

## An audit on the management of hypomagnesaemia on the wards in a district general hospital in the UK

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### Abstract

Hypomagnesaemia (Low serum magnesium) can be a life-threatening condition, if severe, and can co-exist with hypokalaemia and hypocalcaemia (with hypoparathyroidism), though the serum magnesium level is not routinely estimated. Given the fact that many medications commonly used in clinical practice can lower the level of serum magnesium (along with other causes) by various mechanisms and that repletion of serum magnesium is absolutely necessary before correction of hypokalaemia and hypocalcaemia, in case of co-existence, we decided to do a short audit for 3 weeks in the month of January 2023, to get an understanding whether patients with hypomagnesaemia were managed adequately on the Wards, in accordance with the prevailing Guidelines. The findings showed that though the aetiology of low serum magnesium was not established in every case, symptomatic management of the condition was adequate.

**Keywords:** Hypomagnesaemia; Hypokalaemia; Hypocalcaemia; Hypoparathyroidism; Guidelines

### 1. Introduction

Hypomagnesaemia results from low serum magnesium (Normal: 0.7 to 1.1 mmol/L or 1.7-2.5 mg/dL). The condition occurs in case of dietary deficiency, failure to absorb Magnesium properly and in urinary magnesium losses (1). Several drugs including Diuretics, Aminoglycosides and Amphotericin B cause renal magnesium losses whereas PPIs (Proton Pump Inhibitors) by their effect on TRP M6/7 (Transient Receptor Potential Melastatin 6 and 7) channels, present in the apical membrane of enterocytes, inhibit the active gut absorption of magnesium (2). Low magnesium is often associated with hypokalaemia (due to urinary potassium wasting) and hypocalcaemia (due both to lower parathyroid hormone secretion and end-organ resistance to its effect). In hypokalaemia always the serum magnesium level is to be checked and repleted prior to repleting potassium. Low magnesium can exacerbate renal potassium losses. Also, hypocalcaemia does not resolve until the magnesium deficiency has been corrected. Therefore, hypomagnesaemia needs to be treated before hypocalcaemia.

#### *Aim of the audit*

We frequently come across patients with low serum magnesium on the wards and OPD. Low serum magnesium can cause various complications including cardiac and neurological problems. Therefore, it was needed to do an audit to see if such patients were being managed adequately in our hospital. The aim was to find out whether the patients with hypomagnesaemia admitted during the first 3 weeks in January 2023 on the Wards were managed properly in accordance with the prevailing Guidelines.

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## 2. Materials and Methods

The Electronic Health Information System (HIS) for all patients on various Wards (during the first 3 weeks of January 2023) were searched to look for low Magnesium and the management offered. Our Hospital Guidelines were considered along with the existing Guidelines of Oxford, Greater Glasgow and Clyde (GGC) and Gloucestershire for the purpose of the audit.

Criteria on which the audit is based:

- Category- Mild, moderate, severe
- Review the potential aetiology that can lead to hypomagnesemia.
- Family History-Genetic testing may be considered if there is positive family history, unexplained hypomagnesemia, or if discovered early in life.
- Check bone profile (Calcium) and U&Es (Potassium and eGFR)
- Check PTH
- Check whether offending drugs, if any, were stopped.
- Record ECG- for prolonged QTc
- 24 hours renal excretion of Magnesium- whether it was done.
- On examination, vertical nystagmus and tetany may be observed. The following signs need to be checked: (1) Chvostek sign: Tapping on facial nerve leads to twitching of facial muscles, (2) Trousseau sign: Carpopedal spasm induced by inflated blood pressure cuff 20 mm above Systolic BP for over 3 minutes.
- Summarize the treatment options for hypomagnesemia.
- Outline the importance of enhancing care coordination among the interprofessional teams and whether referral was done to Gastro and Renal teams to ensure proper evaluation and management of hypomagnesemia.
- Patient and relatives need to be informed of the complications of hypomagnesaemia

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## 3. Discussion

Hypomagnesemia can be secondary to decreased intake, as seen in the following:

