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THE EFFECT OF INTRAPERITONEAL LOCAL ANAESTHETIC IN COLONIC SURGERY

ARMAN KAHOKEHR

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 انين و مونس شد
از دور ترين فاصله ها به هم رسد يم
و تا اوج بودن با هميم
ACKNOWLEDGMENTS

This work simply could not have been completed without the mentorship, supervision and guidance of Associate Professor Andrew G. Hill. He inspired my introduction into the glittering world of academic surgery by bridging the gap between science and the patient. The valuable lessons I gained in this process will be with me forever and I am inexpressively grateful for this support. Thank you for everything.

Dr Mattias Soop co-supervised this work, provided advice and experience in the field of peri-operative care. I am extremely lucky to have had his expert eyes review this work.

Dr Tarik Sammour for contributing extremely valuable scientific input. But more importantly for his unconditional friendship. He guided me through challenges on a daily basis with sharp thinking, wit, dedication to surgical research, and clinical surgery. He inspires and I hope to learn from his shadow for many years to come.

Dr Emmanuelle Cognard for her ongoing patience, unfaltering companionship, and making sure that nothing was lost in translation. I am in debt to your gratitude.

Maria Vitas and her work at the South Auckland Clinical School. Thank you setting up the foundations from which clinical research can bud from. Her support and dedicated time made this research possible.

Dr Kamran Zargar Shoshtari for sharing his research experiences, teaching and supporting me to take on the challenges of academia. I look forward to our friendship in the years to come.
Ms Erica Natalie George who reflected thoughts and ideas and never asked for anything more. I will never forget our famous rants.

Mr Andrew Connolly and the Department of Surgery at Middlemore Hospital for his ongoing support on the clinical grounds on which this research took part.

Lisa Thompson for leading the nursing team at Manukau Surgery Centre and her enthusiastic involvement in clinical research and Enhanced Recovery Surgery.

Professor John Windsor and The Department of Surgery at The University of Auckland for encouraging me to take on the challenges offered by surgical research. I was lucky to have been a student at the Department of Surgery lead by him.

Drs Matthew Taylor and Francois Stapelberg for expert anaesthetic input and sharing their ideas.

Associate Professor Lindsay Plank for his teaching, advise, statistical and methodological expertise.

The surgical patients, who despite physical and emotional adverse impacts of illness, took part in research in order to improve the experience for others. Thank you for volunteering your bodies and minds.

Dr Rachel Helliwell at the Auckland Medical Research Foundation. This research was carried out during tenure of the Ruth Spencer Medical Fellowship and a supportive research grant was provided by the Auckland Medical Research Foundation. These supportive grants made this work a possibility.


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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>5-HT</td>
<td>5-hydroxytryptamine (serotonin)</td>
</tr>
<tr>
<td>AAG</td>
<td>Alpha-1-acid glycoprotein</td>
</tr>
<tr>
<td>AC</td>
<td>Arm circumference</td>
</tr>
<tr>
<td>ACTH</td>
<td>Adrenocorticotropic hormone</td>
</tr>
<tr>
<td>AMED</td>
<td>Allied and Complementary Medicine Database</td>
</tr>
<tr>
<td>AMC</td>
<td>Arm muscle circumference</td>
</tr>
<tr>
<td>ASA</td>
<td>American Society of Anesthesiologists</td>
</tr>
<tr>
<td>CCTR</td>
<td>Cochrane Controlled Trials Registry</td>
</tr>
<tr>
<td>CCT</td>
<td>Clinical Controlled Trial</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CINAHL</td>
<td>Cumulative Index of Nursing and Allied Health Literature</td>
</tr>
<tr>
<td>Cmax</td>
<td>Concentration maximum</td>
</tr>
<tr>
<td>CMDHB</td>
<td>Counties Manukau District Health Board</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
</tr>
<tr>
<td>CVS</td>
<td>Cardiovascular system</td>
</tr>
<tr>
<td>DHB</td>
<td>District Health Board</td>
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<tr>
<td>DSMB</td>
<td>Data Safety Monitoring Board</td>
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<tr>
<td>DVT</td>
<td>Deep vein thrombosis</td>
</tr>
<tr>
<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay</td>
</tr>
<tr>
<td>ERAS</td>
<td>Enhanced Recovery After Surgery</td>
</tr>
<tr>
<td>GC</td>
<td>Gas Chromatography</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>HDU</td>
<td>High dependency unit</td>
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</table>
ICFS  Identity Consequence Fatigue Scale
ICU  Intensive care unit
IDC  In-dwelling urinary catheter
IL-1β  Interleukin 1β
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 translumenal 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
<table>
<thead>
<tr>
<th>QUORUM</th>
<th>Quality of reports of meta-analyses of randomised controlled trials</th>
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<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SI</td>
<td>le Système international d'unités</td>
</tr>
<tr>
<td>SRS</td>
<td>Surgical Recovery Score</td>
</tr>
<tr>
<td>TAP</td>
<td>Transversus abdominis plane block</td>
</tr>
<tr>
<td>Tmax</td>
<td>Time to reach Cmax</td>
</tr>
<tr>
<td>TSF</td>
<td>Triceps skin fold</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Tumour Necrosis Factor-α</td>
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