Effects of magnesium sulphate on cerebral haemodynamics in healthy volunteers: a transcranial Doppler study

R. Sherman¹, P. Armory¹, P. Moody², T. Hope² and R. P. Mahajan¹*

¹University Department of Anaesthesia and Intensive Care and ²Department of Neurosurgery, University Hospital and City Hospital, Nottingham, UK

*Corresponding author. E-mail: ravi.mahajan@nottingham.ac.uk

Background. Magnesium is increasingly being considered as a neuroprotective agent. We aimed to study its effects on middle cerebral artery blood flow velocity ($V_{mca}$), cerebral autoregulation and cerebral vascular reactivity to carbon dioxide (CRCO₂) in healthy volunteers.

Methods. Fifteen healthy volunteers were recruited. Using transcranial Doppler ultrasonography, $V_{mca}$ was recorded continuously. The strength of autoregulation was assessed by the transient hyperaemic response test, and the CRCO₂ was measured by assessing changes in $V_{mca}$ to the induced changes in end-tidal carbon dioxide. I.V. infusion of magnesium sulphate was then started (loading dose of 16 mmol followed by an infusion at the rate of 2.7 mmol h⁻¹) for 45 min. The cerebral haemodynamic variables were measured again near the end of the infusion of magnesium sulphate.

Results. Total serum magnesium levels were doubled by the infusion regimen. However, there were no significant changes in $V_{mca}$, strength of autoregulation, or CRCO₂. Five of the volunteers reported marked nausea and two developed significant hypotension during the loading dose.

Conclusions. Infusion of magnesium sulphate, in a dose that doubles its concentration in plasma, does not affect $V_{mca}$, strength of autoregulation or CRCO₂ in healthy volunteers. However, it can be associated with nausea and hypotension.


Keywords: blood, haemodynamics; brain, cerebral circulation; ions, magnesium sulphate; measurement techniques, transcranial Doppler ultrasonography

Accepted for publication: April 10, 2003

Magnesium has a recognized role in the treatment of eclamptic seizures, refractory arrhythmias, and asthma.¹ It is neuroprotective in many pre-clinical models of ischaemic and excitotoxic brain injury, and recent studies point to its potential role in stroke, head injury, and subarachnoid haemorrhage.²–⁴

Magnesium may dilate cerebral vessels, and thus be responsible for relieving vasospasm in patients with pre-eclampsia.⁵ Its effects on other aspects of cerebral haemodynamics, such as autoregulation to the changes in perfusion pressure (cerebral autoregulation) and cerebral vascular reactivity to carbon dioxide (CRCO₂), are not well documented, in health or in disease. This knowledge is important for its judicious use, particularly in view of potential increase in its clinical applications in neurological diseases. In the present study, using transcranial Doppler (TCD) ultrasonography, we evaluated the effects of a clinically relevant dose of magnesium sulphate on middle cerebral artery (MCA) flow velocity (FV), cerebral autoregulation, and CRCO₂ in healthy volunteers.

Methods and results

After obtaining approval from the Medical School Ethics Committee and written, informed consent, 15 healthy volunteers, aged between 18 and 40 yr, were recruited.
 Volunteers were excluded if they were overweight (BMI >25 kg m⁻²), had any evidence of cerebrovascular or neurological disease, were taking any vasoactive medications, were pregnant or potentially pregnant, or had history of smoking or of migraine.

All subjects were studied in the supine position with the head resting on a pillow. The left MCA was sonicated through the temporal window using a 2 MHz TCD ultrasound probe (SciMed QVL 120, SciMed, Bristol, UK). The depth of sonication was adjusted to achieve maximal signal. The position of the probe was fixed using a headband. The FV was recorded continuously on digital audiotape for subsequent analysis using specific software (SciMed, Bristol, UK). I.V. access was secured and monitoring was initiated using an electrocardiogram, non-invasive arterial pressure measurement and pulse oximetry (Marquette Tramscope: Marquette Electronics, Milwaukee, WI, USA). Mean arterial pressure (MAP) was measured at 2-min intervals and the partial pressure of end-tidal carbon dioxide (E₂CO₂) was measured continuously using a nose-clip and mouthpiece (Marquette Tramscope: Marquette Electronics).

After an initial period of rest of approximately 10 min, cerebral haemodynamic variables such as Vₘca, cerebral autoregulation, and CRCO₂ were measured in each subject. Venous blood samples were taken for measurement of serum magnesium levels. I.V. infusion of magnesium sulphate was then started. The regimen for the infusion was a loading dose of 16 mmol magnesium over 15 min, followed by an infusion of magnesium at 2.7 mmol h⁻¹ for 45 min. Nearing the end of the infusion, measurements of cerebral haemodynamic variables and serum magnesium were repeated.

