The Use of Magnesium Sulphate in Peridural Anesthesia (spinal, epidural and combined)

Thesis

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First of all thanks to "Allah"

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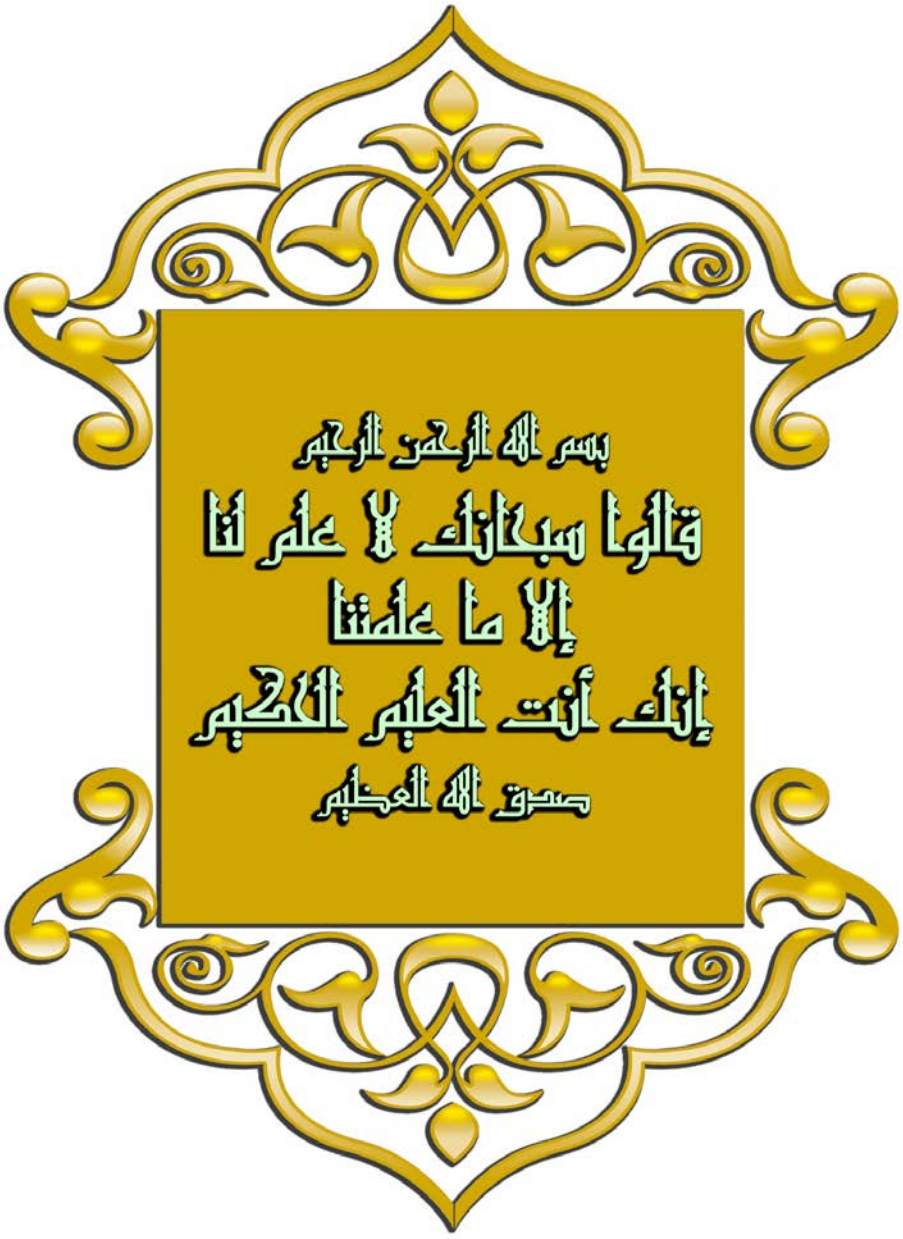
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صدق الله العظيم

List of Abbreviations

Abbrev.	Meaning
AMI	Acute myocardial infarction
AMP	Adenosine monophosphate
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate
ASA	American society of anaesthesiologist
ATP	Adenosine triphosphate
AV	Atrio-ventricular
BBB	Blood brain barrier
BPM	Beats per minute
BTS	British Thoracic Society
CABG	Coronary artery bypass graft
CNS	Central nervous system
COX	Cyclooxygenase
CPB	Cardiopulmonary bypass surgery
CSF	Cerebrospinal fluid
GABA	Gama aminobutyric acid
GMP	Guanosin monophosphate
i.v.	Intravenous
ICU	Intensive care units
IL	Interleukins
LOX	Lipooxygenase
MAP	Mean arterial blood pressure
MBS	Modified Bromage Score
$MgSO_4$	Magnesium sulfate
MLC	Myosin light chain
Mu-OR	Mu-opioid receptors
NGF	Nerve growth factor
NMDA	N-methyl-d-aspartate
nNOS	Nitric oxide synthase
NS	Nociceptive specific neurons
PABA	Para-amino butyric acid
PCEA	Patient controlled epidural analgesia
PKA	Protein kinase A
PKC	Protein kinase C
PLC	Phospholipase C
PNS	Peripheral nervous system
SIGN	Scottish Intercollegiate Guidelines Network
SN	Sinus nodal
SP	Substance P