- Nutritional including Starvation, Chronic alcoholism, Terminal cancer, critically ill patients who are receiving total parenteral nutrition (3)
- Medications: Diuretics, Proton pump inhibitors, Aminoglycoside antibiotics, Amphotericin B, Pentamidine, Digoxin, Cisplatin, Cyclosporine, Antibodies that bind to epidermal growth factor (EGF) receptors and Laxatives (3)
- Redistribution from the extracellular to the intracellular compartment: Treatment of diabetic ketoacidosis with insulin, Refeeding syndrome, Correction of metabolic acidosis, Acute pancreatitis, Alcohol withdrawal syndrome (3)
- Gastrointestinal and Renal losses: Acute and Chronic diarrhoea, Acute pancreatitis, Gastric bypass surgery, Genetic causes (Gitelman's syndrome, Bartter syndrome, Familial hypomagnesemia with hypercalciuria and nephrocalcinosis, MODY caused by HNF1-beta mutation, Autosomal recessive isolated hypomagnesemia caused by EGF mutation, etc), Acquired tubular dysfunction including post-kidney transplant, Recovery from acute tubular necrosis and post-obstructive diuresis (3)

### 3.1. Clinical Features of Hypomagnesaemia:

Signs and symptoms of hypomagnesaemia (more likely if level is < 0.5 mmol/L)

- Neuromuscular and CNS: fasciculations, hyperreflexia, paraesthesia, Vertical nystagmus, seizures, and confusion. Chvostek and Trousseau's sign may be positive as features of latent tetany.
- Cardiac: arrhythmias and ECG changes (Prolonged PR/QTc, wide QRS, Flattened T waves)
- Gastrointestinal; Nausea and Vomiting

### 3.2. Treatment Details (4,5,6,7) and Appendix 2

#### 3.2.1. Treatment of hypomagnesaemia

If the Serum Magnesium is  $< 0.5$  mmol/L

Prescribe 20mmol magnesium IV in 500 ml to 1000 ml of compatible fluid IV (Normal saline or 5% Dextrose) over 6-12 hours. If patient also has hypokalaemia generally give magnesium first; do not combine magnesium and potassium in the same bag (6).

Intravenous administration: Magnesium sulphate 50% is used for making IV solution: 1g (4mmol) in 2ml amps, 5g (20mmol) in 10ml amp.

Higher doses may be given, if necessary, e.g., 40mmol may be given in 100ml of compatible fluid over 2 hours via a central line with appropriate monitoring (6)

Concentrations over 20mmol/100ml should ideally be given via a central line.

With rates above 8mmol/hr close monitoring including ECG is recommended (6).

If the Serum Magnesium is between 0.5 – 0.7 mmol/L

Asymptomatic and if oral access is available (Including enteral feeding tubes)-

Prescribe regular magnesium aspartate 10mmol sachets one twice a day (20mmol/day). Diarrhoea/stoma output may be dose limiting or necessitate IV administration. Monitor magnesium level closely and continue accordingly. Choice of oral/enteral treatment: Magnesium aspartate sachets are not licensed with GFR  $< 30$  ml/min but may be used with caution. Magnesium aspartate sachets may be used via jejunal feeding tubes (unlicensed).

Magnesium oxide tablets or capsules (4 mmol in 160 mg of MgO capsules) and Magnesium glycerophosphate tablets (4 mmol in each tablet) are reserved for specialist use only- usually 24 mmol/day or 2 tablets thrice daily. Higher doses may be administered provided there is no diarrhoea.

If the Serum Magnesium is 0.5 – 0.7 mmol/L

- Asymptomatic and if oral access is not available (6)

Prescribe 8mmol magnesium in 100ml compatible fluid IV over 2 hours. Monitor magnesium level daily.

If the Serum Magnesium is 0.5 – 0.7 mmol/L

- Symptomatic (6)

IV Magnesium Sulphate: 20mmol magnesium IV in 500 ml to 1000 ml of compatible fluid IV (Normal saline or 5% Dextrose) over 6-12 hours.

#### 3.2.2. Hospital Guidelines

In cases of mild, asymptomatic hypomagnesaemia, where potassium levels are normal, attempt to correct magnesium deficits with oral treatment in the first instance.

