Magnesium (Mg$^{2+}$)

Given as Magnesium Sulfate Intravenously

Mechanism of Action

- In pain: non-competitive NMDA receptor antagonist, blocking glutamate and aspartate from binding and preventing extracellular calcium movement into cells
- Like ketamine, thought to attenuate central sensitization and alter perception and duration of pain — hence an antinociceptive effect

Dosing and Uses

- IV dosing ranges are highly variable in the literature, including bolus +/- infusions or infusions alone
- Dosing for anti-nociception is lower than dosing for some other conditions (e.g., pre-eclampsia treatment)
- At UCSF, Mg$^{2+}$ infusions used as part of ERAS pathways (e.g., gynecology, colorectal) and some spine surgeries
- At UCSF, loading dose of 30mg/kg over 30-60min and then 6mg/kg/hr

Evidence to date

- Magnesium used in pain for decades, but much is still unknown regarding pain outcomes, with mixed evidence
- In one systematic review, decreased post-op pain scores at rest at 4h (-0.74) and 24h (-0.36), pain scores with activity at 24h (-0.73), and opioid consumption (by 10mg IV morphine)
- Types of surgery with some evidence for post-op analgesia benefit:
  - Orthopedic, Cardiac, GI, Urologic, Abdominal Hysterectomies
  - Bariatric when combined with ketamine
- In one trial on laminectomies, Mg$^{2+}$ bolus + infusion intra-op had no effect on pain scores or first PCA-use
- In an orthopedic review, Mg$^{2+}$ increased time to first analgesic use and decreased cumulative analgesic use, but no change in pain intensity

References

9. MH Jarahzadeh, ST Harati, H Babaeizadeh, E Yasaei, FR Bashar

Physiology

- Mg$^{2+}$ is a vital cation across physiologic processes and organ systems including cardiovascular, nervous, musculoskeletal, endocrine, and immune
- Primarily intracellular (only <1% in plasma), used in oxidative phosphorylation, glycolysis, and cell signaling
- As an essential element, Mg$^{2+}$ intestinal uptake and renal excretion is highly regulated to maintain homeostasis via a filtration-reabsorption process in the kidney
- Normal plasma range is 1.5-2.5mEq/L
- Urinary excretion increases linearly with plasma concentration to maintain stable level, but this is saturable above a threshold, you can increase Mg$^{2+}$ levels above physiologic ranges.

Other Uses

- Reduced persistent post-surgical pain at 1 year in total knee arthroplasty
- Reduces incidence of post-op shivering by 42%
- Also used in pre-eclampsia (vasodilation, anti-convulsant), asthma exacerbations (bronchodilation), and cardiac arrhythmias (ion-channel regulation)

Side Effects and Toxicity

- Side effects can include: nausea, feelings of warmth/heat, prolonged QT or PR intervals, hypotension, bradycardia, muscle weakness (including respiratory paralysis), prolonged emergence, and prolonged neuromuscular blockade
- Serum levels associated with toxicity effects: loss of DTRs at 7-10mEq/L, respiratory paralysis at 10-13mEq/L, cardiac conduction altered at >15mEq/L, cardiac arrest at >25mEq/L
- Treatment for toxicity is calcium gluconate injection (1000-3000mg depending on serum level)