing orthopaedic surgery. *Pediatric Analgesia, 9*(5), 419-422. doi: 10.1046/j.1460-9592.1999.00370.x

Grant, G. J., Hepner, D., & Barss, V. A. (2010). Adverse effects of neuraxial analgesia and anesthesia for obstetrics. Retrieved June 3, 2012, from http://www.uptodate.com/contents/adverse-effects-of-neuraxial-analgesia-and-anesthesia-for-obstetrics

Grape, S., & Shug, S. A. (2008). Epidural and spinal analgesia. In P. E. Macintyre, S. M. Walker & D. J. Rowbotham (Eds.), *Clinical pain management: Acute pain* (2nd ed., pp. 255-270). London, England: Hodder-Arnold.

Gwirtz, K. H., Young, J. V., Byers, R. S., Alley, C., Levin, K., Walker, S. G., & Stoelting, R. K. (1999). The safety and efficacy of intrathecal opioid analgesia for acute postoperative pain: Seven years' experience with 5969 surgical patients at Indiana University Hospital. *Anesthesia & Analgesia, 88*(3), 599-604.

Hansen, R. (2010). Biopsychosocial model of pain. Retrieved June 14, 2010, from http://www.arachnoiditis.info/website_captures/chronicpainhandbook/Biopsychosocial%20Model%20of%20Pain.htm

Hindle, A. (2008). Intrathecal opioids in the management of acute postoperative pain. *Continuing Education in Anaesthesia, Critical Care & Pain, 8*(3), 81-85. doi: 10.1093/bjaceaccp/mkn016

Ho, K. T., & Gan, T. J. (2009). Opioid-related adverse effects and treatment options. In R. S. Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. 406-415). New York, NY: Cambridge University Press.

Huntington, A. (Ed.). (2012). *The New Zealand nursing workforce: A profile of nurse practitioners, registered nurses and enrolled nurses 2011*. New Zealand: The Nursing Council of New Zealand.

IASP. (2011). IASP Taxonomy. Retrieved August 26, 2012, from http://www.iasp-pain.org/AM/Template.cfm?Section=Pain_Definitions

Jenkins, H. H., Spencer, E. D., Weissgerber, A. J., Osborne, L. A., & Pellegrini, J. E. (2009). Correlating an 11-point verbal numeric rating scale to a 4-point verbal rating scale in the measurement of pruritis. *Journal of Perianesthesia Nursing, 24*(3), 152-155.

Jimenez, N., Seidel, K., Martin, L. D., Rivara, F. P., & Lynn, A. (2010). Perioperative analgesic treatment in Latino and non-Latino pediatric patients. *Journal of Health Care for the Poor and Undeserved, 21*(1), 229-236. doi: 10.1353/hpu.0.0236

Kalso, E. (1983). Effects of intrathecal morphine, injected with bupivicaine, on pain after orthopaedic surgery. *British Journal of Anaesthesia, 55*(5), 415-422. doi: 10.1093/bja/55.5.415

Karaman, S., Kocabas, S., Uyar, M., Hayzaran, S., & Firat, V. (2006). The effects of sufentanil or morphine added to hyperbaric bupivacaine in spinal anaesthesia for Caesarean section. *European Journal of Anaesthesiology, 23*(04), 285-291. doi: 10.1017/S0265021505001869

Kehlet, H., Troels, S. J., & Woolf, C. J. (2006). Persistent postsurgical pain: risk factors and prevention. *The Lancet, 367*(9522), 1618-1625. doi: 10.1016/S0140-6736(06)68700-X

Klepstad, P., Dale, O., Skorpen, F., Borchgrevink, P. C., & Kaasa, S. (2005). Genetic variability and clinical efficacy of morphine. *ACTA Anaesthesiologica Scandinavica, 49*, 902-908. doi: 10.1111/j.1399-6576.2005.00772.x

Kodali, B. S., & Oberoi, J. O. (2011). Management of postoperative pain. Retrieved August 16, 2011, from http://www.uptodate.com/contents/management-of-postoperative-pain

Lai, D. C. (2002). History of pain relief. In C. A. Warfield & H. J. Fausett (Eds.), *Manual of pain management* (2nd ed., pp. 3-5). Philadelphia, PA: Lippincott Williams & Wilkins.

