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The Role of Magnesium Sulfate in the Analgesic Requirements in Bariatric Surgery

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا

إلا ما علمتنا إنك أنت

العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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Maha Salah Omar

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List of Abbreviations

Abbrev.	Full-term
AF	: Atrial fibrillation
AMI	: Acute myocardial infarction
ATP	: Adenosine triphosphate
BBB	: Blood brain barrier
BMI	: Body mass index
CBC	: Complete blood count
CGRP	: Calcitonin gene-related peptide
CNS	: Central nervous system
COPD	: Chronic obstructive pulmonary disease
CPAP	: Continuous positive airway pressure
CPAP	: Positive airway pressure
DM	: Diabetes mellitus
ECG	: Electrocardiogram
ECT	: Electroconvulsive therapy
EDRF	: Endothelium-derived relaxing factor
FEV1	: Forced expiratory volume one
FRC	: Functional residual capacity
FVC	: Forced vital capacity
IM	: Intramuscular
IV	: Intravenous
KFT	: Kidney function tests
LFT	: Liver function tests

LBW	: Lean body weight
NSAIDs	: Nonsteroidal anti-inflammatory drugs
MAP	: Mean arterial blood pressure
Mg	: Magnesium
MV	: Minute ventilation
NMDA	: N-Methyl-D-aspartate
OSA	: Obstructive sleep apnea
PT	: Prothrombin time
PTT	: Partial thromboplastin time
PCA	: Patient-controlled analgesia
PEFR	: Peak expiratory flow rate
PEEP	: Positive end-expiratory pressure
RBS	: Random blood sugar
RV	: Residual volume
SAH	: Subarachnoid Hemorrhage
SIMV	: Synchronized intermittent mandatory ventilation
TEG	: Thromboelastography
TDP	: Torsades de pointes
TIH	: Tourniquet induced hypertension
TBI	: Traumatic brain injury
TIVA	: Total intravenous anesthesia
U.S	: United States of America
VAS	: Visual analog scale
Vd	: Volume of distribution
VT	: Tidal volume

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Abstract

Background: The need for bariatric surgery is rapidly increasing and the concept of laparoscopy have made bariatric surgery a cost-effective and efficient way of treating the morbidly obese when other non-surgical options have been unsuccessful. 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. Laparoscopic approach has emerged as a popular alternative to traditional open abdominal surgery as it combines the benefits of less post-operative pain and ileus and less deterioration of postoperative respiratory functions with subsequent shorter postoperative hospital stay and rapid return to normal activities. However, laparoscopic surgeries are associated with hemodynamic, ventilatory and neuroendocrinal changes which result from the combined effects of pneumoperitoneum, hypercapnia secondary to CO_2 absorption, anesthesia technique and patient position. **Aim of the Work:** This study was performed to evaluate the effect of intravenous magnesium on intra-operative and post-operative narcotic requirements and the incidence of postoperative need for mechanical ventilation in bariatric surgeries. **Patients and Methods:** This randomized clinical study was conducted on 48 adult patients scheduled for elective laparoscopic gastric sleeve operations under general anesthesia in **Ain Shams University Hospitals;** after obtaining approval of research ethical committee and patients' written informed consents, Patients were divided into two equal groups 24 patients per group, both groups received Nalbuphen 0.2 mg/kg in induction & Nalbuphen infusion in the rate of 2 mg/hr for 24 hrs postoperative, group (M) recieved intravenous magnesium sulphate on the dose of 50 mg/ kg in 250 ml of isotonic sodium chloride solution 0.9% after induction & Magnesium sulfate infusion as a total dose of 50 mg/kg given over 24 hrs postoperative. **Results:** results showed that MAP, VAS and CO2 level were significantly less in Mg group than control group & There were no statistically significant differences between the 2 groups as regard demographic data and heart rate **Conclusion:** It can be concluded that MgSO4 could be a useful adjuvant to general anesthesia in laparoscopic gastric sleeve surgeries, since this molecule is inexpensive, relatively harmless and enables anesthesiologists to avoid the hypoventilation effect of large doses of opioids that may be used in bariatric patients. Also the biological basis for its anesthesia promoting ant-nociceptive and hypotensive effects is promising. **Recommendations:** Large scale further studies will definitely help to elucidate its role in the field of anesthesia.

Key words: magnesium sulfate, analgesics, bariatric surgery, narcotics, postoperative mechanical ventilation

Introduction

Over 65% of the U.S adult population is overweight or obese, defined by a Body Mass Index (BMI) $\geq$ 25 kg/m^2 or $\geq$ 30 kg/m^2, respectively. Bariatric surgery is usually performed in patients with a BMI $\geq$ 40 kg/m^2, or a BMI $\geq$ 30 kg/m^2 with comorbidities that are expected to respond to weight loss (i.e. hypertension, diabetes). Obese patients, undergoing bariatric or other surgical procedures, present an increased anesthetic risk because of physiologic changes, comorbidities and technical challenges ***(Flegal & Carroll, 2010).***

Opioids are commonly used for bariatric surgery for pain control because of their potent analgesic effects. Nevertheless, the morbidly obese patient has increased risk for developing adverse effects produced by opioids (such as sedation, apnea, hypoxemia, ileus, and vomiting) ***(Begon & pickering, 2002).***

Postoperative morbidity is increased in obese patients but increased mortality is controversial. The most Common postoperative complications are respiratory. Narcotic-based analgesia may be challenging because of the increased risk of hypoventilation and hypoxemia in obese patients ***(Nafiu et al., 2011).***

