

Guidelines for the Management of Hypomagnesaemia in Adult Clinical Haematology Patients

1. Introduction

Magnesium is essential for a number of intracellular functions and low levels may potentially be life-threatening. Patients within the Clinical haematology department frequently present with hypomagnesaemia and almost all patients will require magnesium replacement in the immediate post-transplant period and on-going magnesium replacement may be necessary for several weeks afterwards.

This guideline summarises the magnesium replacement options both oral and IV within the Adult **Clinical haematology department only**. The recommendations within this guideline are not intended for patients with impaired renal function; patients with impaired renal function will require dose adjustments and should be discussed with a haematology registrar on an individual basis.

See separate section for patients on pentamidine. This guideline does not cover the prescribing of magnesium for specialist uses e.g. pre-eclampsia, asthma or AF.

2. Causes of Hypomagnesaemia

Common causes of hypomagnesaemia seen in haematology patients include:

- Gastrointestinal losses: vomiting, diarrhoea, malabsorption (due to mucositis or Graft versus Host Disease especially in allograft patients)
- Renal losses
- Blood transfusion
- Hypercalcaemia and hypokalaemia
- Dietary deficiency and Re-feeding syndrome
- Syndrome of inappropriate antidiuretic hormone secretion
- Acidosis

Common drugs causing hypomagnesaemia in haematology patients include:

- Cisplatin
- Ciclosporin and tacrolimus
- Pentamidine (see point 6)
- Foscarnet
- Aminoglycosides
- Gentamicin
- Amphotericin B (Ambisome)
- Diuretics
- Proton Pump Inhibitors

3. Main Clinical Manifestations

4. Hypomagnesaemia can cause a number of symptoms and signs, most of which are non-specific and rarely occur unless the magnesium level is less than 0.4 mmol/L. They include:

- Neuromuscular symptoms: tremors, tetany, cramps, seizures, ataxia and muscle weakness.

- Cardiovascular symptoms: arrhythmias, enhanced digitalis toxicity, and nonspecific electrocardiographic changes, including ST-segment depression, altered T waves, or loss of voltage. Severe magnesium deficiency may cause PR prolongation or widened QRS complexes.
- Behavioural symptoms: irritability, confusion, depression and psychoses.

5. Grading

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	: <0.3mmol/L

Note: The majority of magnesium is stored in the bone, muscle and the liver, and it is primarily intracellular - the little that is extracellular is protein bound or ionized therefore hypoalbuminaemic states may cause levels to appear falsely low.

6. Management (See separate section for patients receiving Pentamidine)

The management of hypomagnesaemia depends upon the severity.

Magnesium level and Replacement options

Grade 1: Mild 0.5- 0.7mmol/L	Grade 2: Moderate 0.4-0.5mmol/L	Grades 3 and 4: Severe <0.4mmol/L	Notes
<p>Only replace if patient is symptomatic</p> <p>1st Line Oral: 1st Option: Magnesium Aspartate 10mmol sachets – 1 sachet twice daily 2nd Option: Magnesium glycerophosphate 8mmol (2 x 4mmol tablets) three times a day.</p> <p>2nd Line Intravenous: 10mmol magnesium sulphate in 100ml-1L sodium chloride 0.9% or glucose 5% over</p>	<p><i>Either:</i></p> <p>Oral: 1st Option: Magnesium Aspartate 10mmol sachets – 1 sachet twice daily 2nd Option: Magnesium glycerophosphate 8mmol (2 x 4mmol tablets) three times a day.</p> <p><i>OR</i></p> <p>Intravenous: 20mmol magnesium sulphate in 100ml-1L sodium chloride 0.9% n or glucose 5% over 3-12 hours.</p>	<p>Intravenous: 20mmol magnesium sulphate in 100ml-1L sodium chloride 0.9% or glucose 5% over 3-12 hours.</p> <p>(20mmol magnesium sulphate ≡ 10mL magnesium sulphate 50% injection)</p>	<p>Oral Replacement Oral magnesium salts commonly cause and may worsen diarrhoea.</p> <p>Intravenous Replacement 10mmol over 90 minutes or 20mmol over 3 hours are acceptable infusion rates on the Haem DTU Unit. A slower rate (6-12 hours) should be used on the ward.</p> <p>-Solution must be diluted before IV administration and mixed thoroughly. -Maximum concentration for peripheral IV infusion is 20% (i.e. 0.8 mmol/mL) using a large peripheral vein. -Maximum infusion rate is</p>

