Effects of magnesium sulfate on spinal cord tissue lactate and malondialdehyde levels after spinal cord trauma

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Abstract. Objective. In the present study, the effects of magnesium sulfate (MgSO4) on tissue lactate and malondialdehyde (MDA) levels after spinal cord trauma (SCT) in rabbits were studied. Subjects. Thirty New Zealand rabbits. Interventions. The rabbits were divided equally into three groups: group I was the sham-operated group, group II suffered from SCT but received no treatment, group III was given a dose of 100 mg/kg of magnesium sulfate intravenously at 5th minute after SCT. Measurements. The lactate and MDA levels were measured in contused spinal cord tissue at 60 minutes after SCT. There was a significant increase of lactate and MDA levels in group II (p < 0.05) when compared with groups I and III, and a significant increase in the level of MDA in group III compared with group I, and also a significant decrease compared with group II, which was the trauma group without treatment (p < 0.05). Conclusion. The findings of this study showed that magnesium sulfate can attenuate the increase of tissue MDA and supply a normalization of lactate levels following SCT which may be related to the neuroprotective effects of (MgSO4).

Keywords: lactate, lipid peroxidation, magnesium sulfate, malondialdehyde, spinal cord trauma

Methods

Acute spinal cord trauma is a destructive injury and has two pathophysiological components: primary and secondary injury [1, 2]. Primary injury is the initial mechanical loss to the spinal cord that results in disruption of neural and vascular structures but secondary injury is a progressive cell injury that damages intact, adjacent tissue [1, 2]. During neuronal injury, ATP depletion causes an increase in anaerobic metabolism that leads to lactate accumulation. Excitatory amino acids (EAAs: mainly glutamate and aspartate) are released in excessive amounts from terminals of ischemic or traumatically injured neurons, leading to N-methyl-D-aspartate (NMDA) receptor activation [3-5]. Ion pump failure, due to ATP depletion and NMDA receptor activation, causes an intracellular increase of Ca2+ concentration. Ca2+ overload also inhibits
Pyruvate dehydrogenase. Suppression of the pyruvate dehydrogenase activity inhibits the decarboxylation of pyruvate to acetyl coenzyme-A and consequently causes anaerobic glycolysis, glycogenolysis and lactate accumulation. This accumulation leads to retardation of the extrusion of Ca$^{2+}$ [6]. Increased Ca$^{2+}$ triggers Ca dependent lytic enzymes such as xanthine oxidase, phospholipase and ornitin decarboxylase [7, 8]. These enzymes cause elevation of oxygen free radicals, lipolysis and proteolysis. Activation of phospholipase-C induces the release of free fatty acids that leads to the depletion of membrane phospholipids. This results in altered permeability and further Ca$^{2+}$ influx [9]. Lactate accumulation causes an intracellular Ca$^{2+}$ increase that leads to further ATP depletion and Ca$^{2+}$ influx which results in further lactate accumulation and MDA formation.

Secondary injury may be prevented by pharmacological agents. Magnesium sulfate (MgSO$_4$) is an effective tissue protective agent due to potent blockage of N methyl-D-aspartate (NMDA) receptor activation, and consequently free radical formation, lipid peroxidation and lactate accumulation [10-14]. When tissue concentration of lactate exceeded 20-25$\text{mg/gww}$ (gram wet weight) the destructive effect became perceptible [15, 16]. Eventually, both tissue lactate and MDA may be considerable features associated with progressively worsening cellular effects.

### Statistical analysis

All values are expressed as means ± SD. One way analysis variance and Tukey’s honest significant difference (post hoc) tests were used for the evaluation of lactate and MDA results.

Two-way analysis of variance for repeated measures and paired t test were used for evaluating arterial blood gas and hemodynamic results between groups.

### Results

The mean arterial pressure, blood gases and heart rates were similar in all groups before SCT. There were significant differences in MAP and HR values between group I and the other groups 60 minutes after SCT (p < 0.05) (table 1).

The levels of group I were considered the baseline levels for MDA and lactate. There was a significant increase in group II (p < 0.05) in lactate and MDA levels when compared with groups I and III (table 2).

There was no significant elevation of the lactate level in group III, compared with group I.

### Discussion

In our study, in the sham operated group (group I) and in group III (MgSO$_4$ treated group), the lactate concentrations were below toxic levels, and the MDA levels were also low, showing a good correla-

### Table 1. The heart rate (HR), mean arterial pressure (MAP), arterial oxygen (PaO$_2$), carbondioxide (PaCO$_2$) values of all groups (means ± SD).

