

Recent Advances in Perioperative Magnesium Sulphate

Essay

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(... رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ
وَأَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ وَأُدْخِلْنِي
بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ)

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List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations	i
List of Tables	iv
List of Figures.....	v
Introduction	1
Aim of the Work.....	4
Chapter (1): Magnesium Physiology	5
Chapter (2): Dysmagnesemia.....	16
Chapter (3): Therapeutic uses of Mg sulphate in Anesthesiology	44
Chapter (4): Therapeutic Uses of Magnesium Sulphate in ICU	64
Summary	80
References	83
Arabic Summary	—

List of Abbreviations

ACOG	: American college of obstetricians and Gyneecologists
ADP	: Adenosine diphosphate
AF	: Atrial fibrillation
AQP4	: Aquaporin 4
ASH	: Aneurismal subarachinoid hemorrhage
ATN	: Acute tubular necrosis
ATP	: Adenosine triphosphate
AV	: Atrioventricular
AMI	: Acute myocardial infarction
AAS	: Atomic absorbance spectrophotometry
BUN	: Blood urea nitrogen
BP	: Blood pressure
Ca	: Calcium
CaSR	: Calcium sensing receptor
CABG	: Coronary artery bypasses grafting
CLDN 16	: Claudin 16
CBS	: Classic Bartter syndrome
CNS	: Central nervous system
CPB	: Cardiopulmonary bypass
CPK	: Creatinephoskinase
CVS	: Cardiovascular system
CP	: Cerebral pulsy
CA	: Cardiopulmonary arrest
DCT	: Distal convoluted tubule
DM	: Diabetes mellitus
DCI	: Delayed cerebral ischaemia

ECG	: Eletrocardiography
FESS	: Functional endoscopic sinus surgery
FHHNC	: Familial hypomagnesaemia with hypercalciuria and nephrocalcinosis
GFR	: Glomerular filtration rate
GI	: Gastrointestinal
GS	: Gitleman's syndrome
GINA	: Global Initiative for asthma
HR	: Heart rate
IDH	: Isolated dominant hypomagnesaemia
IRH	: Isolated recessive hypomagnesaemia
IV	: Intravenous
IVRA	: Intravenous regional anesthesia
ICU	: Intensive care unit
IL6	: Interieukin 6
JET	: Junctional ectopic tachycardia
K	: Potassium
LQTS	: Long QT syndrome
Mg	: Magnesium
Mn	: Manganese
Mg CL2	: Magnesium chloride
Mg So4	: Magnesium sulphate
MAC	: Mimmal alveolar concentration
MMP 1	: Matrix metalloproteinase 1
NMDA	: N-methyl-D-aspartate
NMBAS	: Neuromuscular blocking agents
NO	: Nitric oxide
PTH	: Parathyroid hormone
PCC	: Pheochromocytoma
SNAP	: Score of neonatal acute physiology

ROSC	: Return of spontaneous circulation
TAL	: Thick ascending loop of Henele
TEG	: Thrompoelastography
Tmax	: Maximum tubular reabsorption rate
TRP	: Transient Receptor potential
TDP	: Torsades de points
TIVA	: Total intravenous Anesthesia
VOCC	: Voltage operated calcium channels
VF	: Ventricular fibrillation
VT	: Ventricular tachycardia

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Causes of hypomagnesemia	25
Table (2):	Signs and symptoms of hypomagnesaemia:	29
Table (3):	Renal magnesium retention test:	31
Table (4):	Oral and Parenteral Magnesium Preparations:.....	33
Table (5):	Regimens parenteral Mg replacement	34

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Effect of Magnesium Sullphate on Cerebral Oedema and the Blood Brain Barrier	49
Figure (2):	Anticonvulsant Activity of Magnesium Sulphate.....	50
Figure (3):	Vascular Effects of Magnesium Sulphate.....	51
Figure (4):	ECG of Junctional Ectopic Tachycardia.....	56
Figure (5):	ECG of normal sinus rhythm	69
Figure (6):	ECG of Ventricular Fibrillation	69
Figure (7):	ECG of Torsades De Pointes	71

Introduction

Magnesium ions are essential to all living cells. As the second most abundant intracellular cation, magnesium has a crucial role in fundamental metabolic processes such as DNA and protein synthesis, oxidative phosphorylation, enzyme function, ion channel regulation, and neuromuscular excitability (*Naderi et al., 2008*).

Magnesium ions are involved as a cofactor in about 300 known enzymatic reactions in the body and in several important processes such as hormone receptor binding, gating of calcium channel, transmembrane ion flux, regulation of the adenylyl cyclase system, neuronal activity, vasomotor tone, cardiac excitability and neurotransmitter release (*Schulz-Stubner et al., 2001*).

