Effect of Profound Hypermagnesemia on Spinal Cord Glucose Utilization in Rats

Michele D. Szabo, MD, and Gregory Crosby, MD

The purpose of our study was to investigate the effect of hypermagnesemia on spinal metabolic rate. The 2-["C]deoxyglucose technique was used to measure regional glucose utilization in the lumbar spinal cord of paralyzed, mechanically ventilated rats receiving 70% nitrous oxide and an intravenous infusion of either saline (n = 5) or magnesium sulfate (n = 5). Plasma magnesium concentrations were 6.75 ± 0.5 and 0.9 ± 0.5 mM (p < 0.01) in hypermagnesemic and control rats, respectively. Hypermagnesemic rats were hypotensive (88 ± 1 vs. 130 ± 4 mm Hg, p < 0.01) but blood pressure remained within the autoregulatory range. Glucose utilization was reduced 26–45% in spinal gray matter and 53–63% in spinal white matter during hypermagnesemia. We conclude that magnesium is a potent spinal metabolic depressant and that this action, which is unusually prominent in spinal white matter, is a plausible explanation for the recently reported beneficial effect of magnesium therapy during spinal cord ischemia. (Stroke 1988;19:747–749)

Results

Plasma magnesium concentrations were 6.75 ± 0.5 and 0.9 ± 0.5 mM (13.5 ± 1 and 1.8 ± 1 meq/l)
(p<0.01) in hypermagnesemic and control rats, respectively. Apart from hypotension, hypermagnesemia produced no significant changes in the physiologic variables (Table 1). Moreover, since MABP remained within the range of autoregulation of spinal blood flow, it is unlikely that hypotension affected the results.

Hypermagnesemia reduced metabolism in all regions of spinal cord examined (Table 2). Glucose utilization was 26–45% lower than control in spinal gray matter; laminae I–III were affected least and utilization in lamina VII was decreased most. The changes in spinal white matter were even more profound. Hypermagnesemia was associated with a 53–63% decrease in glucose utilization by spinal white matter (Table 2).

Discussion

There have been conflicting opinions regarding the CNS effects of magnesium. Somjen et al first demonstrated that hypermagnesemia (plasma concentration 7.5 mM) does not produce anesthesia in humans and concluded that magnesium's divalent, cationic structure limits its ability to cross the blood-brain barrier. Moreover, although the success of magnesium for treating or preventing seizures in patients with toxemia of pregnancy suggests that magnesium enters the CNS in a therapeutic amount, such therapy does not reduce cerebral metabolic rate in toxemic patients. For example, despite high plasma magnesium concentrations, MABP remained within autoregulatory limits (Table 1); therefore, hypotension probably did not contribute to spinal metabolic depression. This is likely to be true even if autoregulation is altered by magnesium since the spinal metabolic effect of halothane, a general anesthetic that impairs autoregulation, is unaffected by hypotension of this magnitude.

The mechanisms by which magnesium reduces spinal metabolism presumably include effects on synaptic transmission and glycolysis. Magnesium reduces synaptic transmission by competing with ionic calcium and inhibits glycolysis directly by inhibiting the enzyme phosphofructokinase. Both actions of magnesium probably explain the decreased rate of glucose utilization in spinal gray matter but (assuming uniform tissue distribution of magnesium) cannot explain fully the disproportionately larger effect of magnesium on spinal white matter metabolism. White matter typically has a lower rate of metabolism than gray matter (presumably because oligodendroglia are not very active metabolically) and contains no synapses, which have a high rate of substrate consumption. In addition, white matter is usually affected less than gray matter by metabolic depressants, such as general anesthesia, and events that reduce impulse conduction along spinal white matter tracts, such as spinal anesthesia and spinal shock, are associated with comparatively small metabolic effects on the conducting pathways. Thus, the fact that magnesium has a greater effect on spinal white than gray matter is unusual and the explanation is entirely speculative. Perhaps magnesium preferentially inhibits oligodendroglial function or nonsynaptic metabolic processes (such as axoplasmic transport). Alternatively, it is possible that the metabolic effect of magnesium is greater in spinal white than gray matter because magnesium uptake may be higher in white matter.

### Table 1. Physiologic Variables for Control and Hypermagnesemic Rats

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 5)</th>
<th>Hypermagnesemia (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>37.0 ± 0.3</td>
<td>37.3 ± 0.3</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mm Hg)</td>
<td>130 ± 4</td>
<td>88 ± 1*</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.47 ± 0.06</td>
<td>7.34 ± 0.03</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>118 ± 10</td>
<td>102 ± 12</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>37 ± 2</td>
<td>37 ± 2</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.  *p<0.01.

### Table 2. Spinal Glucose Utilization in Control and Hypermagnesemic Rats

<table>
<thead>
<tr>
<th>Lamina(e)</th>
<th>Control</th>
<th>Hypermagnesemia</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>I–III</td>
<td>38 ± 1</td>
<td>31 ± 1*</td>
<td>-26</td>
</tr>
<tr>
<td>IV–VI</td>
<td>47 ± 2</td>
<td>35 ± 2*</td>
<td>-35</td>
</tr>
<tr>
<td>VII</td>
<td>55 ± 2</td>
<td>38 ± 2*</td>
<td>-45</td>
</tr>
<tr>
<td>VIII</td>
<td>54 ± 2</td>
<td>39 ± 2*</td>
<td>-38</td>
</tr>
<tr>
<td>IX</td>
<td>52 ± 2</td>
<td>37 ± 2*</td>
<td>-38</td>
</tr>
</tbody>
</table>

**Gray Matter**

Values are mean ± SEM μmol/100 g/min.  *p<0.01.
Insofar as its effect on spinal gray matter metabolism is concerned, magnesium appears to be very similar to general anesthesia. That is, in absolute terms, the glucose utilization of spinal gray matter during pentobarbital anesthesia and hypermagnesemia (Table 2) are nearly identical. Such is not the case for magnesium’s spinal white matter effects; glucose utilization is nearly 50% lower during hypermagnesemia (Table 2) than barbiturate anesthesia. Spinal metabolic depression, particularly and most prominently of spinal white matter, therefore appears to be a very plausible explanation for magnesium’s protective effect during experimental spinal ischemia. Moreover, even if some of magnesium’s other putatively beneficial properties, such as calcium channel blockade and relaxation of vascular smooth muscle, prove to be of greater significance during ischemia, the fact that magnesium profoundly reduces spinal metabolism is likely to be of additional benefit.

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References


Key Words • glucose • magnesium • spinal cord • rats
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