Lee, A., Chan, S. K. C., Chen, P. P., Gin, T., Lau, A. S. C., & Chiu, C. H. (2010). The costs and benefits of extending the role of the acute pain service on clinical outcomes after major elective surgery. *Anesthesia & Analgesia, 111* (4), 1042-1050. doi: 10.1213/ ANE.0b013e3181ed1317

Lockington, P. F., & Fa'aea, P. (2007). Subcutaneous naloxone for the prevention of intrathecal morphine induced pruritus in elective caesarean delivery. *Anaesthesia, 62*(7), 672-676. doi: 10.1111/j.1365-2044.2007.05098.x

Lotsch, J., Dudziak, R., Freynhagen, R., Marschner, J., & Geisslinger, G. (2006). Fatal respiratory depression after multiple intravenous morphine injections. *Clinical Pharmacokinetics 45*(11), 1051-1060. doi: 0312-5963/06/0011-1051/

Macintyre, P. E., & Ready, L. B. (2001). *Acute pain management: A practical guide* (2nd ed.). London, England: W. B. Saunders.

Macintyre, P. E., Rowbotham, D. J., & Walker, S. G. (2008). *Clinical pain management acute pain* (2nd ed.). London, England: Hodder Arnold.

Maclaren, J. E., & Kain, Z. N. (2007). Perioperative biopsychosocial research: The future is here. *Journal of Clinical Anesthesia, 19*(6), 410-412.

Macrae, W. (2001). Chronic pain after surgery. *British Journal of Anaesthesia, 87*(1), 88-98. doi: 10.1093/bja/87.1.88

Manalo, E., & Trafford, J. (2004). *Thinking to thesis: A guide to graduate success at all levels*. Auckland, New Zealand: Pearson Longman.

Manias, E. (2003). Medication trends and documentation of pain management following surgery. *Nursing and Health Sciences, 5*(1), 85-94. doi: 10.1046/j.1442-2018.2003.00140.x

Manias, E., Aitken, R., & Dunning, T. (2004). Medication management by graduate nurses: Before, during and following medication administration. *Nursing and Health Sciences, 6*(2), 83-91. doi: 10.1111/j.1442-2018.2004.00178.x

Marchand, S. (2008). The physiology of pain mechanisms: From the periphery to the brain. *Rheumatic Diseases Clinics of North America, 34*(2), 285-309. doi: 10.1016/j.rdc.2008.04.003

Marks, R. M., & Sachar, E. J. (1973). Undertreatment of medical inpatients with narcotic analgesics. *Annals of Internal Medicine, 78*(2), 173-181.

Mazoit, J. X., Butscher, K., & Samii, K. (2007). Morphine in postoperative patients: Pharmacokinetics and pharmacodynamics of metabolites. *Anesthesia & Analgesia, 105*(1), 70-78. doi: 10.1213/01.ane.0000265557.73688.32

McCaffery, M., & Pasero, C. (1999). *Pain clinical manual* (2nd ed.). St Louis, MO: Elsevier.

McDonald, D. (1994). Gender and ethnic stereotyping and narcotic analgesic administration. *Research in Nursing and Health, 17*(1), 45-49. doi: 10.1002/nur.4770170107

McNicol, E., Horowicz-Mehler, N., Fisk, R. A., Bennett, b., Gialeli-Goudas, M., Chew, P. W., . . . Carr, D. (2003). Management of opioid side effects in cancer-related and chronic noncancer pain: a systematic review. *The Journal of Pain, 4*(5), 231-256. doi: doi:10.1016/S1526-5900(03)00556-X

McQuay, H. (2009). Historical perspective, unmet needs, and incidence. In R. S. Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. xv-xvi). New York, NY: Cambridge University Press.

Melzack, R., & Wall, P. D. (1965). Pain mechanisms: A new theory. *Science, 150*(3699), 971-979. doi: 10.1126/science.150.3699.971

Michael, G. E., Sporer, K. A., & Youngblood, G. M. (2007). Women are less likely than men to receive prehospital analgesia for isolated extremity injuries. *The American Journal of Emergency Medicine, 25*(8), 901-906. doi: 10.1016/j.ajem.2007.02.001

Midwifery Council of New Zealand. (2011). 2011 Midwifery workforce survey. Retrieved November 3, 2012, from http://www.midwiferycouncil.health.nz/images/stories/pdf/Publications/workforce%20survey%202011.pdf

Ministry of Health. (2010). Hospital-based Maternity Events 2007. Retrieved August 22, 2012, from http://www.health.govt.nz/publication/hospital-based-maternity-events-2007

Ministry of Health. (2011). Targeting more elective operations: Improved access to elective surgery. Retrieved August 22, 2012, from http://www.health.govt.nz/publication/targeting-more-elective-operations-improved-access-elective-surgery

Morrow, A. (2012). Morphine. Retrieved July 28, 2012, from http://dying.about.com/od/opioidpainmedications/a/ms.htm

Murnion, B. P., Gnjidic, D., & Hilmer, S. N. (2010). Prescription and administration of opioids to hospital in-patients, and barriers to effective use. *Pain Medicine, 11*(1), 58-66. doi: 10.1111/j.1526-4637.2009.00747.x

Okie, S. (2010). A flood of opioids, a rising tide of deaths. *The New England Journal of Medicine, 363*(21), 1981-1985. doi: 10.1056/NEJMp1011512

Pasero, C., & McCaffery, M. (2011). *Pain assessment and pharmacologic management*. St. Louis, MO: Elsevier.