Magnesium sulfate has been used in preeclampsia patients in order to prevent seizure. It is also used for the treatment of arrhythmia and asthma and as an anesthetic adjunct in patients undergoing surgery for pheochromocytoma. However, its potentiating effects on perioperative analgesia and muscle relaxation have drawn attention recently. These characteristics of magnesium (anesthetic- and analgesic-sparing effect) enable anesthesiologists to reduce the use of anesthetics during surgery and the use of analgesics after surgery. Magnesium sulfate has a high therapeutic index and cost-effectiveness. Considering these diverse characteristics useful for anesthesia, appropriate use of magnesium sulfate would improve surgical outcome and patients' satisfaction ***(Sang-Hwan Do, 2013).***

The magnesium ion was the first agent discovered to be an NMDA channel blocker. At very high doses, perioperative intravenous magnesium sulfate has been reported to reduce postoperative morphine consumption ***(Asokumar et al., 2009).***

As regards its analgesic effect, although magnesium has been used successfully to potentiate opioid analgesia and in treating neuropathic pain in experimental studies, clinical trials investigating the analgesic efficacy of magnesium have shown conflicting results ***(Seyhan et al., 2013).***

Mechanism of analgesic effect of magnesium sulphate is not clear but inhibition of calcium channels and NMDA receptors seem to play an important role. Woolf et al 1995 studied the dependence of the central sensitisation on NMDA receptor activation in rats and found that NMDA receptor activation is involved in the induction and maintenance of central sensitization processes that characterize post injury pain states. Therefore, NMDA receptor antagonist may play a role in prevention and treatment of perioperative pain ***(Kiran et al., 2011).***

Aim of the Work

This study will be performed to evaluate the effect of intravenous magnesium on intra-operative and post-operative narcotic requirements and the incidence of postoperative mechanical ventilation in bariatric surgeries.

Magnesium: Physiology and Pharmacology

Magnesium is a bivalent ion, with an atomic weight of 24.312. It is the fourth most common mineral salt in humans after phosphorus, calcium and potassium, the second intracellular cation after potassium and the fourth plasma cation after sodium, potassium and calcium ***(Fawcett et al., 1999).***

It is found mainly in the intracellular compartment (99%) and the remaining 1% is in extracellular compartment ***(Navarro-Gonzalez, 1998).*** The normal Serum Mg level is (0.7–1.1 mmol/l or 1.4–2.2mEq/l, or 1.6–2.6 mg/dl). It is divided into three fractions: free (active form), protein-bounded (mainly to albumin) and that contained in anion complexes (phosphates and citrates). These fractions account respectively for 60, 30 and 10% of serum content. Intracellular Mg is existing largely (90%) in bound form in adenosine triphosphate (ATP), in nucleotides, or in enzyme complexes ***(Sanders et al., 1999).***

The daily recommended Mg requirement is 250 to 350 mg in adults with an additional 100 to 150 mg in children, pregnant or nursing women ***(Dacey, 2001).*** Magnesium absorption occurs principally from the ileum and colon. Phytates and oxalates reduce Mg absorption through the formation of a complex that cannot be dissociated ***(Sanders et al., 1999).***

In the kidneys (figure 1), 80% of plasma Mg is ultrafiltered through the glomerulus, with more than 95% being reabsorbed by the consecutive segments of the nephron. The predominant site is the thick ascending limb of the loop of Henle (70%), with the proximal and distal convoluted tubule accounting for 20% and 0-10% of reabsorption, respectively ***(Herroeder et al., 2011).***

Several hormones are involved in the regulation of Mg metabolism, namely parathyroid hormone and vitamin D which stimulate Mg renal and intestinal reabsorption respectively; insulin decreases renal excretion of Mg and enhances its cellular uptake while aldosterone increases its renal excretion ***(Saris et al., 2000).***

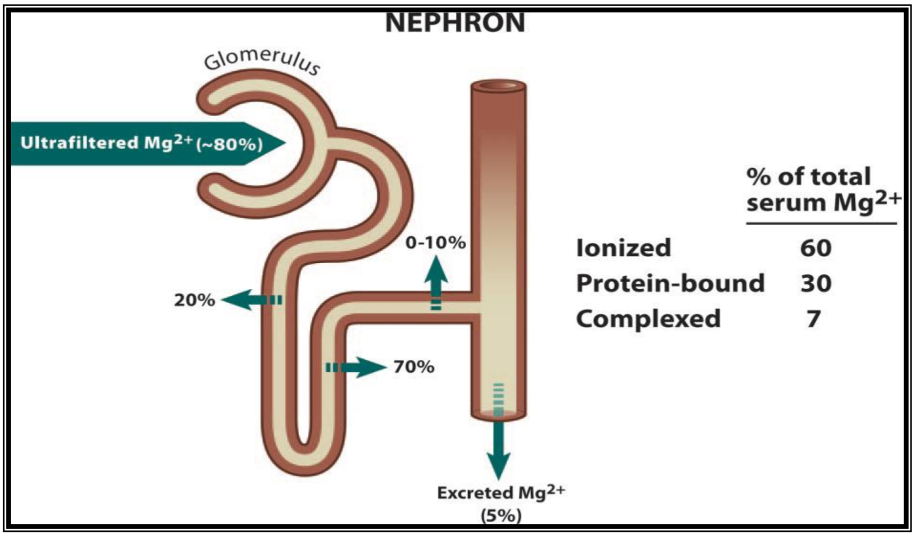

Figure (1): Renal handling of magnesium ***(Herroeder et al., 2011).***