<table>
<thead>
<tr>
<th>Study group</th>
<th>HR</th>
<th>MAP</th>
<th>PaO$_2$</th>
<th>PaCO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before laminectomy</td>
<td>244 ± 6.6</td>
<td>74 ± 2.7</td>
<td>96.39 ± 2.1</td>
<td>28.40 ± 1.6</td>
</tr>
<tr>
<td>60 minutes after laminectomy</td>
<td>247 ± 7.7</td>
<td>75 ± 2.5</td>
<td>97.33 ± 1.8</td>
<td>27.45 ± 1.9</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before spinal cord trauma</td>
<td>242 ± 8.7</td>
<td>73 ± 2.9</td>
<td>97.12 ± 2.3</td>
<td>26.35 ± 1.7</td>
</tr>
<tr>
<td>60 minutes after spinal cord trauma</td>
<td>268 ± 8.1*</td>
<td>68 ± 2.3*</td>
<td>95.16 ± 2.5</td>
<td>27.32 ± 2.1</td>
</tr>
<tr>
<td>Group III</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Before spinal cord trauma</td>
<td>243 ± 9.1</td>
<td>72 ± 2.7</td>
<td>98.22 ± 1.7</td>
<td>29.15 ± 1.5</td>
</tr>
<tr>
<td>60 minutes after spinal cord trauma</td>
<td>257 ± 8.3*</td>
<td>67 ± 2.6*</td>
<td>97.66 ± 2.2</td>
<td>28.15 ± 1.7</td>
</tr>
</tbody>
</table>

* Compared group to I, p < 0.05.

### Table 2. Spinal cord tissue lactate and malondialdehyde (MDA) levels (mean ± SD) of each group.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>15.70 ± 2.40</td>
<td>27.87 ± 2.82</td>
<td>17.93 ± 2.79</td>
</tr>
<tr>
<td>(nmol/gwwet weight)</td>
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<tr>
<td>MDA</td>
<td>74.66 ± 11.08</td>
<td>136.04 ± 9.86</td>
<td>92.51 ± 10.42</td>
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<tr>
<td>(nmol/gwwet weight)</td>
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</tbody>
</table>

Group I: sham operated group. Group II: spinal cord trauma delivered and non- treated group. Group III: spinal cord trauma delivered and MgSO4 treated group.
tion with the lactate concentrations, as mentioned in the introduction. So our results demonstrated that MgSO4 treatment inhibited the increase in tissue lactate and MDA levels. The increases of HR and decrease of MAP values were significant in group II. This may be the detrimental effect of spinal cord trauma.

The tissue lactate and MDA levels reached a high value during the first few minutes of traumatic or ischemic brain injury, it continued to accumulate and the maximum lactate and MDA levels were reached 1 hour after brain injury [17, 18]. Therefore we measured spinal tissue lactate and MDA levels 1 hour after SCT.

Mg2+ plays a pivotal role in the metabolism of carbohydrates, fats, and proteins including glycolysis, oxidative phosphorylation, and protein synthesis [19]. Mg2+ also plays a vital role in regulating ribosomal RNA and DNA structure. From this brief summary, it can be seen that Mg2+ has actions opposite to those of Ca2+ in maintaining membrane integrity and storage utilization of energy [20, 21]. Mg2+ is essential for NADH−K+−ATPase function, and it suppresses the decline in cerebral ischemia and spinal trauma [15, 22, 23]. It was emphasized that NMDA depresses the decline in brain tissue, significantly improved neurological outcome [33] and protected against irreversible damage after spinal ischemia [34], whereas pre-injury dietary depletion of Mg2+ resulted in lower Mg2+ concentration in the brain and worsened the neurological outcome [35]. Post ischemic and post injury intravenous Mg2+ treatment improved histological changes and the neurological outcome in several studies [36, 37]. Mg2+ treatment also attenuated the increase of lactate and MDA levels in other studies [13, 35] and also attenuated [38-40] the decrease of endogenous antioxidant activity in brain tissue after traumatic head injury in rabbits [41].

We conclude that MgSO4 is an important agent in the normalization of lactate levels and in suppressing the increase in MDA levels in traumatic spinal cord tissue. However, further studies should be performed in the clinical use of MgSO4 and its protective effects at a cellular level.

References


EFFECTS OF MAGNESIUM SULFATE ON SPINAL CORD TISSUE LACTATE