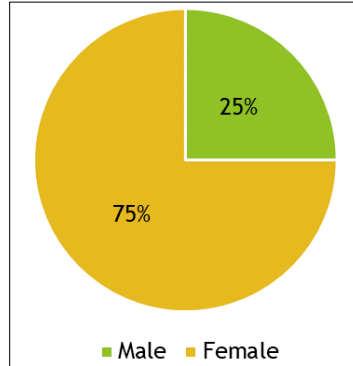
Currently, Magnesium Aspartate sachets are the only licensed magnesium replacement product in use at our hospital. However, Magnesium Oxide and Magnesium Glycerophosphate tablets are also used. Recheck serum magnesium after 5 days. All, oral magnesium products may cause diarrhoea. If the patient has diarrhoea or high output stoma, consider IV treatment.

- For Intravenous correction of hypomagnesaemia (perform ECG).
  - IV Magnesium Infusion is indicated if Mg is  $< 0.5$  mmol/L
  - If eGFR above 30- Give 24mmol of magnesium over 12hours in 500ml of Normal saline or 5% Dextrose
  - If eGFR is below 30- Give 12mmol of magnesium over 12hours in 500ml of Normal saline or 5% Dextrose
  - If eGFR is below 15- Give 6 mmol of magnesium over 12hours in 500ml of Normal saline or 5% Dextrose

- Oral Magnesium aspartate is used with caution if the eGFR is <30ml/min and in bradycardia (consult a Cardiologist).

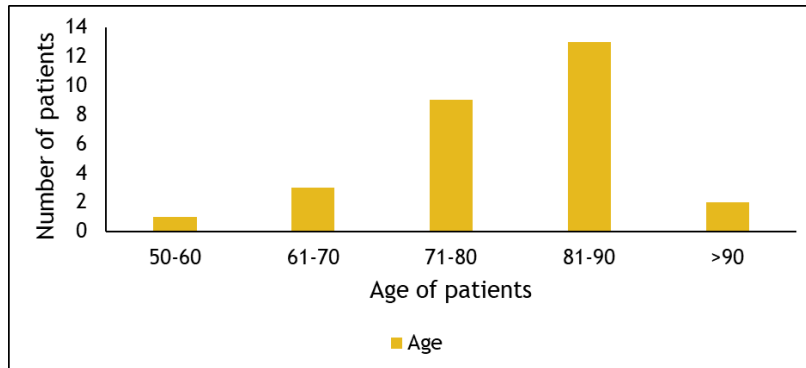
#### 4. Results

- Total number of patients: 28
- Male: Female = 7 (25%): 21(75%)



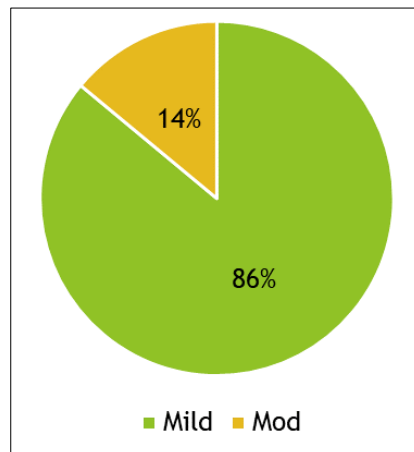
**Figure 1** Gender distribution

- Age distribution: 50-60 = 1, 61-70 = 3, 71-80 = 9, 81-90 = 13, >90 = 2



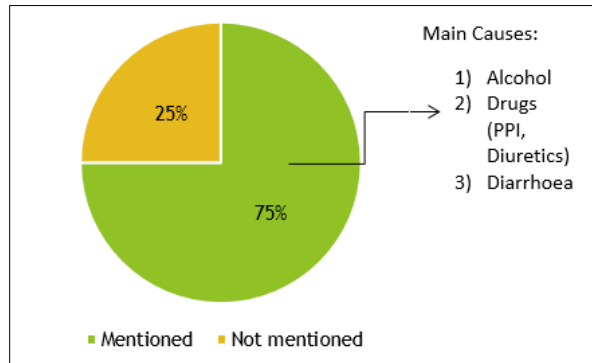
**Figure 2** Age distribution

- Category: Mild = 24 (86%), moderate = 4 (14%), severe= 0



**Figure 3** Category of hypomagnesaemia

- Aetiology that resulted in hypomagnesaemia (mentioned): 21(75%)

