British Journal of Anaesthesia 1995; 74: 92–94

Effect of magnesium on coagulation as measured by thrombelastography

M. F. M. JAMES AND G. NEIL

Summary

Magnesium has long been assumed to have anticoagulant properties, but the effect has been poorly quantified. The thrombelastograph (TEG) was used to evaluate the effect of magnesium using blood from volunteers. Magnesium sulphate was added to one blood sample and another sample was used as a control. Both samples were tested simultaneously and the results evaluated against the magnesium concentration measured in each sample. At serum magnesium concentrations < 3 mmol litre^{-1}, there were no significant effects of magnesium. With increasing magnesium concentrations there was a statistically significant but small prolongation of the r time, k time and $r+k$ time. Maximum amplitude was affected only at magnesium concentrations > 7 mmol litre^{-1}. Magnesium has only minimal effects on coagulation which are unlikely to be clinically important. (*Br. J. Anaesth.* 1995; **74**: 92–94)

Key words

Blood, coagulation. Measurement techniques, thrombelastography. Ions, magnesium

It has long been suggested that magnesium may have antiplatelet and antithrombotic properties [1] but there have been few studies which have demonstrated this effect conclusively. The literature has been reviewed extensively by Arsenian who argued that some of the beneficial effects of magnesium in myocardial infarction may result from the mild anticoagulant effects [2]. While an anticoagulant effect of magnesium could be beneficial in some circumstances, such an effect could make placement of extradural catheters hazardous in patients receiving magnesium therapy, and may result in an increased risk of surgical bleeding in patients given magnesium salts during operation. We therefore conducted an *in vitro* study of the effects on coagulation, as measured by the thrombelastograph (TEG), of varying magnesium concentrations across the concentration range likely to be seen in clinical practice.

Methods and results

Venous blood (10 ml) was sampled from 30 healthy, conscious volunteers and separated immediately into two aliquots of 4 ml each in polypropylene plastic tubes. Magnesium sulphate 50% was added to one aliquot in volumes of 2–9 µl with the objective of increasing the plasma concentration of magnesium in that specimen to 2–9 mmol litre^{-1}. The other sample was not treated. Specimen tubes containing each sample were inverted several times to ensure thorough and similar mixing of the blood in each tube. Specimens from each sample (0.360 ml) were added to the TEG within 3 min of sampling and simultaneous traces recorded of the normal blood and magnesium treated samples. The remainder of each sample was sent for laboratory analysis of serum magnesium concentration (xyledile blue method). The TEG trace was recorded for 1 h and the r and k times, alpha angle (α), maximum amplitude (MA) and amplitude 60 min were measured for each sample.

The results obtained from the test blood were allocated to groups depending on the measured serum concentration of magnesium (Mg^{2+}). The groups were 1–3, 3–5, 5–7 and > 7 mmol litre^{-1}. All untreated samples were allocated to a control group. The TEG measurements were compared for each magnesium group to the control group using analysis of variance for repeated measures with 95% confidence interval testing to identify significantly different groups. The magnesium concentrations were also tested using regression analysis for correlation with the measured TEG variables.

There was a significant slope to the regression line for most TEG variables against serum Mg^{2+} concentration but the correlation was poor. At serum Mg^{2+} concentrations less than 3 mmol litre^{-1} there was no detectable effect on any part of the TEG trace. At serum Mg^{2+} concentrations greater than 3 mmol litre^{-1} there was a small but statistically significant prolongation of the r time, k time and $r+k$ time (table 1). At serum Mg^{2+} concentrations greater than 5 mmol litre^{-1}, significant effects of magnesium were also seen on MA. Amplitude at 60 min was not affected at any concentration of magnesium. The α angle was significantly affected only at serum Mg^{2+} concentrations greater than 7 mmol litre^{-1}.

M. F. M. JAMES, MBCHB, PHD, FRCA, G. NEIL, MDIPMEDTECH, Department of Anaesthesia, University of Cape Town, Anzio Road, Observatory, Cape, South Africa 7925. Accepted for publication: August 1, 1994.

Correspondence to M.F.M.J.

Table 1 TEG variables measured at varying serum concentrations of magnesium (Mg). * Statistically significant difference from control value

