NHS
North East and
North Cumbria

Management of Hypomagnesaemia in Adults in Primary Care

Magnesium is an essential constituent of many enzyme systems, particularly those involved in energy generation; the largest stores are in the skeleton. Changes in normal concentration (0.7 – 1.0mmol/L) can therefore have significant effects on body function [1].

Hypomagnesaemia is a state in which someone has abnormally low concentration of magnesium in their blood. The condition can occur if people do not get enough magnesium in their diet, if they are not able to absorb magnesium properly, or if they lose too much magnesium in their urine [2]. Hypomagnesaemia often causes secondary hypocalcaemia (low calcium) and hypokalaemia (low potassium) [1,3].

Hypomagnesaemia has been associated with the following conditions [2-5]:

- Malabsorption (e.g. Coeliac disease, Crohn's disease, Ulcerative Colitis, short bowel syndrome, chronic diarrhoea, Steatorrhoea)
- Chronic alcoholism
- Drug therapy (e.g. proton pump inhibitors*, laxatives, thiazide or loop diuretics, digoxin, theophylline, amphotericin, aminoglycosides, immunosuppressants, cisplatin, cyclosporin & tacrolimus)
- Inherited kidney conditions (e.g. Bartter's and Gitelman's syndrome)
- Renal disorders (e.g. post-kidney transplant, dialysis, renal tubular disorders)
- Diabetes (due to glucose-induced diuresis secondary to poor glucose control)
- Disorders of the parathyroid gland
- Malnutrition / dietary deficiency / Anorexia
- Re-feeding syndrome

** In 2012 the MHRA stated that severe hypomagnesaemia had been reported infrequently in patients treated long term with PPIs. They advised that for patients expected to be on prolonged treatment, and especially for those who take PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and repeat measurements periodically during treatment [6].*

Often hypomagnesaemia does not cause any symptoms, but if the magnesium concentration is low enough (typically <0.5mmol/L) patients can present with [2,3]:

- nausea & vomiting
- lethargy, muscle weakness, ataxia and tremors
- seizures
- ventricular arrhythmias and ECG abnormalities
- vertigo

The laboratory will phone all initial magnesium concentrations that are ≤0.4mmol/L to the requestor (or deputising service) to facilitate rapid patient management.

There are no national guidelines for the monitoring and treatment of acute hypomagnesaemia, and practice varies widely across hospital Trusts.

Although this document offers guidance, the dose and duration of oral magnesium to correct hypomagnesaemia and subsequent monitoring should be determined on an individual patient basis.

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Monitoring

It is advised that magnesium should be measured in patients who are symptomatic and/or are likely to have magnesium deficiency due to drug therapy or clinical condition. If treatment is commenced, it is advised to wait at least 2 days before repeating as it takes up to 48 hours for the magnesium to redistribute through the body. Concentrations should then be checked weekly until they return to normal range. Additional electrolyte imbalances are often associated with hypomagnesaemia, particularly calcium and potassium, it's therefore good practice to check and monitor these levels.

Management

Hypomagnesaemia can be defined as mild, moderate or severe based on serum magnesium concentration [3] and should be considered alongside the presence/absence of symptoms and/or ECG changes which may indicate clinically significant hypomagnesemia and potentially serious dysrhythmias.

Mild deficiency	0.5 – 0.7 mmol/L	Only require oral replacement if symptomatic
Moderate deficiency	0.4 – 0.5 mmol/L	Advise oral replacement if asymptomatic May need IV replacement if symptomatic
Severe deficiency	<0.4 mmol/L	Usually requires admission for IV replacement

- If concentrations are between 0.4 -0.7mmol/L then oral magnesium replacement should be considered in symptomatic patients or those at high risk of the effects of hypomagnesaemia.
- If possible, correct the underlying cause e.g. stop causative medications (consider switch from PPI to H2-receptor antagonist), support alcohol cessation, treat diarrhoea etc. [7]
- Oral magnesium therapy should be considered first-line.
- The standard dose of oral magnesium to prevent recurrence of hypomagnesaemia is 24mmol daily in divided doses over 5-7 days depending on cause and severity.
- Magnesium aspartate sachets and glycophosphate chewable tablets are available as licensed formulations.
- Oral magnesium salts commonly cause diarrhoea which may be improved by administration with or after food or at a reduced dose.
- If oral therapy is not tolerated OR serum magnesium is not responding to treatment OR hypomagnesaemia recurs despite oral treatment, refer to the relevant specialty according to the suspected underlying cause. This is particularly important if long term intravenous magnesium is likely to be required [7].

Precautions for Prescribing

- Magnesium is renally excreted and should be used with caution in patients with renal impairment (eGFR <30 mL/minute/1.73m^2) as they are at a higher risk of adverse effects [3,4]
- Magnesium salts should be used with caution in patients with myasthenia gravis, patients with hepatic impairment at risk of developing renal impairment, and respiratory insufficiency [4]
- Patients who are taking concurrent digoxin may exhibit signs and symptoms of digitalis toxicity which require omission or reduction of digoxin dose until hypomagnesaemia is corrected.
- Magnesium Glycerophosphate should not be used in patients if Phosphate levels are high.

Dosing

The standard dose of oral magnesium to prevent recurrence of hypomagnesaemia is 24mmol daily in divided doses.

Drug	Product	License Status UK	Formulary Status [10]	Recommended Dose	Directions for Administration	Separation of Administration
Magnesium Aspartate	**Oral Powder Sachets** Each sachet contains 6.5 g (10 mmol Mg^{2+})/sachet	**Licensed**	**GREEN** *1st line treatment & prevention*	1–2 sachets daily	Dissolve sachet contents in 50–200 mL water, tea or orange juice Can be administered in 200mL water via a gastric, duodenal, and nasal feeding tube	Oral magnesium should preferably not be taken at the same time as other drugs since they might impair absorption. Oral magnesium might damage enteric coatings designed to prevent dissolution in the stomach.
Magnesium Glycerophosphate	**Chewable Tablets** ***Use preparation with the cheapest acquisition cost*** Each tablet contains Mg^{2+} 4 mmol	**Licensed**	**GREEN**	1–2 tablets 3 times a day *Dose to be adjusted according to the serum total magnesium conc.*	Chewable tablets may be broken into quarters and chewed or swallowed with water	
	Oral tablets and capsules	**Unlicensed**	**Non-Formulary**			
	Oral Suspension 1mmol/mL	**Unlicensed**	Can be used if supply problems with chewable tablets			

Oral magnesium and other medicinal products may mutually influence each other's absorption, a time interval of 2 to 3 hours should generally be respected if possible.
This specifically applies to:

- Fluorides and tetracycline: if they must be used, the doses must be separated by 2 to 3 hours or more to prevent their admixture in the gut.
- Aminoquinolines, quinidine and quinidine derivatives nitrofurantoin, penicillamine, iron, bisphosphonates, eltrombopag, nitroxoline: to avoid impairment of absorption, magnesium preparations should be taken 3 to 4 hours before or after the administration of those drugs.

Please refer to the current BNF and SPCs for further information and details of interactions.

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