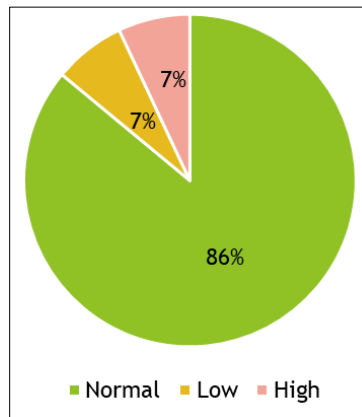


**Figure 4** Documentation of aetiology of hypomagnesaemia

- Family History of hypomagnesaemia taken - none (0%)

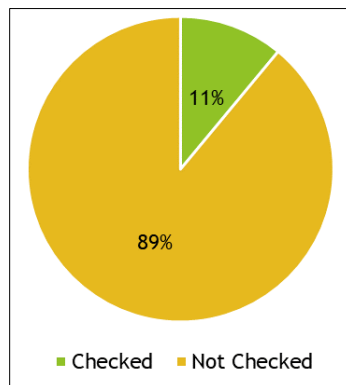
Genetic testing referral considered (needed if there is a positive family history or unexplained hypomagnesemia, or if discovered early in life) -none (0%)

- Bone profile checked -28 patients or 100% and U&Es done -28 patients or 100%; eGFR < 30 in 2 patients: Potassium: Low -9 patients or 32%, Calcium: Low -2 patients or 7%, High- 2 patients or 7%, Normal- 24 patients (86%)



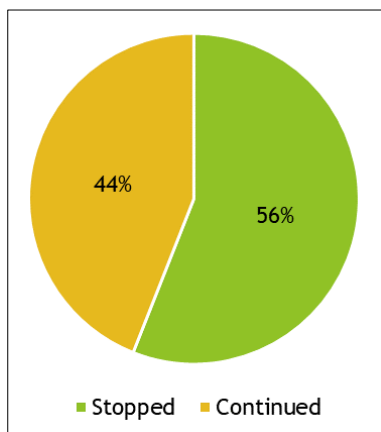
**Figure 5** Serum Calcium level

- PTH checked: 3 patients (11%)



**Figure 6** Serum PTH checked

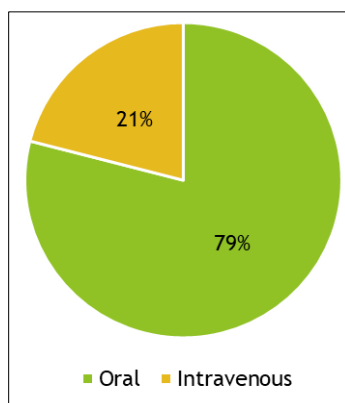
- Whether the patients were on offending drugs: 18/28 (64%), patients were either on PPI or diuretics or both; drugs stopped in 10/18 (56%) patients



**Figure 7** Whether offending drugs were stopped

- Whether ECGs were done: 28 patients (100%) – mention of prolonged QTc in 4 (14%) patients and arrhythmias 0%
- Assessment of Renal excretion of Magnesium done - none (0%)
- Examination done for vertical nystagmus and tetany; Chvostek sign and Trousseau sign checked - not mentioned in any patient (0%); confusion was present in 7 patients (but may be from other causes)
- The correct treatment options for hypomagnesaemia followed- 28 patients (100%)

Oral Magnesium Aspartate was given in 22 patients (79%); 4 patients had IV Magnesium sulphate because of low Serum Magnesium of <0.5 mmol/L and 2 patients had IV Magnesium for diarrhoea/increased stoma output.



**Figure 8** Method of Magnesium replacement

- Treatment dose of Magnesium supplements modified in case of low eGFR (100%): with eGFR< 30, 1 patient received Magnesium aspartate sachet 1 daily (10 mmol of magnesium) and 1 patient received IV magnesium sulphate 50% 10 mmol over 6 hours.
- Referral to ensure proper evaluation and management of hypomagnesaemia: Renal team - none (0%) and Gastro-intestinal Team - 7 patients (25%); 6 had pre-existing GI/Liver conditions and 1 had Liver abscess
- Patients or relatives informed of the importance of hypomagnesaemia and complications -4 (14%)

## 5. Summary and Conclusion

- Most of the patients were above 80 years of age (15 or 54%)
- There were 4 patients (14%) in the study with Serum Magnesium between 0.4 to 0.5 mmol/l
- The aetiology was not documented or found out in 7 patients (25%)
- There was no mention of the family history of hypomagnesaemia and no genetic referral considered in any case.