90minutes. (10mmol magnesium sulphate ≡ 5mL magnesium sulphate 50% injection)	(20mmol magnesium sulphate ≡ 10mL magnesium sulphate 50% injection)		36mmol/hour. Refer to the OUH IV Magnesium Monograph
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7. Management of hypomagnesaemia in patients receiving Pentamidine

Intravenous pentamidine is used in the treatment of and prophylaxis against Pneumocystis Jiroveci Pneumonia, (refer to Clinical Haematology [Pneumocystis Jiroveci Pneumonia guidelines](#), NSSG/BMT/Clinical management).

Cardiac arrhythmias have been reported in isolated cases with the administration of pentamidine, this is a particular risk in uncorrected hypokalaemia and or hypomagnesaemia. It is therefore important to ensure both the potassium and magnesium are within the normal limits prior to administration.

Checking levels

- Patients with known recurrent hypomagnesaemia or have risk factors for hypomagnesaemia (such as diarrhoea or medications known to cause low magnesium) should have their magnesium level checked **24 hours prior** to pentamidine administration.
- All other patients should have their magnesium checked **72 hours prior** to pentamidine administration.

Magnesium level and Replacement options in patients receiving Pentamidine

Magnesium Level	Grade 2: Moderate 0.5- 0.7mmol/L	Grades 3 and 4: Severe <0.5mmol/L	Notes
Replacement Options in patients receiving Pentamidine	Intravenous: 10mmol magnesium sulphate in 100ml-1L sodium chloride 0.9% or glucose 5% over 90 minutes. (10mmol magnesium sulphate ≡ 5mL magnesium sulphate 50% injection)	Intravenous: 20mmol magnesium sulphate in 100ml-1L 0.9% sodium chloride 0.9% or glucose 5% over 3-12 hours (20mmol magnesium sulphate ≡ 10mL magnesium sulphate 50% injection)	Intravenous Replacement 10mmol over 90 minutes or 20mmol over 3 hours are acceptable infusion rates on the Haem DTU Unit. A slower rate (5-12 hours) should be used on the ward. -Solution must be diluted before IV administration and mixed thoroughly. -Maximum concentration for

			<p>peripheral IV infusion is 20% (i.e. 0.8 mmol/mL) using a large peripheral vein. -Maximum infusion rate is 36mmol/hour.</p> <p>Refer to the OUH IV Magnesium Monograph</p>
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8. Notes:

- These recommendations are for patients with normal renal function only; patients with renal impairment will require dose reduction and should be discussed with a haematology registrar on an individual basis.
- Magnesium levels should be monitored at least weekly after discharge, the frequency may need to be increased depending upon response to treatment. Levels should be taken at least 48 hours after administration. Note; serum magnesium concentrations are usually elevated for 1-2 days following treatment, it takes 36-48 hours for the magnesium to fully redistribute to the body tissue.
- Concomitant hypokalaemia or hypocalcaemia should also be checked and corrected as appropriate.
- Major adverse effects of intravenous magnesium therapy are due to the development of hypermagnesaemia following too rapid administration or excessive administration of magnesium, symptoms may include: nausea, vomiting, flushing of the skin, thirst, hypotension, drowsiness, confusion, loss of tendon reflexes due to neuromuscular blockade, muscle weakness, respiratory depression, cardiac arrhythmias, coma and cardiac arrest. If toxicity is suspected treatment should be stopped immediately and an antidote, calcium gluconate may require to be given.

9. References

- Coleman J, Worvill C, Craig J. [Intravenous Magnesium Monograph](#). Oxford University Hospitals. February 2014.
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- Fuller T (2009) Hypomagnesaemia. Accessed online via www.medscape.com on 19.06.2011.
- Saif WM (2008) Management of Hypomagnesaemia in Cancer Patients Receiving Chemotherapy. Journal of Supportive Oncology. 6(5); 243-248
- White R, McGlen S. [Guidelines for the Acute Management of Hypomagnesaemia in Adults](#). Oxford University Hospitals NHS Trust. May 2015.

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Review

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