Intravenous Magnesium

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ABSTRACT

Objective: *To review the function and use of intravenous magnesium in magnesium depleted and non-magnesium depleted patients.*

Data sources: *A review of studies reported from 1966 to 1998 and identified through a MEDLINE search of the English-language literature on the use of intravenous magnesium.*

Summary of review: *Magnesium is a metalo-coenzyme that participates in numerous enzymatic reactions including all reactions that involve the formation and utilization of ATP. The cardiovascular, neurological and metabolic disorders caused by magnesium deficiency are associated with an increase in morbidity and mortality and can be rapidly corrected by magnesium therapy. There is also evidence that intravenous magnesium alters ion channels, NMDA receptors, and calcium metabolism, causing effects that are beneficial in a range of cardiovascular, respiratory and metabolic disorders, in the absence of magnesium deficiency. In these disorders intravenous magnesium sulphate is usually administered as an initial bolus varying between 8 - 16 mmol over 5 min, followed by an infusion of 2 – 4 mmol/h, to keep the plasma magnesium between 1.5 - 3 mmol/L.*

Conclusions: *Magnesium is required in patients who are magnesium depleted and is also of benefit in non-magnesium depleted patients with pre-eclampsia. It may also be of benefit in non-magnesium depleted patients with acute coronary syndromes, arrhythmias, acute asthma, stroke, seizures and spinal cord injury.* (**Critical Care and Resuscitation 1999; 1: 162-172**)

Key Words: Magnesium sulphate, intravenous magnesium, hypomagnesaemia, magnesium deficiency

Intracellular magnesium participates in over 300 phosphate transfer reactions, including all reactions that involve the formation and utilization of ATP. It has a critical role in the transfer, storage and utilization of energy within the body. Magnesium is also required for protein and nucleic acid synthesis and for a number of mitochondrial reactions. Magnesium deficiency occurs in up to 65% of critically ill patients and is associated with an increase in mortality.[1-4] There are also a variety of disorders in non-magnesium depleted patients where intravenous magnesium appears to have a therapeutic benefit. This review considers normal magnesium metabolism and examines the use of intravenous magnesium sulphate in magnesium deficient and non-magnesium deficient states.

MAGNESIUM HOMEOSTASIS

In the 70 kg adult, total body magnesium is approximately 1000 mmol; 60% is bound in bone, 39% is in the intracellular fluid compartment (35.5% bound, 2.5% free) and 1% is in the extracellular compartment. The plasma levels of magnesium range from 0.70 - 0.95 mmol/L and its distribution is, 33% protein bound (25% to albumin, 8% to globulin), 60% ionized (0.4 - 0.6 mmol/L), and 6% complexed with citrate and phosphate.[5] A circadian rhythm to serum magnesium has also been reported with levels tending to be lowest from 1100 to 1600 hours.[6] The total intracellular magnesium concentration is 15 mmol/L, whereas the ionized intracellular magnesium concentration ranges between 0.5 - 1.0 mmol/L (i.e. the ionic concentrations of magnesium are approximately the same outside and inside the cell).[7]

A shift of magnesium into or out of cells may increase or decrease the plasma magnesium concentration without altering the total body

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magnesium. For example, alkalosis and excess catecholamine states (e.g. phaeochromocytoma, trauma, acute myocardial infarction, catecholamine infusions) reduces, and acidosis increases, the extracellular magnesium concentration due to magnesium redistribution. Haemolysis may also spuriously elevate the plasma magnesium level.[8]

The daily oral magnesium intake is 8 - 20 mmol, 40% of which is absorbed in the jejunum and ileum by passive absorption. The glomerular filtration of magnesium is 100 mmol/day; 15% is absorbed in the proximal tubule, 70% is reabsorbed in the loop of Henle (most of which is reabsorbed in the thick ascending limb),[9,10] 10% is reabsorbed in the distal tubule and 5% is usually excreted (which ranges between 2.5 to 8 mmol/day).[11] The maximum renal tubular reabsorption for magnesium is at the normal plasma magnesium level, thus any increase in plasma magnesium is rapidly excreted by the kidney. In magnesium deficiency the renal loss can reduce to 0.05 - 0.10 mmol/day; and with normal renal function up to 200 mmol/day may be excreted.[4] The minimum daily requirement for magnesium is approximately 0.5 mmol/day.[12]

