

**The Efficacy of Local Anaesthetic
Infiltrated at the Incision Site for
Post-Operative Pain Management
Following Abdominal Surgery:
An Application to Fast-Track Surgery**

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DECLARATION

I, Sumithra Krishnan certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Date

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ABSTRACT

Post-operative pain is the most commonly encountered and therapeutically difficult problem on a surgical ward. Pain can be a preventable outcome of surgery but its treatment is inadequate for many patients, as 30-70 % of patients continue to suffer from pain post-operatively. Current pharmacological approaches used for pain management consist mainly of opioids, which cause serious adverse effects and may increase patient morbidity and prolong recovery. Therefore, this may be reduced with appropriately delivered local anaesthesia, as a favourable adjuvant.

The aim of this study was to test whether a continuous 96 hour infusion of the local anaesthetic, levobupivacaine, using a commercial infiltration device (Painbuster[®], IFlow Corp, USA), delivered into the deeper muscle layers where pain fibres penetrate, can minimise or eliminate the need for opioid analgesia following laparoscopic or open abdominal surgery. The novel aspects of the study include the higher dosage of the local anaesthetic, the longer duration of infusion, and the location of the catheter in the deeper tissue layers aimed at maximising response, all as part of a fast-track surgery approach.

Patients scheduled for laparoscopic or open abdominal surgery who consented into this randomised double-blinded placebo-controlled trial, were allocated (2:1) to receive either the active drug (0.5% levobupivacaine infusion) or placebo (0.9% saline infusion) in the Painbuster[®]. Blood samples were collected over the 96 hr infusion period in order to measure the total plasma levobupivacaine concentration and patients were placed under a fast-track surgery protocol intended to enhance recovery. Patients had available opioids via a patient-controlled-analgesia system for break-through pain. Pain scores and total opioid consumption were used as an index of efficacy.

Eighty-one patients were recruited in the study: laparoscopic active (n=31); laparoscopic placebo (n=20); open active (n=24) and open placebo (n=6). The four treatment groups were well controlled for age, body mass index and gender. There was a trend towards lower opioid consumption and pain scores in the open active group compared to the open placebo group, however, paradoxically the

laparoscopic active group had higher opioid consumption and pain levels than the laparoscopic placebo group at particular time-points, which may be influenced by the presence of stomas, drains and gender differences. Although a significant difference in length of hospitalisation was evident between laparoscopic and open cases (laparoscopic- 6.5 days; open- 9.8 days, $p= 0.003$), the active treatment was not associated with an earlier time of bowel movement and mobilisation nor reduction in hospitalisation. The mean patient total plasma levobupivacaine concentrations were below the toxicity threshold, but need to be interpreted in the light of increased protein binding (to AAG) post-operatively, as total concentrations may over-estimate the risk of toxicity.

These findings suggest that a 96 hr continuous local anaesthetic infusion post abdominal surgery may be a favourable method of pain control in patients undergoing open surgery. This could be due to the well located catheter, the increased local anaesthetic concentration and a longer post-operative infusion period.

PUBLICATIONS AND PRESENTATIONS DURING CANDIDATURE

Publications

Krishnan S, Tou S, Hewett P, Karatassas A, Field J, Morris R. Continuous local anaesthetic infusion in open and laparoscopic colorectal surgery: a double blind randomised study. For submission to the Aust NZ J Surg, Manuscript in Preparation.

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Awards

Best Poster Presentation Winner, TQEH Research Day, Oct 2010, Adelaide, Australia.

LIST OF ABBREVIATIONS

AAG	Alpha1-acid glycoprotein
ACTH	Adrenocorticotropic hormone
APS	Acute Pain Services
BMI	Body Mass Index
Cb	Bound drug concentration
CCK	Cholecystokinin
CGRP	Calcitonin gene-related peptide
Cl_{int}	Intrinsic clearance
CONSORT	Consolidated Standards of Reporting Trials
Ct	Total drug concentration
Cu	Unbound drug concentration
DOSA	Day of Surgery Admission
FDA	Food and Drug Administration
Fu	Unbound Fraction
Fu%	Fraction unbound (as a percentage)
HAL	Hand Assisted Laparoscopy
HPLC	High Performance Liquid Chromatography
ICU	Intensive Care Unit
IV	Intravenous
LA	Laparoscopic Active
LLOQ	Lower Limit of Quantification
LP	Laparoscopic Placebo
NMDA	N-Methyl-D-aspartic acid
NSAID	Non-Steroidal Anti-Inflammatory Drug
OA	Open Active

OP	Open Placebo
PAC	Pre-Admission Clinic
PCA	Patient Controlled Analgesia
PCEA	Patient Controlled Epidural Analgesia
PCOA	Patient Controlled Oral Analgesia
PHR	Peak Height Ratio
PROSPECT	PROcedure SPECific postoperative pain management
QC	Quality Control
TQEH	The Queen Elizabeth Hospital
Tmax	Time to peak concentration
VAS	Visual Analogue Scale
VNRS	Verbal Numerical Rating Scale