Pirat, A., Tuncay, S. F., Torgay, A., Candan, S., & Arslan, G. (2005). Ondansetron, orally disintegrating tablets versus intravenous injection for prevention of intrathecal morphine-induced nausea, vomiting, and pruritus in young males. *Anesthesia & Analgesia, 101* (5), 1330-1336. doi: 10.1213/01.ANE.0000180830.12355.D9

Pleym, H., Spigset, O., Kharasch, E. D., & Dale, O. (2003). Gender differences in drug effects: Implications for anaesthesiologists. *ACTA Anaesthesiologica Scandinavica, 47*(3), 241-259.

Podgoreanu, M. V., & Mathew, J. P. (2006). Genomic basis of perioperative medicine. In P. G. Barash, B. F. Cullen & R. K. Stoelting (Eds.), *Clinical anesthesia* (5th ed., pp. 133-148). Philadelphia, PA: Lippincott Williams & Wilkins.

Rachinger-Adam, B., Conzen, P., & Azad, S. C. (2011). Pharmacology of periferal opiod receptors. *Current Opinion in Anesthesiology, 24*(4), 408-413. doi: 10.1097/ACO.0b013e32834873e5

Rathmell, J. P., Lair, T. R., & Nauman, B. (2005). The role of intrathecal drugs in the treatment of acute pain. *Anesthesia & Analgesia, 101*(5S Suppl.), S30-S43. doi: 10.1213/01.ane.0000177101.99398.22

Rathmell, J. P., Pino, C. A., Taylor, R., Patrin, T., & Viani, B. A. (2003). Intrathecal morphine for postoperative analgesia: A randomized, controlled, dose ranging study after hip and knee arthroplasty. *Anesthesia & Analgesia, 97*(5), 1452-1457. doi: 10.1213/01.ANE.0000083374.44039.9E

Roden, D. M., & George, A. L. (2002). The genetic basis of variability in drug responses. *Nature Reviews Drug Discovery, 1*(1), 37-44. doi: 10.1038/nrd705

Sarvela, J., Halonen, P., Soikkeli, A., & Korttila, K. (2002). A double-blinded, randomized comparison of intrathecal and epidural morphine for elective cesarean delivery. *Anesthesia & Analgesia, 95*(2), 436-440. doi: 10.1213/01.ANE.0000019205.58614.20

Sharma, A., Chugh, Y., Kastury, N., & Kapoor, A. K. (2009). Management of itching. *Journal, Indian Academy of Clinical Medicine*. Retrieved July 26, 2012, from http://medind.nic.in/jac/jacm.shtml

Sheen, M. J., Ho, S. T., Lee, C. H., Tsung, Y. C., Chang, F. L., & Huang, S. T. (2008). Prophylactic mirtazapine reduces intrathecal morphine-induced pruritus. *British Journal of Anaesthesia, 101*(5), 711-715. doi: 10.1093/bja/aen241

Siddik-Sayyid, S. M., Yazbeck-Karam, V. G., Zahreddine, B. W., Adham, A. M. B. F., Dagher, C. M., Saasouh, W. A., & Aouad, M. T. (2010). Ondansetron is as effective

as diphenhydramine for treatment of morphine-induced pruritus after cesarean delivery. *ACTA Anaesthesiologica Scandinavica, 54*(6), 764-769. doi: 10.1111/j.1399-6576.2010.02231.x

Sinatra, R. S. (2009). Oral and parental opioid analgesics for acute pain mangement. In R. S. Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. 188-203). New York, NY: Cambridge University Press.

Sites, B. D., Beach, M., Gallagher, J. D., Jarrett, R. A., Sparks, M. B., & Lundberg, C. J. F. (2004). A single injection ultrasound-assisted femoral nerve block provides side effect-sparing analgesia when compared with intrathecal morphine in patients undergoing total knee arthroplasty. *Anesthesia & Analgesia, 99*(5), 1539-1543. doi: 10.1213/01.ANE.0000136470.51029.52

Smith, H. S. (2008). *Opioid therapy in the 21st century*. New York, NY: Oxford University Press.