MAGNESIUM DEFICIENCY

Hypomagnesaemia is defined as a plasma level of less than 0.7 mmol/L and when caused by magnesium depletion (in the absence of abnormal renal magnesium losses), is associated with a 24 h urine magnesium excretion of less than 1 mmol. While a strong correlation has been reported between serum total and ionized magnesium levels,[13] magnesium depletion may exist in the presence of a normal total plasma magnesium level[5,14] and a normal ionized plasma magnesium level.[2]

Erythrocyte, mononuclear cell and muscle magnesium levels have been used to more accurately assess total body magnesium status. However, erythrocyte[15] and mononuclear cell[16] magnesium concentrations have been found to be no better than plasma magnesium, and skeletal or cardiac muscle magnesium estimations have the disadvantages of being invasive and technically difficult when determining magnesium status. Recently, techniques for measuring intracellular free magnesium, using microelectrodes and magnetic resonance imaging with radiolabled phosphorous, and magnesium-sensitive dyes have been reported,[17,18] although they are used largely as research tools and currently have little clinical application.

In patients with severe magnesium deficiency and normal renal function the renal excretion is minimal (e.g. 0.05 - 0.10 mmol/day). As the majority of an intravenous dose of magnesium is normally excreted in the urine in 24 h, 30 mmol of magnesium administered over 8 h and a 24 h collection of urine (commencing at the beginning of the magnesium infusion) can be used as an estimation of magnesium balance. If less than 70% of the dose (i.e. < 20 mmol) is excreted, the patient is magnesium deficient.[19] However, as renal dysfunction is common in the critically ill patient, magnesium excretion studies are infrequently performed in the intensive care unit.

Table 1. Causes of Magnesium Deficiency

Gastrointestinal disorders
Malabsorption syndromes
Starvation, malnutrition, liquid protein diets
Gastrointestinal tract fistulas
Short-bowel syndrome
Prolonged nasogastric suction
Diarrhoea
Pancreatitis
Parenteral nutrition
Alcoholism
Endocrine Disorders
Hyperparathyroidism
Hyperthyroidism
Conn's syndrome
Diabetes mellitus
Hyperaldosteronism (primary and secondary)
Renal losses
Renal tubular acidosis
Post obstructive diuresis
Diuretic phase of acute tubular necrosis
Bartter's syndrome
Gitelman's syndrome
Drugs
Aminoglycosides
Carbenicillin, ticarcillin
Amphotericin B
Osmotic, thiazide and loop diuretic therapy
Cis-platinum
Cyclosporine

Aetiology: Hypomagnesaemia may be caused by magnesium redistribution or magnesium depletion due to decreased intake or increased loss[20] (Table 1). While loop, osmotic and thiazide diuretics are associated with magnesium depletion, potassium sparing diuretics (spironolactone, amiloride and triamterene) are also magnesium sparing, and do not cause magnesium depletion. Carbonic anhydrase has little effect on magnesium balance.[21]

Clinical features: The clinical features of hypomagnesaemia are uncommon and tend to occur only when the plasma level is less than 0.5 mmol/L.[22,23]

They usually manifest as neurological, cardiovascular or metabolic disturbances (Table 2).

Table 2. Clinical features of hypomagnesaemia

Neurological
Confusion, irritability, delirium, convulsions
Depression, psychosis
Ataxia, athetoid movements
Weakness, tremors, cramps, tetany
Trousseau and Chvostek signs
Cardiovascular
Tachyarrhythmias
Enhanced digoxin toxicity
Biochemical
Resistant:
hypokalaemia
hypocalcaemia
renal tubular acidosis
diabetic keto acidosis
lactic acidosis

Cardiovascular disturbances

The influence magnesium has on potassium and calcium metabolism in myocardial and smooth muscle tissue explains, to a large degree, its effect on the cardiovascular system.

