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MANAGEMENT OF HYPOMAGNESAEMIA

Hypomagnesaemia (HoM) is a serum magnesium level ($s[Mg]$) $<0.7\text{mmol/L}$. Magnesium is mainly an Intracellular (IC) ion and the $s[Mg]$ may be normal despite significant total body depletion. The serum contains only $\sim 0.5\%$ of total body Mg (TBMg)^[1-3].

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| <p>Symptoms and Signs (S/S) (Similar to hypocalcaemia)^[1-3]</p> | <p>Are generally non-specific and could be attributed to other frequently associated electrolyte deficiency; occur when $s[Mg]$ falls to $<0.5\text{mmol/l}$. S/S are prominent when the reduction in $s[Mg]$ occurs rapidly or is large.</p> <ol style="list-style-type: none"> 1. Neuromuscular effects: weakness, hyper-excitability (tetany, tremor, seizures), coma 2. Cardiac: widened QRS, T abnormalities; severe HoM: prolonged PR and QT; arrhythmias: atrial and ventricular; increased risk of digitalis toxicity 3. Metabolic: Hypokalaemia; Hypocalcaemia – common associations |
| <p>Common Causes ^[1-3]</p> <p>The cause is usually clear from the history</p> | <ol style="list-style-type: none"> a. Increased GI losses: PPI (possibly impaired Mg absorption), vomiting, diarrhoea, laxatives abuse, malabsorption; rarely reduced intake b. Increased Renal losses: Diuretics, CNIs, CTx, Osmotic diuresis (e.g. hyperglycaemia), resolving ATN – post-renal transplant, Familial, e.g. Gitelman's/Barter's syndromes (rare) c. Re-distributive (uncommon): DKA, Insulin therapy |

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| Investigations ^[1-3] | UEs, s[Ca]. If cause unclear from the history: 24hr urine Mg to differentiate renal from GI losses |
| Abbreviations: GI=Gastrointestinal; PPI=Proton Pump Inhibitor; CNI=Calcineurin Inhibitors; CTx=Cytotoxic medications; ATN=Acute Tubular Necrosis; hr=Hour | |

Treatment, follow the sequential flowchart:

| s[Mg] (mmol/l) | Treatment ^[1-7] |
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| 0.5–0.7 (Mild) – usually asymptomatic | <ul style="list-style-type: none"> • Prompt identification and treatment of the underlying cause • Stop offending drugs: PPI, optimise diuretics • Monitor and seek expert advice as appropriate • Treat as per the next box guidance if symptomatic, or on a clinical risk benefit decision^[1,5] |
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| 0.3–0.49 (Moderate) Asymptomatic | <p>Apply all treatment measures listed above +</p> <ul style="list-style-type: none"> • Oral Mg^a: 24 (up to 50) mmol Mg daily. Mg glycerophosphate (1 tablet = 4mmol Mg) 2 tablets tds with or after food. Try an alternative if ineffective or causing side effects – diarrhoea is common • Mg dosing is empirical – monitor s[Mg] (Ca, K, PO₄) daily; ≥5 days treatment is usually required to replete the IC Mg stores. • Long term replacement may be needed if a reversible cause is not found and removed. |
| | ↓ |
| 0.3–0.49 (Moderate) Symptomatic | <p>Apply all treatment measures listed above +</p> <ul style="list-style-type: none"> • IV Mg^b under continuous ECG monitoring: use a large vein (may cause tissue damage if extravasted), and infusion pump. • Give magnesium sulphate 50% (2mmol/mL; Ig=4mmol)^[6]: <ul style="list-style-type: none"> ○ Day 1: 20mmol (5gms) in ½ or 1L 5% D (or saline) over 3hrs; repeat as necessary ○ Day 2 onwards: 20mmol in 500mL 5% D (or saline) over six hours <div style="border: 1px solid black; padding: 5px; margin: 5px 0;"> <p>Lower diluent volumes in volume overload states If haemodynamically unstable, e.g. VT: give 8mmol over 10–15 minutes, repeat once if necessary^[6].</p> </div> <ul style="list-style-type: none"> • Monitor s[Mg] after each dose, and daily. <i>UP to 160 mmol may be required to correct the deficiency over several days [6].</i> • Continue for 2–3 days with oral (preferably) Mg after s[Mg] normalisation to replete the IC stores. • Monitor PR, BP, RR, UOP, and for signs of hypermagnesaemia |

