Opioid Free General Anesthesia for Laparoscopic Bariatric Surgery

Thesis

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List of Abbreviations

ABG	:	Arterial blood gases
APVR	:	Abdominal Pressure insufflated Volume Relation
AR	:	Adrenergic receptor
BIS	:	Bispectral index
BMI	:	Body mass index
CNS	:	Central nervous system
CNS	:	Central nervous system
CO_2	:	Carbon dioxide
CPAP	:	Continuous positive airway pressure
CPAP	:	Positive airway pressure
EEG	:	Electroencephalogram
ERAS	:	Enhanced recovery after surgery
FRC	:	Functional residual capacity
FRC	:	Functional residual capacity
FRC	:	Functional residual capacity
FVC	:	Forced vital capacity
HR	:	Heart rate
IAP	:	Intra abdominal pressure
IAV	:	Intra abdominal volume
ICP	:	Intra-cerebral pressure

List of Abbreviations (Cont.)

LBW	:	Lean body weight
NMDA	:	N-Methyl-D-Aspartate
NSAIDs	:	Nonsteroidal anti-inflammatory drugs
OHS	:	Obesity hypoventilation syndrome
OSA	:	Obstructive sleep apnoea
$PaCO_2$	:	Partial pressure of arterial CO_2
PCA	:	Patient-controlled analgesia
PEEP	:	Positive end-expiratory pressure
RBF	:	Renal blood flow
RV	:	Residual volume
SD	:	Standard deviation
SPSS	:	Statistical Program for Social Science
TOF	:	Train of four
VAS	:	Visual analog scale
X^2	:	Chi-square

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Introduction

Obesity is a significant health problem with clearly established health implications. Both in developed and underdeveloped countries the total number of obese people and their fraction of the population are increasing. The World Health Organization has declared obesity as the epidemic of the twenty-first century ***(Johan, 2012).***

The body mass index (BMI), calculated as the weight in kilograms divided by the height in meters squared, has been used in clinical and epidemiological studies as a predictor of health risk. A BMI of 25 Kg/m2 is considered normal, >30 Kg/m2 obese, >35 Kg/m2 morbidly obese and >55 Kg/m2 super morbidly obese ***(Ukleja and Stone, 2004).***

Obesity is usually associated with increased risk for coronary artery disease, hypertension, dyslipidemia, diabetes mellitus, gallbladder disease, degenerative joint disease, obstructive sleep apnea and psychosocial impairment ***(Feld et al., 2006).***

The need for bariatric surgery is rapidly increasing and the concept of fast-track surgery and laparoscopy have made bariatric surgery a cost-effective and efficient way of treating the morbidly obese when other non-surgical options have been unsuccessful ***(Adams and Murphy, 2000).***

Bariatric surgery is effective in reducing obesity related co-morbidities as well as achieving major long-term weight loss and improvement in quality of life. Compared with conservative management, bariatric surgery leads to a 29% reduction in the long-term risk of death. Bariatric surgical techniques are divided into three groups: restrictive procedures, pure malabsorptive procedures, and mixed restrictive/ malabsorptive procedures (Roux-en-Y gastric bypass) ***(Sjostrom et al., 2007).***

Opioids given intra-operatively as well as post-operatively could play a significant part in postoperative pulmonary morbidity. On one side, postoperative pain ranges from mild to moderate and lasts for a short period of less than 24 h in laparoscopic surgery. On the other side, opioids may not be highly effective in alleviating such pain without causing much sedation, and impending rapid recovery and early mobilization ***(Feld et al., 2006).***

It has been recommended that opioid drugs have to be avoided for analgesia in the morbidly obese patient because of the risk of respiratory depression. This requires that alternative drugs be used in place of opioids to provide analgesia during surgery. Several drugs, including clonidine, ketamine, magnesium, lidocaine, ketorolac, and steroids have all been shown to be analgesic. Combining these drugs may potentiate analgesia by separate actions and decrease the risk of

side effects by lowering the effective dose for each agent ***(Liu et al., 2001).***

Opioid free anesthesia (OFA) is a method to optimize enhanced recovery after surgery (ERAS). Enhanced recovery after surgery (ERAS) protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining preoperative organ function and reducing the profound stress response following surgery. The key elements of ERAS protocols include preoperative counselling, optimization of nutrition, standardized analgesic, anesthetic regimens and early mobilization ***(Wilmore and Kehlet, 2001).***

Aim of the work

The purpose of this study is to evaluate the efficacy and safety of giving general anesthesia without the use of any opioids either systemic or intraperitoneal in bariatric surgery.