Intracellular magnesium augments inward rectification of potassium (i.e. allows potassium to pass into the cell more readily than out of the cell by blocking potassium channels from the inner surface of the sarcolemma)[7,24]. Inward rectification of potassium is inhibited when magnesium is sufficiently reduced,[25] increasing early after depolarizations (i.e. oscillations in the transmembrane potential occurring before the cell has had a chance to repolarised fully) leading to repetitive membrane depolarisations (i.e. triggered activity) which may manifest clinically as polymorphic ventricular tachycardia (an effect which is suppressed by intravenous magnesium).

Magnesium has also been described as 'nature's physiologic calcium blocker', inhibiting Ca^{2+} induced myocardial muscle contraction by, inhibiting the release of Ca^{2+} from the sarcoplasmic reticulum, increasing the uptake of Ca^{2+} by the sarcoplasmic reticulum (by stimulating the Ca-ATPase activity) and competing with Ca^{2+} at certain binding sites on troponin C and myosin.[26] Unlike the synthetic calcium-blockers, increasing extracellular Mg^{2+} has not been shown to block the entry of Ca^{2+} into the cell through the slow channel,[26] although increasing intracellular magnesium experimentally inhibits calcium entry through the dihydropyridine-sensitive channels.[27] While magnesium has a calcium inhibitory effect, at plasma levels < 10 mmol/L, it appears to have no negative inotropic effect.[28]

Arrhythmias: The ECG changes associated with hypomagnesaemia include prolongation of the QT_c segment, U waves (although these are most likely due to an associated hypokalaemia), and ventricular and atrial tachycardias.[29,30] Magnesium deficiency also increases the incidence of digoxin induced arrhythmias and reduces the ventricular response to digoxin in atrial fibrillation (both effects are reversed with intravenous magnesium sulphate).[21] Bolus (e.g. 4 - 8 mmol) followed by continuous intravenous infusions (e.g. 4 - 8 mmol/h) of magnesium sulphate is the treatment of choice in all hypomagnesaemic induced cardiac arrhythmias.[29,31-33]

Cardiac failure: In hypomagnesaemic patients, cardiac failure[34] and cardiogenic shock[35] have been described and treated successfully with intravenous magnesium sulphate infusions. In acute pernicious (i.e. sho-shin) beri-beri, thiamine resistance can occur if magnesium depletion coexists.[36]

Angina: Hypomagnesaemia has been reported to cause coronary artery spasm[37] (which is reversed with intravenous magnesium sulphate),[38,39] and has been associated with sudden death in patients with ischaemic heart disease.[40] Patients with chronic low plasma and myocardial levels of magnesium have also been reported to have a high incidence of atherosclerotic ischaemic heart disease and acute myocardial infarction.[41,42]

Neurological disturbances

The neurological disturbances associated with magnesium depletion include confusion, irritability, depression, weakness, tremors, cramps, tetany, psychosis, ataxia, athetoid movements, delirium and convulsions. Trousseau and Chvostek signs have also been reported, although these signs are rare.

Metabolic disturbances

Magnesium depletion often causes hypokalaemia (due to hypomagnesaemia causing impaired Na/K ATPase activity, impaired K-Na-Cl cotransport and increased efflux through K channels,[43] which in turn lead to an increased renal potassium loss[44]). In one study more than 40% of hypokalaemic patients had an associated hypomagnesaemia.[45] In hypokalaemic patients, magnesium may be repleted with potassium in a molar ratio of 1:8.[46] The magnesium depletion induced hypocalcaemia is caused by an impaired synthesis and/or release of PTH and impaired peripheral action of PTH (which is not associated with hyperphosphataemia).[47] If hypomagnesaemia is not corrected, then the associated hypocalcaemia and

hypokalaemia are often resistant to therapy. Magnesium deficient Type I renal tubular acidosis has also been reported.[48]

Treatment: Magnesium sulphate is the most widely available intravenous preparation, and while intravenous salts of chloride and aspartate have also been used, it is the magnesium ion (and not its anion) that modulates the biological effects.[21]

Treatment of acute magnesium deficiency consists of intravenous magnesium sulphate, 0.15 mmol/kg being given for each 0.1 mmol/L of plasma magnesium less than 0.7. This is usually administered as a bolus of 10 mmol over 10 minutes (if it is administered too rapidly it may cause unpleasant flushing) followed by an infusion of 20-60 mmol over the next 24 h. Plasma levels of magnesium should be measured on admission and daily thereafter. When normal plasma levels are achieved, 4 - 8 mmol/day of magnesium are administered. If renal failure exists, the intravenous dosages should be halved and the plasma magnesium levels closely monitored. Magnesium administration should cease if the plasma level is > 1.5 mmol/L.

This dose has also been recommended for all critically ill patients with normal renal function who have no symptoms of magnesium deficiency.[3,4,23] Oral magnesium chloride may be administered to patients with mild or chronic magnesium deficiency and normal gastrointestinal function.

NON-MAGNESIUM DEFICIENT DISORDERS

Magnesium therapy has also been used for a wide range of non-magnesium deficient cardiovascular, neurological, gynaecological, respiratory and other miscellaneous disorders (Table 3). For example;

Cardiovascular disorders

In normomagnesaemic patients, intravenous magnesium sulphate, when used to elevate plasma concentrations up to 2 mmol/L, causes coronary and systemic vasodilation (reducing coronary artery spasm and blood pressure, respectively), inhibits platelet function (by inhibiting fibrinogen binding to the platelet GPIIb/IIIa receptor[49]) prolongs bleeding time[50] and has antiarrhythmic effects.[51] It also causes a slight decrease in heart rate (a direct effect on the sinus node), and prolongs the PR interval (due to an increase in the PA and AH interval without altering the HV interval), with no effect on the QRS (except at high doses) or QT_c duration.[21,52-54] Magnesium decreases the sympathetic tone by causing a sympathetic ganglia blockade[55], and prior magnesium treatment reduces postganglionic sympathetic nerve fibre noradrenaline release (and storage) during stimulation.[56,57] Magnesium may also enhance parasympathetic tone.[58] However, during a magnesium infusion, plasma noradrenaline and neuropeptide-Y-like activity increases.[59]

Table 3. Normomagnesaemic disorders where intravenous magnesium treatment has been used

Cardiovascular disorders
Atrial and ventricular tachyarrhythmias
Acute coronary syndromes
Acute hypertension associated with,
Tetanus
Phaeochromocytoma
Post coronary artery bypass surgery
Neurological disorders
Seizures
Stroke
Cerebral vasospasm
Spinal cord injury
Obstetric disorders
Pre-eclampsia
Eclampsia
Tocolytic
Respiratory disorders
Asthma
COAD exacerbation
Miscellaneous disorders
Post-operative analgesia
Tetanus
Aluminium phosphide poisoning

Arrhythmias: Both intravenous bolus (8 mmol over 1 minute) and continuous intravenous infusions of magnesium sulphate have been used to treat ventricular ectopics and ventricular tachycardia.[60,61] It is the treatment of choice in digoxin induced tachyarrhythmias,[62-64] torsades de pointes,[60,65] multifocal atrial tachycardia,[66,67] and in halothane[68] or lithium[69] induced cardiac arrhythmias, and has been recommended to treat alternating ventricular fibrillation and asystole during cardiac arrest.[70] In one study, magnesium sulphate was more effective than amiodarone in converting acute atrial tachyarrhythmias in critically ill patients.[71] In a prospective randomised controlled study of in-hospital cardiac arrest, magnesium (8 mmol bolus followed by 32 mmol over the next 24 h), did not improve immediate or long-term morbidity or mortality.[72]

