NHS
Dorset
Clinical Commissioning Group

The management of hypomagnesaemia in primary care

Magnesium is a cofactor in enzyme systems involving energy metabolism and protein and nucleic acid synthesis. It also plays a role in the active transport of calcium and potassium ions across cell membranes, important to nerve impulse conduction, muscle contraction, and heart rhythm.

Normal plasma magnesium concentration ranges from 0.70 - 1.05 mmol/L. Only about 1% total body magnesium is found in extracellular fluid; the remainder is in bone and soft tissue. About 25% of plasma magnesium is bound to albumin so high or low albumin concentrations will affect magnesium levels.

Changes in magnesium levels occur very slowly (over months or years). Serum magnesium does not always correlate with total body magnesium – it is possible to see a serum level within the reference interval, but a total body magnesium deficit with a chronic magnesium deficiency usually as a result of inadequate dietary magnesium. The reverse (a low serum level and normal total body magnesium) is also possible and is usually seen with drugs which increase excretion of magnesium.

Early signs of deficiency include loss of appetite, nausea, vomiting, fatigue, and weakness. As deficiency worsens, numbness, tingling, muscle contractions and cramps, seizures, personality changes, abnormal heart rhythms, and coronary spasms can occur. Severe deficiency can result in hypocalcaemia or hypokalaemia.

Magnesium deficiency has been associated with the following conditions:

- Gastrointestinal loss, including malabsorption, malnutrition, Crohn's disease, coeliac disease
- Chronic alcoholism
- Poorly controlled type 2 diabetes
- Renal disorders
- Drug therapy – e.g. PPIs, diuretics, cisplatin, gentamicin, ciclosporin, foscarnet, amphotericin, pentamidine

The MHRA advise that prolonged use of PPIs has been associated with case reports of hypomagnesaemia, some serious. It suggests measuring magnesium levels before starting PPI treatment and periodically during prolonged treatment, especially in those who will take a PPI concomitantly with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics).

What does Dorset CCG recommend?

Dorset CCG advises that magnesium levels should be measured in patients who are symptomatic and are likely to have diminished magnesium levels because of their therapy (e.g. long term PPIs and/or other medicines) and pre- existing conditions (Appendix One).

Robust evidence of the superiority of one oral magnesium preparation over another does not exist. Tolerability of a particular preparation may limit the dosage. Caution should be exercised when switching between magnesium preparations as magnesium preparations have differing bioavailability.

<u>First line</u>

Magnesium-L-aspartate (Magnaspartate®) is the preferred choice for treatment and prevention of magnesium deficiency in adults, adolescents and children from 2 years. Magnesium-L-aspartate (Magnaspartate®) is a 10 mmol sachet formulation to be mixed with water and for adults taken up to twice a day. It is the most cost-effective licensed preparation available.

<u>Second line</u>

Magnesium glycerophosphate is available for patients unable to tolerate the magnesium-L-aspartate sachet formulation. Currently the only licensed magnesium glycerophosphate preparation is Neomag® (4 mmol chewable tablets). This is licensed in treatment and prevention of magnesium deficiency in adults, adolescents and children from 4 years.

All other magnesium preparations and salts (citrate) remain unlicensed

Magnesium glycerophosphate liquid 5 mmol/5mL (MagnaPhos®) is unlicensed but manufactured to GMP standards and currently the most cost effective liquid available for those unable to take the licensed preparations.

Dosing

The BNF states that for adults, magnesium may be given by mouth in a dose of 24mmol Mg daily in divided doses. See BNFc for children's doses.

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- No longer accessible

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Appendix One– Flow chart for patients presenting with possible PPI-associated hypomagnesaemia

A. **Repeat prescription for PPIs?** Has the patient been taking PPIs for more than 5yrs, are they **over 70**; with poor dietary intake; malabsorption syndromes; chronic diarrhoea, taking other medicines which decrease magnesium levels e.g. diuretics?

OR

B. **First prescription for PPIs?** Is the patient **over 75**; poor dietary intake; malabsorption syndromes; taking other medicines which decrease magnesium levels?

NB If renal failure or Crohn's disease – **REFER TO SPECIALIST**

YES to A

If YES to A: consider

1. Have they been taking PPIs for 5 years or longer?
2. Do they have; loss of appetite, cramps, nausea, fatigue, weakness?
3. Are they taking meds (diuretics) which predispose to hypomagnesaemia?
4. Is their diet adequate? Are they likely to have GI loss of magnesium?
5. Do they have chronic alcoholism**?**

YES to B

Monitor Mg annually

YES to questions 1-5

NO to questions 1-5

Test Magnesium levels (and Ca^{2+} and K^{+})

Serum Mg^{2+} 0.5–0.7mmol/L:
Give Oral supplementation

Serum Mg^{2+} <0.5mmol/L:
IV infusion required

TREAT

- Stop PPI, Rx ranitidine 150mg bd
- Reduce dose of diuretic if appropriate or trial of amiloride/spironolactone
- Provide dietary advice- increase dietary green vegetables, peas and nuts, whole grains

And

Prescribe 3 month trial of magnesium supplementation

- **First Line:** Magnaspartate, 1-2 sachets/day (10-20mmol/day)
- **Other options:** Mg glycerophosphate (Neomag®) 6/day (24mmol/day); Magnesium glycerophosphate liquid [unlicensed] (24mmol/day)

Monitor and provide advice about AEs especially diarrhoea

TREAT

RBCH: GP referral to TIU for IV $Mg2^{+}$ infusion
Poole: GP referral to Ansty ward
DCH: GP referral to an acute medicine consultant physician to decide whether to admit or treat in the ambulatory care unit

Re-test Mg^{2+} after 3 months

Mg^{2+}> 0.7
Stop Mg^{2+}; review at appropriate intervals

Mg^{2+} = 0.7
Reduce dose, repeat test in one month to check result

Mg^{2+} <0.7
REFER to secondary care endocrinology