Introduction

Regional anesthesia techniques are widely used for lower extremity orthopedic surgery and offer several benefits compared to general anesthesia. One of the most important issues is the ability to provide extended post operative pain control that is superior to that provided by systemic opioids alone ***(Doty & Sukhani, 2006).*** Regional anesthesia is a safe, effective and cheap anesthesia over general anesthesia ***(Bali et al., 2007).***

Spinal and epidural techniques have been the standard regionl techniques for major lower extremity orthopedic surgery over the last two decades. However combined spinal epidural anesthesia has evolved as an ideal technique for these procedures ***(Wong, 2006).*** It combines the rapid onset and intensity of spinal blockade with the use of minimal dose of local anesthetics for a shorter duration, and the flexibility of epidural intra- operative reinforcement if necessary and postoperative epidural analgesia ***(Bali et al., 2007).***

The majority for lower extremity orthopedic surgery are the elderly and many have multiple coexisting medical conditions. Ensuring haemodynamic stability in these patients requires selection of the appropriate technique with a focus on maintaining a safe and desirable level of blockade, and limiting extensive sympathectomy ***(Wong, 2006).***

Polypharmacological approach is the most common practice as regarding regional anesthesia, as no single agent has yet been identified to spescifically inhibit nociception without associated side effects ***(Edmund et al., 2002).***

Opioids such as fentanyl is commonly added to local anesthetics to produce spinal and epidural anesthesia. However, significant side effects such as pruritis, respiratory depression, haemodynamic instability and occasionally sever nausea and vomiting may limit their use ***(El Kerdawy, 2008).***

Non-competitive N-methyl D-aspartate NMDA receptor antagonists can have an effect on pain when used alone, but it has also been shown that they can reveal the analgesic properties of opioids ***(Begon et al., 2002).***

Magnesium is the fourth most abundant cation in the body and the second most abundant intracellular cation. It has numerous physiological activities including antinociceptive effects in animal and human pain models ***(Lee et al., 2007).*** These effects are primarily based on the regulation of calcium influx into the cell, natural physiologic calcium antagonism ***(Iseri & French, 1984)*** and antagonism of NMDA receptors ***(Ascher & Nowak, 1987).***

Whatever the route of administration intravenous, intrathecal or epidural, the true site of action of magnesium is propably at the spinal cord NMDA receptors. However

intravenous magnesium for modulation of antinociception via NMDA receptor antagonism has insufficient blood-brain barrier penetration to achieve effective CSF concentrations ***(Ko et al., 2001).***

Intrathecal and epidural magnesium can provide a low-cost, simple change in clinical anesthesiology practice leading to significant decrease in patient's peri-operative analgesic needs and their safety has been evaluated in animal ***(Begon et al., 2002)*** and human ***(Bilir et al., 2007)*** studies that concluded that magnesium seems to have a good safety profile with no serious side effects.

Some clinical studies proved the effective analgesic property of magnesium as an adjuvant to intrathecal opioids prolonging the duration and thus improving the quality of spinal anesthesia ***(Ozaleli et al., 2005).***

Other clinical study proved that using epidural magnesium reduces post-operative analgesic requirements ***(Bilir et al., 2007).***

Aim of the Work

The aim of this study is to evaluate in a systematic approach the exact effects of magnesium sulphate when added to the commonly used protocols for spinal, epidural and combined spinal - epidural blocks used in Ain Shams University hospitals for lower extremity orthopedic surgery.

Pharmacology of Local Anaesthetics

Chemistry:

Local anaesthetic agents have a similar molecular configuration consisting of a lipophilic aromatic ring connected to a hydrophilic amine group (Fig. 1). The linking chain may be used to classify the agents as an ester, amide, ketone or ether ***(Sudoh et al., 2003).***

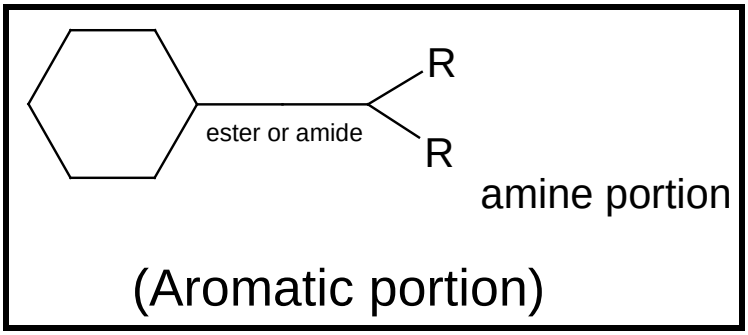

Figure (1): Chemical structure of local anaesthetic agents ***(Whiteside and Wildsmith, 2000).***

Ester local anaesthetics include cocaine, procaine, 2-chloroprocaine, tetracaine and benzocaine ***(McLure and Rubin, 2005).*** Apart from cocaine, which is a naturally occurring compound, ester drugs result from the combination of para-aminobenzoic acid and amino-alcohol. The esters tend to be unstable in solution and clinically they only diffuse poorly through tissues. They are hydrolyzed by plasma cholinesterase and their duration is increased in patients with absent, low or atypical plasma cholinesterase. They are metabolized to para-aminobenzoic acid (PABA) which may cause allergic reactions