Cerebral autoregulation was assessed using the transient hyperaemic response (THR) test. The test involves establishing continuous measurement of Vₘca, cerebral autoregulation, and CRCO₂ were measured in each subject. Venous blood samples were taken for measurement of serum magnesium levels. I.V. infusion of magnesium sulphate was then started. The regimen for the infusion was a loading dose of 16 mmol magnesium over 15 min, followed by an infusion of magnesium at 2.7 mmol h⁻¹ for 45 min. Nearing the end of the infusion, measurements of cerebral haemodynamic variables and serum magnesium were repeated.

Table 1 summarizes the results. The infusion regimen almost doubled the levels of magnesium in the plasma. There were no significant changes in MAP or E₂CO₂. Also, Vₘca, THR, SA, and CRCO₂ remained unchanged.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Magnesium infusion</th>
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<tbody>
<tr>
<td>MAP (mmHg)</td>
<td>87 (8)</td>
<td>88 (6)</td>
</tr>
<tr>
<td>E₂CO₂ (kPa)</td>
<td>5.5 (0.4)</td>
<td>5.5 (0.5)</td>
</tr>
<tr>
<td>Vₘca (cm s⁻¹)</td>
<td>62 (13)</td>
<td>61 (13)</td>
</tr>
<tr>
<td>THR</td>
<td>1.44 (0.13)</td>
<td>1.47 (0.17)</td>
</tr>
<tr>
<td>SA</td>
<td>1.05 (0.14)</td>
<td>1.06 (0.14)</td>
</tr>
<tr>
<td>CRCO₂ (%)</td>
<td>38 (8)</td>
<td>37 (8)</td>
</tr>
<tr>
<td>Serum magnesium (mmol litre⁻¹)</td>
<td>0.78 (0.06)</td>
<td>1.57 (0.12)</td>
</tr>
</tbody>
</table>
Comment
This study shows that a clinically relevant dose of magnesium, that almost doubles its concentration in plasma, has no significant effects on \( V_{\text{mca}} \), cerebral autoregulation and \( \text{CRCO}_2 \) in healthy volunteers. In view of the increasing therapeutic use of magnesium, these are important ‘negative’ findings.

The effects of magnesium on cerebral vessels remains undefined, although it is suggested to have a vasodilatory effect and to relieve vasospasm in pre-eclamptic patients. In a study by Belfort et al., infusion of magnesium did not have significant effects on MAP or \( V_{\text{mca}} \) in pre-eclamptic patients. In a recent study in patients with subarachnoid haemorrhage, infusion of magnesium did not change \( V_{\text{mca}} \) significantly. Our results in healthy volunteers are in agreement with these reports. In addition, we have shown that cerebral autoregulation and \( \text{CRCO}_2 \) also remain unchanged.

The dose regimen of magnesium infusion used in this study has been shown previously to increase serum magnesium concentration rapidly to double the physiological level. This regimen is likely to be adopted for the forthcoming clinical trials of magnesium in stroke. Its lack of significant effects on cerebral autoregulation and \( \text{CRCO}_2 \) would suggest that, in patients receiving magnesium, the unaffected parts of the brain would tend to retain the capacity to autoregulate the blood flow. Our results, however, cannot be extrapolated to the injured or affected parts of the brain.

During the course of the study several unexpected adverse events occurred. This is contrary to previous studies, which have shown magnesium to be generally free from troublesome side effects. Two of our volunteers developed hypotension toward the end of the loading dose. This required the loading dose to be stopped temporarily. The arterial pressure, in both these volunteers, recovered within 2 min of stopping the loading dose. Five of the volunteers reported marked nausea during the loading dose, two of whom also suffered retching. We were surprised by the unexpected higher incidence of side effects in this study compared with earlier reports. We postulate that this may be a result of the rate of change in serum magnesium concentration rather than the absolute level, as all these side-effects began within 4 min of commencing, and abated within 2 min of completing, the loading dose. Maybe the loading dose should be given over a longer period of time to prevent the adverse events.

In conclusion, in healthy volunteers, i.v. infusion of magnesium does not affect \( V_{\text{mca}} \), cerebral autoregulation, or \( \text{CRCO}_2 \), but can be associated with nausea and hypotension.

Acknowledgements
This study was funded by the Research Funds, Department of Neurosurgery, Queen’s Medical Centre, Nottingham.

References
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