Physiology and Pharmacology

Magnesium Sulfate

Physiology and Pharmacology

About 50% of body Mg stores are in bone; 46% exist as intracellular cations; and 1% are in the extracellular fluid. One fifth of intracellular Mg is localized within the skeletal muscle. Normal serum Mg ranges from 1.5mg/dl to 2.0mg/dl, where about 20% is protein bound and the remainder exists as free or complexes ***(Lowenthal, 1988).***

Mg is the fourth most common cation in the body, it has a fundamental role as a co-factor in more than 300 enzymatic reactions involving energy metabolism; nucleic acid synthesis, gating of ca channels; muscle contraction; neuronal activity; cardiac excitability; muscle contraction and transmembrane ion flux ***(Altura, 1994).***

Approximately 2 grams of Mg are filtered daily by the kidney and 100 milligrams excreted in the urine. Therefore 95% of the filtered load of Mg is reabsorbed by the kidney and 5% is excreted in the urine. Reabsorption of Mg occurs by both an active and a passive mechanism. When Mg deficiency exists, the kidney can compensate by reducing the amount of Mg excreted in the urine to less than 0.5% of the filtered load. Conversely, during states of hypermagnesemia such as Mg infusion, the kidney can excrete 40% to 70% of the filtered load of Mg ***(Slatopolsky and Klah, 1998).***

• Pharmacokinetics

When MgSO4 is administered IV, the onset of action is immediate and the duration of action is about 30 minutes. Following IM administration of the drug, the onset of action occurs in about 1 hour and the duration of action is 3 to 4 hours. Mg sulfate crosses the placenta and distributes into breast milk following parenteral administration. MgSo4 is excreted by the kidneys at a rate that is directly proportional to its serum concentration and glomerular filtration rate ***(Lu and Nightingale, 2000).***

• Pharmacodynamics

Magnesium and perioperative analgesia:

NMDA receptors play a major role in central nocioceptive transmission, modulation and sensitization of acute pain states. In addition to their central location, previous studies identified NMDA receptors peripherally in the skin, muscles and joints that play a role in sensory transmission of noxious signals and their activation were found to potentially play a role in nociception ***(Woolf, 1995).***

Many authors have studied the antinociceptive effects of Mg when used an adjuvant to more conventional analgesics in the perioperative period ***(Herroeder et al., 2011).***

There are two possible mechanisms of Mg as an adjuvant for perioperative analgesia: The 1st theory

includes the action of Mg as Ca channel blocker. The analgesic action of some calcium channel blockers could be mediated by an increase of the nociceptive threshold resulting from interference with calcium influx and the subsequent release of excitatory neurotransmitters implicated in nociception and inflammatory response. The 2nd theory includes inhibition of NMDA receptors which are amino acid receptors responsible for excitatory synaptic transmission that can be inhibited by ketamine and Mg. These NMDA receptors antagonists can prevent the induction of central sensitization due to peripheral nociceptive stimulation. It has been suggested that NMDA antagonism could play a role in prevention and treatment of established pain states by blocking dorsal horn NMDA receptors activation induced by excitatory amino acid transmitters, such as glutamate and aspartate ***(Pockett, 1995).***

Furtheremore, NMDA antagonists have a peripheral antinociceptive effect through their analgesic and anti-inflammatory effect. NMDA antagonists reduce the excitability of nociceptive input terminals of C-fibers, which play a role in the central processing of pain. The anti-inflammatory action of NMDA antagonists in the peripheral tissues occurs through antagonizing the release of inflammatory mediators such as histamine, cytokines and serotonin, which excite the nociceptors ***(Liu et al., 2001).***

Many studies results showed that the perioperative application of IV MgSO4 was associated with less analgesic requirement, less patient discomfort and a better quality of sleep in the postoperative period without any adverse effects ***(Tramer et al., 1996).***