

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 pain¹**— hence an antinociceptive effect

Dosing and Uses

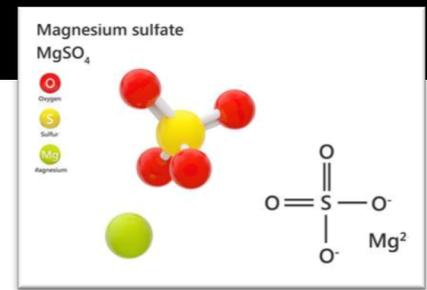
- IV dosing ranges are highly variable in the literature, including bolus +/- infusions or infusions alone
- Dosing for anti-nociception is lower than dosing for some other conditions (e.g., pre-eclampsia treatment)
- At UCSF, Mg^{2+} infusions used as part of ERAS pathways (e.g., gynecology, colorectal) 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 review¹, 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^{8,9}:
 - Orthopedic, Cardiac, GI, Urologic, Abdominal Hysterectomies
 - Bariatric when combined with ketamine¹²
- 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 intensity¹⁴**

References

1. GS De Oliveira, LJ Castro-Alves, JH Khan, RJ McCarthy. Anesthesiology 2013.
2. H-S Na, J-H Ryu, S-H Do. Role of Magnesium in Pain. Book Chapter in: Magnesium in CNS 2011.
3. P Houllier. Annu Rev Physiol 2014.
4. ER Norwitz (Eds CJ Lockwood, VA Barss). Uptodate Preeclampsia 2020.
5. AG Euser, MJ Cipolla. Stroke 2009.
6. RH Green. BMJ Clin evid 2016.
7. WL Baker. Eur Heart J Cardiovasc Pharmacother 2017.
8. B-L Guo, et al. Pain Physician 2015.
9. MH Jarahzadeh, ST Harati, H Babaeizadeh, E Yasaei, FR Bashar
10. TK Oh, et al. J Clin Med 2019.
11. H Kawakami, D Nakajima, T Mihara, H Sato, T Goto. Anesthesia & Analgesia 2019.
12. H Jabbour et al. Obesity Surgery 2019.
13. S Ghaffaripour, H Mahmoudi, H Eghbal, A Rahimi. Cureus 2016.
14. Y-N Peng, F-C Sung, M-L Huang, C-L Lin, C-H Kao. Medicine 2018



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^{1,2}
- As an essential element, **Mg^{2+} intestinal uptake and renal excretion is highly regulated to maintain homeostasis** via a filtration-reabsorption process in the kidney²
- **Normal plasma range is 1.5-2.5mEq/L**
- Urinary excretion increases linearly with plasma concentration to maintain stable level, but this is saturable³— 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 arthroplasty¹⁰
- Reduces incidence of post-op **shivering** by 42%¹¹
- Also used in **pre-eclampsia⁵** (vasodilation, anti-convulsant), **asthma exacerbations⁶** (bronchodilation), and **cardiac arrhythmias⁷** (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 blockade⁴
- 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)⁴