- Bone profile was checked in 100% cases, but the PTH was checked in 11% cases. Offending drugs were continued in 8/18 patients (44%)
- Prolonged QTc in ECG was mentioned in 14% patients.
- 24 hours urinary excretion of Magnesium was not done in any patient.
- Physical examinations for signs of hypomagnesaemia were not mentioned in any patient.
- The correct treatment options for hypomagnesaemia were followed in 100% patients.
- All 4 patients with Serum Magnesium < 0.5 mmol/L received IV magnesium Sulphate and in the 2 patients with eGFR < 30, the dose reduction of Magnesium supplementation was done.
- 25% patients had been referred to the GI team.
- 14% of patients or their relatives were explained the importance and consequences of low Serum Magnesium
- Serum Magnesium level is not often checked routinely. However, low serum magnesium is quite common and can co-exist with low serum calcium and potassium. Unless, hypomagnesaemia is treated, hypocalcaemia and hypokalaemia cannot be corrected. Also, very low serum magnesium can be life threatening. This audit aims to help the society in understanding the significance and complications of low serum magnesium and the way forward to managing such patients as mentioned above.

### *Recommendations*

- In all cases it is necessary to review the potential aetiology that can lead to hypomagnesaemia.
- Family History is to be taken and Genetic testing may be considered if there is a positive family history, unexplained hypomagnesemia, or if discovered early in life
- Check PTH along with bone profile and U&Es in all cases of hypomagnesaemia
- If possible, the offending drugs need to be stopped- for example PPIs can be replaced with Famotidine or Nizatidine
- ECG results are to be documented in all cases- whether there is prolonged QTc/ arrhythmias
- Physical examinations for nystagmus and tetany need to be checked with Chvostek sign and Trousseau sign
- To follow the treatment options for hypomagnesaemia according to the Guidelines for example to reduce the dose if the eGFR is <30 and to replace magnesium IV if the level is < 0.5 mmol/L or if there is diarrhoea or increased stoma output
- To check for 24 hrs urine magnesium, if no apparent cause is found
- To ensure referral to Renal and Gastro-intestinal Team for proper management as and when necessary
- Patient and/or their relatives need to be informed of the importance of hypomagnesaemia and the complications which can occur
- Re-audit in 1 year.

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### **Compliance with ethical standards**

#### *Acknowledgments*

We would like to acknowledge all Endocrine colleagues and the Secretaries for helping us with the data collection towards preparation of the audit.

#### *Disclosure of conflict of interest*

No conflict of interest.

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## **Appendix 1 (8)**

### Grading of Hypomagnesaemia

Severity of hypomagnesaemia is graded according to the National Cancer Institute-Common Terminology Criteria for Adverse Events (CTCAE), version 4, as follows:

- Grade 1 Mild: 0.5-0.7 mmol/L
  - Grade 2 Moderate: 0.4-0.5 mmol/L
  - Grade 3 Severe: 0.3-0.4 mmol/L
  - Grade 4 Life Threatening: < 0.3 mmol/L
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## **Appendix 2 (9)**

### Magnesium sulphate IV in Life threatening emergencies

- Severe acute asthma, continuing respiratory deterioration in anaphylaxis: 1.2–2 g IV, to be given over 20 minutes (2g is equivalent to 8 mmol)
- Emergency treatment of serious arrhythmias: 2 g IV, to be given over 10-15 minutes, dose may be repeated once if necessary.
- Treatment of seizures and prevention of seizure recurrence in eclampsia: Initially 4 g IV, to be given over 5–15 minutes, followed by (by intravenous infusion) 1g/hour for 24 hours after seizure or delivery (whichever is later), if seizure recurs, give an additional dose of 2–4 g by intravenous injection over 5–15 minutes.