INTRAOPERATIVE AND POSTOPERATIVE STUDY OF MAGNESIUM SULPHATE AS PART OF BALANCED GENERAL ANAESTHESIA

Thesis

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Anaesthesia

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INTRODUCTION AND AIM OF THE WORK

The magnesium ion blocks the ion channel of N-methyl-D-aspartate (NMDA) receptor in a voltage-dependent fashion *(Nowak et al., 1984)*. Also, increased extracellular magnesium concentration in vitro cause a non-competitive NMDA blockade *(Harrison and Simmonds, 1985)*. Several studies have shown that intrathecal administration of magnesium sulfate alone produced a small degree of antinociception or no nociception but resulted in potentiated antinociception when magnesium was coadministrated intrathecally with morphine *(Kroin et al., 2000)*. However, magnesium transference from blood to Cerebrospinal Fluid (CSF) across the Blood-Brain Barrier (BBB) in unclear in normal humans. In one study, when the propofal infusion rate was held constant and the fentanyl dose was adjusted to hemodynamic endpoints, opioid requirements were reduced *(Koining et al., 1998)*. This result suggests that the effect of magnesium on anaesthesia should be studied further.

Accordingly, the aim of this work is to study the perioperative effects of continuous intravenous

administration of magnesium sulfate. To be more precise, two main aspects are included in this study. Firstly, intraoperative effects of magnesium sulfate on stress response and anaesthetics requirements. Secondly, its postoperative analgesic effects when combined with regional analgesia without opioid administration.

MAGNESIUM PHYSIOLOGY

(A) Magnesium in the organism:

Total body magnesium: magnesium is a bivalent ion, like calcium, with an atomic weight of 24.312. The human body contains 1 mole (24g of Mg).It is the fourth most common mineral salt in the organism after phosphorus, calcium and potassium *(Saris et al., 2000)*, the second intracellularcation after potassium, and the fourth plasma cation after sodium,potassium and calcium *(Fawcett et al., 1999)*.

Distribution in the body:It is concentrated mainly in bone (60%), muscle (20%) and soft tissues (20%). Only a fourth of the Mg contained in bone and muscle is exchangeable *(Sanders et al., 1999)*. Extracellular Mg represents only 1%of the total. In serum, Mg is divided into three fractions: ionized (active form), protein-bound and that contained in anion complexes (phosphates and citrates). These three fractions account respectively for 65, 27, and 8% of serum content. Three-fourth of plasma Mg is ultrafiltrable *(Sanders et al., 1999)*.

Daily Mg requirements: The daily recommended Mg requirement is 250 to 350mg (10.4-14.6mmol) in adults *(Dacey, 2001)* and an additional 100 to 150 mg

in children and pregnant or nursing women (Sanders et al., 1999). 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 (5mmol/day) in decreasing quantity from the small intestine to colon. The fraction of absorbed Mg decreases as the quantity ingested increases. Mg depletion corresponds to obligatory and uncontrolled digestive losses (around 60% of ingested Mg) and variable losses through renal excretion. Digestive losses are increased by diarrhea or biliary fistula. Urinary excretion of Mg is normally 5mmol/day, but can be reduced to 0.5mmol/day in the event of severe deficiency. The level is regulated by variations in renal reabsorbion, as a function magnesemia, relativeto inputs and bone mobilization *(Sanders et al., 1999)*.

(B) Magnesium homeostasis:

No single homeostatic control has been demonstrated for magnesium *(Quamme, 1997)*.

[A]Cellular Homeostasis:

If total exchangeable Mg in the body is considered as the Mg pool regulated by the kidney then it would take more than three days for the kidney to turn over exchangeable Mg only once.

Therefore processes taking place at cell membrane, rather than the kidney, must be important for maintaining cellular versus extracellular Mg concentration.

Therefore the kidney is responsible for long term (chronic) regulation of Mg homeostasis and the cells and possibly also bone are responsible for short term (acute) regulation. The mechanisms that regulate Mg excretion are not well understood *(Fawcett et al., 1999)*.

[B]Renal homeostasis:

Quamme, (1997) has mentioned that the renal handling of magnesium is normally a filtration reabsortion process. Some (20-30%) of filtered Mg is reabsorbed in the proximal tubules. The major portion of filtered Mg (65%) is reabsorbed in the loop of Henle, mainly in the thick ascending limb. The loop of Henle appears to be the major nephron site where magnesium reabsorption is controlled. About 10% of the filtered Mg is delivered into the distal nephron where only a small fraction of the filtered Mg is reabsorbed, and the transport capacity is readily exceeded with increased Mg delivery *(Kelepouris and Agus, 1998)*.

Morgan and Mikhail, (2000) suggested that the exact mechanisms involved in Mg homeostasis in remain unclear, they involve interaction of the gastrointestinal tract (absorption), bone (storage) and the kidneys which is the primary route for elimination averaging 6-12mEq/d.

Factors that affect Mg handling by the kidney:

(1) Plasma Mg concentration:

The most striking changes in Mg excretion occur in response to alterations in plasma Mg concentration. With marked acute or chronic hypermagnesemia due to high dietary intake or intravenous Mg infusion, urinary Mg excretion can approximate the filtered load of Mg. Conversely, severe hypomagnesemia results in almost complete renal conservation of Mg. Thus a major determinant of renal Mg excretion appears to be the plasma magnesium concentration *(Quamme, 1997)*.

Quamme, (1997) has suggested that the large increase in Mg excretion occur following hypermagnesemia due to:

- Increased filtered load
- Reduction in fractional reabsorption in the proximal tubules and

- Reduction in reabsorption in the ascending limb of loop of Henle.

(2) Parathyroid hormone (PTH):

The interrelationship between Mg and PTH is complex. PTH secretion may be modulated by changes in plasma Mg concentration as it is bchanges in calcium concentration. PTH may enhance renal Mg reabsorption and the resulting effects may depend on the opposing forces of elevated serum calcium and Mg concentrations *(De Rouffiganc and Quamme, 1994)*.

(3) Adenosine mono-phosphate (AMP) mediated hormones:

Including PTH, ADH, calcitonin and glucagon. It had observed that all four hormones generally enhance sodium, chloride, potassium and magnesium reabsorption in the loop of Henle and distal tubule. This observation suggested that these may not be specific regulatory mechanisms at least for Mg. Accordingly control of renal Mg excretion by these factors is a combination of the independent hormonal effects apparently acting in concert with each other to provide electrolyte balance *(De Rouffiganc and Quamme, 1994)*.

(4) Thyroid hormone: