

USE OF MAGNESIUM SULPHATE IN CRITICAL CARE

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Magnesium sulphate has long been used in the treatment of eclampsia to control the fits. It has been shown to reduce the central nervous system irritability and to enhance the threshold of the central neurones to fire spontaneously. This observation led to many investigators to search any possible role for magnesium sulphate in the prevention of eclamptic fits by using it in pre-eclamptic patients. However the results were conflicting. The tocolytic effects of this drug in this category of patients led to many unwanted consequences, including prepartum / post-partum haemorrhage and uterine atony.¹⁻³ This effect was presumed to be due to its effect on uterine smooth muscle as well as blood vessels. No effect was found on the coagulation profile itself.⁴

An interesting co-finding of use of the drug in eclamptic patients was that the drug had a protective role against cerebral palsy in very low birth weight infants. Nelson and Greathner confirmed this finding in their retrospective study⁵. They found that overall survival was improved in infants, weighing <1500g, born to mothers, who received Mg SO₄ due to preeclampsia or as a tocolytic agent. This association was also confirmed by Blair and co-workers.⁶

Magnesium sulphate has a role in the treatment of premature infants, admitted to neonatal critical units with persistent pulmonary hypertension. It has been used with satisfaction for this purpose. The drug causes significant decrease in AaDo₂ at 36 hours,⁷ but the decrease of oxygenation index does not reach significance even after 72 hours.

Over the past few years the role of magnesium sulphate has been widely investigated in the treatment of acute asthma. Beta - adrenergic agonists are useful for the emergency treatment of asthma, but these have unwanted side-effects, e.g increased systolic blood pressure, corrected QT interval (QTc), serum glucose and insulin and decreased RR interval, diastolic blood pres-

sure, serum potassium, phosphate, and calcium. Concurrent use of magnesium sulphate with terbutaline has been shown to enhance these effects, modestly. But in patients with stable cardiac and metabolic function, no serious adverse actions have been reported.⁸ It has been shown that when given with standard protocol drugs, magnesium sulphate improves FEV₁ at 120 to 240 minutes, and reduces hospital admission rate. This effect is more pronounced in acute severe asthmatics, whereas moderate asthma and chronic stable asthma did not respond to any significant levels,⁹⁻¹¹. The drug may safely be used as adjunctive treatment for acute exacerbation of chronic obstructive pulmonary disease. A dose of 1.2g over 20 minutes after beta-agonist administration, is safe and modestly efficacious in the treatment of acute exacerbations of chronic obstructive pulmonary disease, and its bronchodilator effect is greater than that of a beta-agonist given alone and lasts beyond the period of magnesium sulfate administration.¹²

The use of magnesium sulphate in acute stroke has been demonstrated recently. Magnesium ions act as endogenous vasodilators of the cerebral circulation and act pharmacologically as noncompetitive antagonists of the N-methyl-D-aspartate receptor by virtue of their role as endogenous voltage-sensitive blockers of the ion channel. The preclinical efficacy of magnesium has been demonstrated in standard models of stroke. It has been shown that the drug has neuroprotective action in focal brain ischaemia and reduces early mortality and has no deleterious haemodynamic effects. Further trials are required to confirm efficacy. It has been suggested that to gain optimum benefits out of this regimen, a loading dose of 16mmol, followed by 65mmol over 24 hours gives best results.¹³⁻¹⁴

The role of magnesium in treating acute myocardial infarction (AMI) has been controversial. Several small clinical trials indicate that magnesium may have a role in treating AMI early, whereas the other results suggest

that magnesium is of questionable benefit. Chirstenson and co-workers have suggested that magnesium infusion during a coronary occlusion has a significant benefit in reducing the infarct size (IS). Magnesium may have a beneficial clinical role in AMI, especially if administered before reperfusion as bolus followed by a constant infusion.¹⁵ Fourth International study of Infarct Survival (ISIS-4) compared efficacy of early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction, and concluded that magnesium sulphate was equal if not superior to captopril, as far as the mortality rate was concerned.¹⁶ This is achieved probably by direct vasodilatory effect, thereby reducing the infarct size, and also by an antithrombotic effect.¹⁷⁻¹⁸⁻¹⁹

Although MgSO₄ has been claimed to be effective in different cardiac arrhythmias, especially in patients suspected of having myocardial ischaemia, only prolongation of RR interval at AV nodal level in atrial tachycardia could be proven to be prolonged. It had no effect on ventricular fibrillation, ventricular tachycardia, atrial fibrillation or heart block of any degree. The reduction in mortality that has been shown with this form of treatment is not attributable to suppression of life threatening rhythm disturbances.²⁰⁻²⁴

Magnesium sulphate, once regarded only as a laxative agent, has thus found many uses, and has emerged as a useful tool in the hands of critical care physician.

REFERENCES

1. Duley L; Neilson JP, Magnesium sulphate and pre-eclampsia. Trial needed to see whether it's as valuable in pre-eclampsia as in eclampsia [letter], *BMJ [Clinical Research ed]*. 1999;7901;3-4.
2. Duley L, Neilson J, Watkins K More studies are needed before giving magnesium sulphate for pre-eclampsia [letter; comment] *BMJ (Clinical Research ED.)* 1999;318;809.
3. Jones P, Johanson R, Baldwin KJ, Lilford R, Jones P, Changing belief in obstetrics; impact of two multicentre randomised controlled trials [letter], 1998;352;1988-1989.
4. James MF, Neil G. Effect of magnesium on coagulation as measured by thrombelastography. *Br. J. Anaes*; 1995;74
5. Nelson Kb, Greather JK, Can magnesium sulfate reduce the risk of cerebral palsy in very low birthweight infants ? *Pediatrics*, 1995;95;263-269.
6. Blair E; Palmer L, Stanley F , Cerebral palsy in very low birth weight infants, pre-eclampsia and magnesium sulphate, *Pediatrics*, 1996;97;780-782.
7. Wu TJ, Teng RJ, Tsou KI. Persistent pulmonary hypertension of the newborn treated with magnesium sulfate in premature neonates. *Pediatrics*, 1995;96;472-474.
8. Skorodin MS; Freebeck PC, Yetter B, Nelson JE, Van de Graff WB, Walsh JM, Magnesium sulfate potentiates several cardiovascular and metabolic actions of terbutaline. *Chest*, 1994;105;701-705
9. Fitz Gerald JM Mangesium sulfate is effective for sever acute asthma treated in the emergency department. *Western Journal of Medicine* 2000;172;96.
10. Bloch H, Silverman R, Mancherje N, Grants S, Jagminas L, Scharf SM, Intravenous magnesium sulfate as an adjunct in the treatment of acute asthma *Chest*, 1995;107;1576-1581.
11. Bernstein WK; Khastgir T, Kastgir A, Hernandez E, Miller J; Schonfeld SA, Nissim JE, Chemow B, Lacc of effectiveness of magesium in chronic stable asthma, A prospective, randomized double-blind, placebo-controlled, crossover trial in normal subjects and in pateitns with chronic stable asthma. *Arch of Int Medicine*. 1995;155;271-276.
12. Skorodin MS; Tenholder MF; Yetter B; Owen KA; Waller RF; Khandelwahl S; Maki K; Rohail T; D'Alfonso N, Magnesium sulfate in exacerbations of chronic obstructive pulmonary disease. 1995;155;496-500.
13. Muir KW; Lees KR , A randomized, double-blind, placebo-controlled pilot trial of intravenous magnesium sulfate in acute stroke. *Stroke*, 1995;26;1183-1188
14. Muir KW; Lees KR Dose optimization of intravenous magnesium sulfate after acute stroke. *Stroke*.1998;29;918-923
15. Christensen CW; Rieder MA; Silverstein EL; Gencheff NE , Magnesium sulfate reduces myocardial infarct size when administered before but not after coronary reperfusion in a canine model, *Circulation* 1995;92;2617-2621
16. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. *LANCET*, 1995;345;669-685
17. Ravn HB; Moeldrup U; Brookes CI; Ilkjaer LB; White P; Chew M; Jensen L; Johnsen S; Birk-Soerensen L; Hjortdal VE, Intravenous magnesium reduces infarct size after ischemia/reperfusion injury combined with a thrombogenic lesion in the left anterior descending artery. *Arteriosclerosis, Thromobosis, & Vascular Biology*, 1999;19;569-574
18. Shibata M; Ueshima K; Harada M; Nakamura M; Hiramori K; Endo S; Sato N; Mukaida H; Suzuki T; Suzuki T; Inada K, Effect of magnesium sulfate pretreatment and significance of matrix metalloproteinase-1 and interleukin-6 levels in coronary reperfusion therapy for patients with acute myocardial infarction. *ANGIOLOGY*, 1999;50;573-582
19. Elder AN , Giving i.v. magnesium in acute m.i. *NURSING*, 1995;25;32VV,32XX-32YY
20. Winters SL; Sachs RG; Curwin JH, Nonsustained polymorphous ventricular tachycardia during amiodarone therapy for atrial fibrillation complicating cardiomyopathy. Management with intravenous magnesium sulfate. *CHEST*, 1997;111;1454-1457.
21. Roffe C; Fletcher S; Woods KL, Investigation of the effects of intravenous magnesium sulphate on cardiac rhythm in acute myocardial infarction. *BRITISH HEART JOURNAL*, 1994;71;141-145
22. Ingemansson MP; Carlson J; Olsson SB, Modification of intrinsic AV-nodal properties by magnesium in combination with glucose, insulin, and potassium (GIK) during chronic atrial fibrillation. *JOURNAL OF ELECTROCARDIOLOGY*, 1998;31;281-292
23. Chamberlain DA, Antiarrhythmic drugs in resuscitation. *Heart*, 1998;80;408-411
24. Magnesium sulfate., *Dimensions of critical care nursing*, 1999;18;24