TEG parameter	Control ($n = 30$)	Mg (mmol litre^{-1}) 1–3 ($n = 7$)	3–5 ($n = 9$)	5–7 ($n = 10$)	> 7 ($n = 4$)
r time (min)					
Mean	7 3	8.1	9.2*	9.7*	10.4*
SD	1.2	1.3	2.0	1.4	1.9
Range	5–10	5–9	6–11	6.5–11.5	8 5–12.5
k time (min)					
Mean	3.4	3.9	4.6*	4.2*	5.1*
SD	0 9	0.7	1 1	0.9	0.7
Range	2–5.5	3–5 5	2–6	3–6	4 5–6
$r+k$ time (min)					
Mean	11.1	12.0	14.2*	13.9*	15.4*
SD	1 9	1.6	1.6	2.1	2.3
Range	7.5–15	9–14	8–17	9.5–17 5	13–17.5
α Angle (°)					
Mean	35 6	34.7	30.9	32 8	27.5*
SD	6.7	3.9	7.6	6.0	5.7
Range	22–52	29–38	22–47	24–44	19–32
MA (mm)					
Mean	50.2	53.6	51.9	45.7*	46.5
SD	4.7	4.0	6.8	6.6	2.4
Range	38–57	48–58	41–63	38–56	44–46
Amplitude at 60 min (mm)					
Mean	48.4	54 7	51.5	46 7	45.2
SD	5.4	2.6	7.2	5.4	0.9
Range	38–56	51–57	41–63	38–56	44–46

Comment

The TEG is a well established device for measuring whole blood clotting times and has been assessed thoroughly for its role in the detection and management of coagulation problems [3]. Increasing the magnesium concentration of the samples to between 1 and 3 mmol litre^{-1} had no effect on TEG variables and this is in good agreement with the *in vivo* study by Wall and colleagues [4]. At higher serum concentrations, initiation of coagulation, as measured by the r and k times, was prolonged, but although statistically significant, the clinical relevance is minimal as prolongation of the $r+k$ time was small and the values remained within the normal range. Even at serum Mg^{2+} concentrations > 7 mmol litre^{-1} the effect of the initiation of coagulation was minimal. The speed of clot formation, as measured by the α angle, was also minimally affected with a statistically significant effect occurring only at values > 7 mmol litre^{-1}. MA, which is a measure of clot strength and is a function of the dynamic properties of fibrin and platelets, was unaffected by serum Mg^{2+} concentrations < 5 mmol litre^{-1}. Even though serum Mg^{2+} concentrations > 5 mmol litre^{-1} did produce a significant reduction in MA, this reduction was so small as to be of little clinical significance. Thrombolysis, as measured by amplitude at 60 min, was not affected at any concentration of magnesium.

Magnesium is used widely for the management of pre-eclamptic toxaemia of pregnancy and, if magnesium were to interfere with coagulation, this might have implications for the placement of extradural catheters and surgical procedures in these patients. Magnesium has minimal effects on those aspects of coagulation measured by TEG and this seems to be borne out clinically [4]. With the range of Mg^{2+} concentrations used in obstetrics (1.5–4 mmol litre^{-1}) there appear to be no clinically important effects of magnesium on coagulation profiles.

Magnesium has been used during surgery in the control of cardiovascular disturbances associated with intubation, during resection of phaeochromocytomas, and in the management of arrhythmia [5]. It has also been used for the production of hypotension during cerebral aneurysm surgery [6]. In these studies, serum Mg^{2+} concentrations of 2–13.5 mmol litre^{-1} have been produced and coagulation abnormalities have not been observed. It seems unlikely, therefore, that infusions of magnesium sulphate resulting in hypermagnesaemia will affect coagulation in such a way as to produce clinically significant bleeding in patients undergoing regional anaesthesia or surgical procedures. However, a word of caution regarding regional anaesthesia is necessary. If magnesium inhibits platelet–endothelium interactions in a similar way to the effect exerted by aspirin, then this will not be detected by the TEG as the platelet–endothelium interface is not tested with this instrument.

In conclusion, a wide range of serum magnesium concentrations had only a small effect on the coagulation profile, as measured by the TEG. Magnesium concentrations > 3 mmol litre^{-1} have a statistically significant but probably clinically unimportant effect on coagulation and magnesium is unlikely to have adverse effects in patients in whom magnesium is being used therapeutically. The possibility that magnesium may interfere with platelet activity at the level of interaction of platelets and

endothelium remains and has not been examined in the present study.

References

1. Durlach J. *Magnesium in Clinical Practice*. London: John Libbey, 1988; 235–236.
2. Arsenian MA. Magnesium and cardiovascular disease. *Progress in Cardiovascular Disease* 1993; **35**: 271–310.
3. Mallett SV, Cox DJ. Thrombelastography. *British Journal of Anaesthesia* 1992; **69**: 307–313.
4. Wall MH, Chadwick HS, Chandler W, Ross BK. Thromboelastography in healthy laboring women and in women receiving magnesium for premature labor. *Anesthesiology* 1993; **79**: A993.
5. James MFM. Clinical use of magnesium infusions in anesthesia. *Anesthesia and Analgesia* 1991; **74**: 129–136.
6. Crozier TA, Radke J, Weyland A, Sydow M, Seyde W, Markakis E. Haemodynamic and endocrine effects of deliberate hypotension with magnesium sulphate for cerebral aneurysm surgery. *European Journal of Anaesthesia* 1991; **8**: 115–121.