Hypertension: Intravenous magnesium sulphate causes a direct peripheral arteriolar vasodilation which may be associated with a generalised warm and tingling sensation and reduction in blood pressure.[73] Continuous infusions have been used to treat acute hypertension

associated with pre-eclampsia, tetanus[74] and phaeochromocytoma.[75]

Cardiac failure: Intravenous magnesium sulphate does not have a direct effect on myocardial contractility in normal individuals.[28]

Angina: In patients with unstable angina an infusion of intravenous magnesium sulphate (8 mmol bolus followed by 3 mmol/h for 24h) has been reported to be associated with a reduction in CKMB release, a more rapid regression of T wave changes, and reduced adrenaline excretion, when compared with a placebo.[76,77] Magnesium has also been reported to be of benefit in patients with variant angina.[38,39]

Acute myocardial infarction: an infusion of intravenous magnesium sulphate (8 mmol over 5 minutes, followed by 65 mmol over 24 h) has been reported to be associated with a decrease in mortality in normomagnesaemic patients with acute myocardial infarction;[51,78-80] even when thrombolytic and aspirin therapy was used, mortality was reduced by a further 25% (i.e. by 2.5 patients per 100 patients).[51] The serum magnesium concentration usually increased to 1.55 mmol/L, in patients without renal failure[51] and if the bolus was not followed by an infusion, the serum magnesium level returned to normal after 20 minutes.[81] The time of intravenous magnesium administration in acute myocardial infarction may be critical, as magnesium given at a mean of 3 h after the onset of chest pain appears to be beneficial whereas magnesium given at a mean of 8 h is not.[82] In the experimental model magnesium reduces the myocardial infarct size when given before coronary reperfusion (i.e. before thrombolysis) but not after.[83] The elevated plasma magnesium is thought to reduce the reperfusion injury by blocking intracellular calcium[84] and attenuating free radical generation.[85]

In the fourth international study of infarct survival (ISIS-4), no significant advantage was recorded with intravenous magnesium sulphate (8 mmol in 15 minutes followed by 72 mmol in 24 h) in any patient group (e.g. with or without thrombolytic therapy, and in those in whom it was infused before thrombolytic reperfusion had probably occurred).[86] However, the optimal 24 h dose of magnesium may be between 50 to 65 mmol and that doses of > 75 mmol (ISIS-4 used 80 mmol/24h) may increase mortality (due to an increase in bradyarrhythmias and heart failure);[87] accordingly, some believe that the use of magnesium in myocardial infarction warrants reexamination.[88]

Cardiac surgery: In one study an intravenous infusion of 8 mmol of magnesium (over 20 minutes) decreased the incidence of ventricular arrhythmias and increased the cardiac index in post cardiac surgery patients.[89] In another study, intravenous magnesium sulphate (16 mmol continuously from the time of anesthetic induction to aortic cross-clamping followed by 32 mmol starting after the release of aortic cross-clamp until 24 hours later) improved myocardial recovery following cardiac surgery.[90] It increased left ventricular stroke work index, reduced the incidence of ventricular arrhythmias and reduced postoperative hypertension compared with the control group.[90] Intravenous magnesium sulphate (2 - 8 mmol bolus over 2 - 5 minutes, up to 30 - 40 mmol during the first 12 h post operative period) may also be used to control hypertensive episodes (and episodes of shivering and tachycardia). It also reduces the postoperative analgesic requirement[91] and promotes normal sleep.[92]

Magnesium is also added to cardioplegic solutions to prevent myocardial substrate derangements during reperfusion.[93]

Neurological disorders

The magnesium ion blocks the NMDA ion channel in a voltage-dependent fashion, although electrophysiologically, extracellular magnesium behaves as a noncompetitive NMDA antagonist.[94]

Seizures: Magnesium sulphate is used to control seizures associated with eclampsia, beginning with 10 - 15 mmol of magnesium sulphate administered intravenously over 5 minutes, followed by an infusion of 4 mmol/h, to achieve blood levels of 2.0 - 3.0 mmol/L. While, magnesium sulphate has not been found to be effective in terminating experimental myoclonic status epilepticus,[95] it has been used successfully in terminating experimental hippocampal seizure activity[96] and as an antiepileptic agent in clinical practice for seizures unrelated to eclampsia (e.g. seizures associated with cerebral ischaemia[97] and porphyria[98]).