Somogyi, A., Barratt, D., & Coller, J. (2007). Pharmacogenetics of opioids. *Discipline of Pharmacology & Therapeutics, 81*(3), 429-444. doi: 10.1038/sj.clpt.6100095

Sternbach, R. A. (1963). Congenital insensitivity to pain: A critique. *Psychological Bulletin, 60*(3), 252-264. doi: 10.1037/h0042959

Suchdev, P. K. (2002). Pathophysiology of pain. In C. A. Warfield & H. J. Fausett (Eds.), *Manual of pain management* (2nd ed., pp. 6-12). Philadelphia, PA: Lippincott Williams & Wilkins.

Szarvas, S., Harmon, D., & Murphy, D. (2003). Neuraxial opioid-induced pruritus. *Journal of Clinical Anesthesia, 15,* 234-239. doi: 10.1016/SO952-8180(03)00501-9

Tan, E.-C., Lim, E., Teo, Y.-Y., Lim, Y., Law, H., & Sia, A. (2009). Ethnicity and OPRM variant independently predict pain perception and patient-controlled analgesia usage for post-operative pain. *Molecular Pain, 5*(32), 1-8. doi: 10.1186/1744-8069-5-32

Tey, H. L., & Yosipovitch, G. (2010). Itch in Ethnic populations. *ACTA Anaesthesiologica Scandinavica, 90,* 227-234. doi: 10.2340/00015555-0867

Tollison, C. D., Satterthwaite, J. R., & Tollison, J. W. (Eds.). (2002). *Practical pain management* (3rd ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Toomey, M., & Biddle, C. (2006). Update for nurse anesthetists: Itching, the "little" big problem as an orphan symptom. *AANA Journal, 74*(5), 379-384.

Törn, K., Tuominen, M., Tarkkila, P., & Lindgren, L. (1994). Effects of sub-hypnotic doses of propofol on the side effects of intrathecal morphine. *The British Journal of Anaesthesia, 73*(3), 411-412.

Tran, M. L. (2002). Opioids. In C. A. Warfield & H. J. Fausett (Eds.), *Manual of pain management* (2nd ed., pp. 265-269). Philadelphia, PA: Lippincott Williams & Wilkins.

Trescot, A., Datta, S., Lee, M., & Hansen, H. (2008). Opioid pharmacology. *Pain Physician, 11*(2 Suppl.), S133-S153.

U.S. Department of Health and Human Services. (2012). Route of Administration. Retrieved August 4, 2012, from http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/DataStandardsManualmonographs/ucm071667.htm

Vadivelu, N., Whitney, C. J., & Sinatra, R. S. (2009). Pain pathways and acute pain processing. In R. S. Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. 3-20). New York, NY: Cambridge University Press.

Van Hulle Vincent, C., & Gaddy, E. (2009). Pediatric nurses' thinking in response to vignettes on administering analgesics. *Research in Nursing and Health, 32*(5), 530-539. doi: 10.1002/nur.20337

Wallace, M. S., & Staats, P. S. (2005). *Pain medicine and management: Just the facts*. New York, NY: McGraw Hill.

Wang, J. K., Nauss, L. A., & Thomas, J. E. (1979). Pain relief by intrathecally applied morphine in man. *Anesthesiology, 50*(2), 149-151.

Waxler, B., Dadabhoy, Z. P., Stojiljkovic, L., & Rabito, S. F. (2005). Primer of post operative pruritus for anesthesiologists. *Anesthesiology, 101*(6), 168-178.

Way, W. L., Fields, H. L., & Schumaker, M. A. (2004). *Opioid analgesics* (9th ed.). New York, NY: Lange Medical Books/McGraw-Hill.

Weiser, T. G., Regenbogen, S. E., Thompson, K. D., Haynes, A. B., Lipsitz, S. R., Berry, W. R., & Gawande, A. A. (2008). An estimation of the global volume of surgery: A modelling strategy based on available data. *The Lancet, 372*(9633), 139-144. doi: 10.1016/S0140-6736(08)60878-8

Wellington, J., & Chia, Y. Y. (2009). Pain variables influencing acute pain mangement. In R. S. Sinatra, O. A. de Leon-Casasola, B. Ginsberg & E. R. Viscusi (Eds.), *Acute pain management* (pp. 33-40). New York, NY: Cambridge University Press.

World Health Organization. (2012). Baby friendly hospital initiative. Retrieved December 2, 2012, from http://www.who.int/nutrition/topics/bfhi/en/

Yaksh, T. L. (1999). *Spinal drug delivery*. Amsterdam, Netherlands: Elsevier.

Zanger, U. M., Raimundo, S., & Eichelbaum, M. (2004). Cytochrome P450 2D6: Overview and update on pharmacology, genetics, biochemistry. *Naunyn-Schmiedebergs Archives of Pharmacology, 369*(1), 23-37. doi: 10.1007/s00210-003-0832-2