In 1950, magnesium was used in anesthesia mainly to control seizures in gravidas (*Schutz-Stubner et al., 2001*). In the last years, the use of magnesium sulphate has been increasing to include situations out of the gynaecological field. It has been used as a pharmacological agent in a variety of clinical situations such as tachyarrhythmia, myocardial and neuronal ischemia, and asthma (*Tramer et al., 1996*).

Magnesium sulphate has been used in the treatment of serious arrhythmias during anesthesia. These may include arrhythmias associated with adrenaline administration, bupivacaine

induced, hypokalaemia, myocardial infarction and digitalis toxicity (**James et al., 1992**).

It is also used for cerebral protection through reduction in the presynaptic release of excitatory neurotransmitter, blockade of calcium channels and an increase in the cerebral blood flow (**Dohi et al., 2005**).

Analgesic and anti-nociceptive properties of magnesium ions have been investigated based on their specified central and peripheral Nmethyl-D-aspartate (NMDA) antagonism (**Tramer et al., 2002**). 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**).

The administration of a bolus of magnesium immediately after spinal anesthesia in elderly patients and starting the infusion as well prevent lowering the arterial blood pressure as prolonged and severe hypotension carries a risk of significant morbidity and mortality in these patients (**Martin et al., 2009**).

Intravenous magnesium sulphate infusion helps to control the rigidity and mild spasms in tetanus. Attygalle et al had stated that the dose of magnesium required in the very severe form of tetanus may have unacceptable cardiovascular side effects (*Attygalle et al., 2002*).

Intraoperative magnesium administration significantly reduced muscle relaxant and opioid requirements; more importantly, it also reduced postoperative pain and opioid use (*Oguzhan et al., 2008*).

Aim of the Work

The aim of this work is to identify applications of magnesium sulphate in anesthesia as its indications have been increasing over the last years.

Chapter (1)

Magnesium Physiology

Mg in the organism:

Magnesium (Mg) is a bivalent ion; the human body contains one mole (24 g) of Mg. It is the fourth most common mineral salt in the organism after phosphorus, calcium and potassium, the second intracellular cation after potassium, and the fourth plasma cation after sodium, potassium and calcium. Extracellular Mg represents only 1% of the total (*Saris et al., 2000*).

Requirements & Absorption:

The recommended Mg requirement is 250 to 350 mg per day (10.4–14.6 mmol) in adults and an additional 100 to 150 mg in children and pregnant or nursing women. Food input is ensured essentially by cocoa powder, chocolate, almonds, peanuts, walnuts, vegetables, cereals and seafood. From 30 to 50% of ingested Mg is absorbed (5 mmol per day) in decreasing quantity from the small intestine to the colon. Fibres, phytates and oxalic acid appear to reduce Mg absorption moderately through the formation of a complex that cannot be easily dissociated. The binding of Mg to anions (phosphates) or fatty acids reduces the quantity of absorbable Mg (*Sanders et al., 1999*).

Administration of Mg:

Mg can be administered orally or intravenously. Intramuscular injection is also possible but painful. Oral administration of a daily dose of more than 50 mmol can cause

vomiting and diarrhea. In anesthesia and intensive care, the preferred administration route is IV. Two injectable forms of Mg are available, namely Mg chloride and sulfate. Ten millilitres of a 10% Mg chloride (MgCl_2) solution provide 1 g of Mg salts (= 118 mg elemental Mg), and 10 mL of a 10% Mg sulfate (MgSO_4) solution provide 1 g of Mg salts (= 98 mg elemental Mg) (*Dacey, 2001*).

Dosage of Mg:

Dose of Mg differs according to indications, and several dosage recommendations have been proposed. When Mg sulfate is used to correct a Mg deficit, the objective is to restore normal serum concentrations, in which case slow infusion of up to 10 g per day is appropriate. When Mg is used for its pharmacological properties, more rapid infusion is often necessary to obtain the high plasma concentrations desired. The recommended procedure is rapid I.V infusion of 1 to 2 g of MgSO_4 over a ten-minute period followed by continuous I.V infusion of 0.5 to one g per hr (reduced to 0.25 g per hr for patients with renal insufficiency). Administration is performed under continuous electrocardiographic monitoring, and serum concentrations of Mg or ionized Mg are determined every six hours (*Dacey, 2001*).

Mg when given too quickly, flushing can occur, and bradycardia, cardiac arrhythmia, and cardiac arrest have been reported. There is also the increased risk of the toxic effects of Mg resulting in renal impairment (*Walker, 2000*).