It is believed by some that the antiepileptic activity associated with intravenous magnesium sulphate in eclampsia is a nonspecific anticonvulsant effect, due to its ability to reverse the underlying pathophysiology of eclamptic seizures (i.e. reverses cerebral vasoconstriction[99]) and not as an NMDA receptor inhibitor[100] (as only a small amount of magnesium crosses the blood brain barrier in patients with preeclampsia undergoing magnesium therapy[101]). However, as the small rise in CSF magnesium level (by up to 18% above physiological concentrations[102]) is a significant one, others believe that magnesium has a central anticonvulsant action involving the N-methyl-D-aspartate receptor[103] (e.g. as a noncompetitive NMDA antagonist[94]). In the experimental model, magnesium sulphate has also been found to reduce the seizure activity associated with hyperbaric oxygen toxicity.[104]

Stroke. While the NMDA receptor antagonists eliprodil, aptiganel and lubeluzole have also shown little

promise in patients with stroke, encouraging results have been found with magnesium sulphate.[105,106] A trial evaluating intravenous magnesium sulphate (16 mmol, followed by 65 mmol over 24 h) for acute stroke is currently underway.[107]

Cerebral vasospasm with subarachnoid haemorrhage. Intravenous and intrathecal magnesium sulphate have been used successfully in the experimental model to reverse cerebral vasospasm.[108]

Spinal cord injury. In the experimental model, intrathecal magnesium sulphate has been used to prevent spinal cord injury during aortic cross clamping.[109] In clinical practice, intravenous magnesium has been reported to offer some protection to the spinal cord during the repair of the aorta (acting as an N-methyl-D-aspartate antagonist).[110]

Gynaecological disorders

Pre-eclampsia. Continuous management of hypertension and hyper-reflexia, in patients who are admitted to hospital for delivery, using a loading dose of 16 mmol of intravenous magnesium sulphate over 5 min, followed by 4 mmol/h and continued for 24 h after delivery, is more effective than phenytoin in preventing eclampsia.[111] This dose of magnesium sulphate is also more effective than diazepam or phenytoin in controlling eclamptic seizures.[112] If renal failure occurs, the magnesium infusion is modified using plasma magnesium levels.

Therapeutic plasma levels of magnesium are between 2 and 3.5 mmol/L, and should be monitored 6 to 12-hourly, as respiratory paralysis may occur at plasma levels of greater than 5.0 mmol/L.[113]

Tocolysis. Intravenous magnesium sulphate (4 mmol/h to keep the serum level at 2-3 mmol/L) in association with a $beta_2$ agonist, has been used successfully as a long term tocolytic agent.[114,115]

Respiratory disorders

Asthma: Magnesium sulphate (5 mmol) intravenously, has been reported to relieve broncho-spasm, in mild asthmatic attacks[116,117] and in patients resistant to beta-adrenergic agonists.[115] High dose intravenous magnesium sulphate (40 - 80 mmol over 1 h) has also been used to reverse life threatening and refractory status asthmaticus,[118] although, two prospective studies reported no benefit from magnesium sulphate in patients with acute asthma.[119,120] In one randomised double blind controlled trial, nebulised magnesium sulphate (3 ml 3.2% solution) had a significant bronchodilatory effect in acute asthma which was as effective as 2.5 mg of nebulised salbutamol.[121] However, intravenous magnesium sulphate has been found to be of no benefit to airflow limitation in chronic stable asthmatics.[122]

Exacerbation of COPD. In one double blind randomised study, intravenous magnesium sulphate (5 mmol over 20 minutes after 2.5 mg of nebulised salbutamol), was found to be safe and efficacious in the treatment of acute exacerbations of chronic obstructive pulmonary disease.[123] Its bronchodilator effect was greater than that of the salbutamol given alone and it lasted beyond the period of magnesium sulfate administration.