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| <table border="1"> <tr> <td style="width: 20%;"><0.3 (Severe)</td> <td style="text-align: center;">Apply all treatment measures listed above</td> </tr> </table> | <0.3 (Severe) | Apply all treatment measures listed above |
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| <p>Hypomagnesaemia frequently causes secondary hypocalcaemia (PTH-end organ resistance and reduced PTH secretion) and hypokalaemia, rendering them refractory to correction until the magnesium deficit is corrected^[8].</p> <p>Hypomagnesaemia-related hypocalcaemia: correction of Mg deficiency first, unless severe hypocalcaemia symptoms present, will often lead to spontaneous normalisation of calcium.</p> <p>Abbreviations: PPI=Proton Pump Inhibitor; CNIs=Calcineurin Inhibitors; CTx=Cytotoxic Agents; ATN=Acute Tubular Necrosis; IV=Intravenous; Ca=Calcium; K=Potassium</p> <p>^aAlternative oral preparations if Mg glycerophosphate intolerant: Maalox 10–20ml qds (10ml Maalox=6.8mmol Mg) may take 6–8 weeks. The aluminium (with constipating effect) contained in Maalox may reduce the chance of diarrhoea. Magnesium Citrate 150mg tablets; contains 6.2mmol Mg/tablet. Oral preparations are not well absorbed from the GIT, hence the use of magnesium sulphate as an osmotic laxative^[4]. <i>Counsel the patient, as all are unlicensed.</i> Magnaspartate (sachets 6.5g/10mmol: 1–2/day) is replacing the oral preparations in the United Kingdom recently licensed^[9].</p> <p>^bIV Mg: Magnesium sulphate is the salt of choice. Ideally, the infusion rate should be no >4mmol/hr. Fluid restricted patients: the maximum concentration is 20% (20mmol in 25ml=0.8mmol/ml) via a peripheral vein. A practical regimen, less likely to cause venous irritation, is 20mmol magnesium diluted to 100ml, infusion over 5hrs.</p> | | |

- Avoid parenteral Mg in patients with heart block or myocardial damage^[5].
- Renal impairment: Mg is renally excreted and should be used cautiously because of the higher risk of adverse effects. If eGFR <30 reduce dose to $\leq 50\%$ under close monitoring^[1,5,6].
- Use cautiously in myasthenia gravis and respiratory insufficiency^[5].

IV Mg: induces a rapid but temporary elevation in $s[Mg]$ that partially inhibits the stimulus to Mg re-absorption in the loop of Henle. Consequently, up to 50% of the infused Mg will be excreted in the urine. In addition, Mg uptake by the cells is slow; therefore adequate repletion requires sustained correction, preferably oral, as above^[10].

IV Mg: is advocated in some acutely ill patients without documented sMg depletion. The American College of Cardiology and the American Heart Association recommend 1–2 grams of magnesium sulphate as an IV bolus over five minutes for torsades de pointes treatment^[3].

Patients with chronic renal magnesium wasting, including Bartter’s, Gitelman’s syndrome and cisplatin nephrotoxicity or diuretic-induced hypomagnesaemia who cannot discontinue diuretic therapy, may benefit from the addition of a potassium-sparing diuretic, e.g. Amiloride. These drugs may lower magnesium excretion by increasing its reabsorption in the distal nephron^[3,10].

Magnesium deficiency has been implicated in asthma, and some studies suggest that magnesium therapy is effective^[1].

Monitoring: s[Mg] should be checked daily as serum levels may be artificially high whilst magnesium equilibrates with the intracellular compartment. Monitor serum levels of calcium and other electrolytes in patients with hypomagnesaemia.

Adverse effects of Magnesium therapy:

Oral Mg is usually well tolerated; high doses can cause diarrhoea. Adverse effects of parenteral Mg include skin flushing, hypocalcaemia, hypotension and AV block. Hypermagnesaemia is unlikely to occur following oral magnesium supplementation, except in patients with renal failure. Significant hypermagnesaemia is rare, patients at higher risk of include the elderly and patients with renal impairment^[5,6].

Symptoms of hypermagnesaemia: include flushing, hypotension due to peripheral vasodilatation, muscle weakness, loss of deep tendon reflexes due to neuromuscular blockade, respiratory depression, confusion, coma, cardiac arrhythmias and cardiac arrest.

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