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THE EFFECT OF INTRAPERITONEAL LOCAL ANAESTHETIC IN COLONIC SURGERY

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*A thesis submitted in partial fulfilment of the requirements for the degree of
Doctor of Philosophy in Surgery, The University of Auckland, 2010.*

ABSTRACT

Millions of years of symbiosis between micro-organisms in the colon and the host have resulted in a unique neural system to detect adverse stimuli. The vagus nerve links the intraperitoneal cavity directly to the brainstem, hence bypassing somatic nerve blockade often utilised after major abdominal surgery. This thesis describes the intraperitoneal *autonomic wound* as a target for intervention after major abdominal surgery to accelerate recovery. Chapter One introduces the topic. Chapter Two focuses on events that lead to prolonged convalescence, and presents the hypothesis that the intraperitoneal *autonomic wound* is an important and potential target for interventions when the *somatic wound* is controlled. Current interventions are also reviewed. Chapter Three describes a systematic review on the use of intraperitoneal local anaesthetic (IPLA) in order to assess this clinical intervention. It will be shown that this intervention may lead to important clinical benefits. Chapter Four systematically reviews published data on the intravascular (systemic) level of drug after IPLA compared to other techniques. Chapter Five brings this information together in the form of a pilot study concerned with safety of concomitant IPLA and epidural anaesthesia infusions. A protocol was devised in order to infuse ropivacaine into the epidural and intraperitoneal space whilst monitoring safety. Chapter Six describes the methodology used to carry out a double-blinded placebo controlled randomised clinical trial infusing IPLA after colon resection within the context of an Enhanced Recovery after Surgery (ERAS) program (IPLA trial). In chapter Seven the results of the IPLA trial are presented. It will be seen that benefits of IPLA were observed, including improvement in functional recovery, reduced systemic markers of inflammation, reduced neuro-endocrine upset, and significantly reduced pain and opioid consumption over the epidural somatic blockade. Chapter Eight summarises these findings and makes the conclusion that it is possible to target the intraperitoneal wound in order to further enhance recovery after surgery. Chapter Nine draws a conclusion on the topic of this thesis.

DEDICATION

This thesis is dedicated to my entire family

To my parents Ehsan Kahokehr and Farideh Pouya

This work was possible because of your unconditional love, dedication, and commitment

I love you both

ستاره ای بدرخشید و ماه مجلس شد
دل رمیده ما را انیس و مونس شد

از دور ترین فاصله ها به هم رسدیم
و تا اوج بودن با همیم

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GLOSSARY

5-HT	5-hydroxytryptamine (serotonin)
AAG	Alpha-1-acid glycoprotein
AC	Arm circumference
ACTH	Adrenocorticotrophic hormone
AMED	Allied and Complementary Medicine Database
AMC	Arm muscle circumference
ASA	American Society of Anesthesiologists
CCTR	Cochrane Controlled Trials Registry
CCT	Clinical Controlled Trial
CI	Confidence interval
CINAHL	Cumulative Index of Nursing and Allied Health Literature
Cmax	Concentration maximum
CMDHB	Counties Manukau District Health Board
CNS	Central nervous system
CONSORT	Consolidated Standards of Reporting Trials
CVS	Cardiovascular system
DHB	District Health Board
DSMB	Data Safety Monitoring Board
DVT	Deep vein thrombosis
ELISA	Enzyme-linked immunosorbent assay
ERAS	Enhanced Recovery After Surgery
GC	Gas Chromatography
GI	Gastrointestinal
HDU	High dependency unit

ICFS	Identity Consequence Fatigue Scale
ICU	Intensive care unit
IDC	In-dwelling urinary catheter
IL-1 β	Interleukin 1 β
IL-6	Interleukin 6
IL-8	Interleukin 8
IL-10	Interleukin 10
IP	Intraperitoneal
IPLA	Intraperitoneal local anaesthetic
LA	Local anaesthetic
LC	Laparoscopic cholecystectomy
LOC	Locus coeruleus
MED	Mean Equivalent Dose
MRRC	Maaori Research Review Committee
MODS	Multiple organ dysfunction syndrome
MSC	Manukau Surgery Centre
NA	Noradrenaline
NOTES	Natural orifice transluminal endoscopic surgery
NTS	Nucleus tractus solitarius
PACU	Post anaesthetic care unit
PAG	Peri-aqueductal grey matter
PCA	Patient controlled opioid analgesia
PE	Pulmonary embolism
POF	Post operative fatigue
PONV	Postoperative nausea and vomiting
PubMed	Public/Publisher MEDLINE

QUORUM	Quality of reports of meta-analyses of randomised controlled trials
RCT	Randomised Controlled Trial
SD	Standard Deviation
SI	le Système international d'unités
SRS	Surgical Recovery Score
TAP	Transversus abdominis plane block
Tmax	Time to reach Cmax
TSF	Triceps skin fold
VAS	Visual analogue scale
TNF- α	Tumour Necrosis Factor- α