ARDS. In the experimental animal, magnesium sulphate (keeping plasma level between 2-3 mmol/L) has been shown to reduce pulmonary oxygen toxicity.[124]

Miscellaneous disorders

Tetanus. Alternating episodes of severe hypotension and hypertension may occur in patients with tetanus in spite of deep sedation, and has been successfully managed by intravenous magnesium sulphate (8 - 12 mmol/h, to maintain the serum magnesium between 2 - 4 mmol/L).[125] Magnesium sulphate has also be used to control tetanic spasms[126] and in one report mechanical ventilation was avoided in eight patients with tetanus by using 10 mmol as a loading dose followed by an infusion of 4 - 6 mmol/h (increasing as required, to control spasms while retaining the patella tendon reflex to avoid overdosage).[127]

Postoperative analgesia. Intravenous magnesium sulphate (2 - 8 mmol over 2 - 5 minutes, and up to 30 - 50 mmol during the first 12 h post operative period, in the presence of normal renal function) reduces shivering, tachycardia, postoperative analgesic requirements and promotes normal sleep.[92] The side-effect of recurarisation (magnesium inhibits the release of acetylcholine from the motor nerve terminal) can be reduced by administration of calcium chloride.[128]

Other. Magnesium sulphate (30 mmol for the first 24 h followed by 16 mmol/24 h for 5 days[129]) has been used to treat aluminium phosphide poisoning[130] (where it appears to act as an antioxidant).[131] It has also been used in the treatment of experimental malignant hyperpyrexia[132] (to inhibit calcium release from the sarcoplasmic reticiulum[133]). Intravenous magnesium sulphate (4 mmol) has also been shown to rapidly relieve headaches (particularly in patients with low ionised magnesium levels[134]) and in the chronic fatigue syndrome.[135] It has also been used during induction of anaesthesia for coronary artery bypass grafting (10 – 14 mmol i.v.) to attenuate the endotracheal haemodynamic response.[136]

SIDE EFFECTS

The adverse effects of intravenous magnesium

sulphate include an unpleasant flushing, nausea and vomiting, particularly if it is administered too rapidly.

The lethal effects of severe hypermagnesaemia (i.e. > 10 mmol/L) are neurological (e.g. fixed dilated pupils,[137] neuromuscular block with respiratory failure) and cardiovascular (e.g. junctional or sinus bradycardia, sinoatrial block, AV block, and asystole[138]). While some believe that a rationale exists for the use of intravenous magnesium in patients with high plasma potassium levels[21], magnesium can potentiate myocardial conduction abnormalities (e.g. sinus arrest, AV nodal block, first-, second- or third-degree heart block and asystole) and therefore is probably contraindicated in patients with hyperkalaemia. However, in hyperkalaemia associated with digoxin poisoning, intravenous magnesium sulphate may eliminate refractory ventricular tachycardia and decrease the serum potassium.[139] The plasma levels and clinical effects of hypermagnesaemia are shown in table 4.

Table 4. Plasma levels and clinical effects of hypermagnesaemia

Plasma concentration (mmol/L)	*Clinical effects*
0.7-1.0	Normal range
2.0-3.5	Therapeutic range for eclampsia
3.0-5.0	ECG changes
4.0-5.0	Areflexia
6.0-7.0	Respiratory arrest
10-12.5	Cardiac arrest

Treatment. Treatment of hypermagnesaemia is directed towards increasing its excretion, which may require dialysis. Intravenous calcium chloride may be used for rapidly treating the cardiac conduction defects[47].

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