Neuroprotective effects of preischemia intraarterial magnesium sulfate in reversible focal cerebral ischemia

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The known cytoprotective properties of MgSO_4 led the authors to study its effects on infarct size in rats when administered intraarterially before reversible focal ischemia. Following an intracarotid infusion of MgSO_4 in the amount of 30 mg/kg (24 animals), 90 mg/kg (18 animals), or an equal volume of vehicle (23 animals), middle cerebral artery occlusion was produced in rats by means of an intraluminal suture technique. Reperfusion occurred after 1.5 (42 animals) or 2 hours (23 animals) of ischemia.

Automated, volumetric measurements of 2',3',5'-triphenyl-2H-tetrazolium chloride–stained coronal brain sections demonstrated a statistically significant decrease in infarct size for MgSO_4 treatment groups compared to controls. Cytoprotection was greater in animals subjected to 1.5 hours of ischemia (28.4% reduction in infarct volume, p < 0.001, Student’s t-test), than in those having 2 hours of ischemia (19.3% reduction, p < 0.05). Animals given 90 mg/kg MgSO_4 prior to 1.5 hours of ischemia (12 animals) showed a 59.8% reduction in infarct volume compared to controls (11 animals, p < 0.001) and a 43.1% reduction compared to the 30 mg/kg group (11 animals, p < 0.001). Analysis of variance demonstrated the statistically significant effects of MgSO_4 doses on infarct volume across all groups (F = 22.95, p < 0.0001).

The neuroprotective effect of intraarterial MgSO_4 in this model is robust, dose dependent, and related to the duration of ischemia. The compound may be valuable for limiting infarction if given intraarterially before induction of reversible ischemia during cerebrovascular surgery.

KEY WORDS • cerebral ischemia • cerebral protection • cerebrovascular surgery • magnesium • N-methyl-d-aspartate receptor antagonists

T R A N S I E N T focal cerebral ischemia that occurs during cerebrovascular surgery may result in permanent neurological injury due to the release of excitotoxic neurotransmitters, influx of calcium ions into neurons, free radical generation, lipid peroxidation, and protein degradation. A reliable pharmacological regimen designed to reduce or eliminate cerebral infarction when given prior to reversible, focal ischemia could be of great benefit in cerebrovascular surgery.

Much evidence implicates the influx of calcium ions via the N-methyl-D-aspartate (NMDA) receptor complex in the pathogenesis of cerebral ischemic injury. Accordingly, a variety of pharmacological agents designed to prevent NMDA receptor activation or to modify the cascade of events that follow this activation have been synthesized. These compounds have been effective in limiting ischemic injury in experimental stroke models, however, although some are presently being evaluated in clinical trials, neurotoxic and behavioral side effects have limited the use of these cytoprotective agents. Conversely, MgSO_4 is a readily available, inexpensive NMDA receptor antagonist with a well-established clinical profile in obstetrical and cardiovascular practice. Its efficacy and toxicity have already been evaluated in a pilot trial involving acute stroke patients. We believe this compound could be of value in preventing ischemic injury during cerebrovascular surgery.

Magnesium ions have been shown to limit neuronal injury in both in vivo and in vitro experiments. They play an important role in neuronal cellular physiology by competing with calcium ions in the extracellular space, acting as an endogenous calcium channel blocker and gating NMDA receptor–associated ion channels in a voltage-dependent fashion. In the latter case they function as noncompetitive antagonists of excitatory amino acid receptors. Magnesium may also be of value in treating cerebral ischemia because it exerts a dose-dependent inhibition of vascular smooth-muscle contraction, resulting in vasodilatation. On the basis of these data, we conducted the present study to determine the efficacy of MgSO_4 as a cytoprotective agent in a rat model of reversible focal cerebral ischemia.
Materials and Methods

Surgical Procedure

Our experimental protocol was approved by the Institutional Animal Care and Use Committee of Dartmouth College and was conducted according to the accepted standards of the National Institutes of Health. Male Sprague–Dawley rats weighing between 300 and 360 g were used for the experiments. Anesthesia was induced by administration of 4% halothane in oxygen and the animals were allowed to breathe spontaneously. Anesthesia was maintained with 1% to 1.5% halothane inhalation. The right femoral artery and vein were cannulated for blood sampling, measurement of arterial blood pressure and administration of fluids and drugs. A rectal temperature probe was connected to a temperature controller coupled to a heating blanket; core temperature was maintained within the normal physiological range (37.5 ± 0.6°C). To be certain that cerebral temperature correlated closely with core temperature, 20 rats underwent simultaneous monitoring of core and temporal muscle temperatures. Temporal muscle temperatures were determined using an optical fiber thermometer probe. There was no significant difference in temperature between sites during infusion of vehicle or MgSO4, induction of ischemia, or at the time of reperfusion. Arterial blood pressure was monitored and blood samples were evaluated for pH, PaCO2, PaO2, and serum glucose before ischemia was induced and for 45 minutes thereafter. Blood samples for measurement of plasma magnesium concentration were obtained just before injection of the MgSO4, 15 minutes and 60 minutes after establishing middle cerebral artery (MCA) occlusion and after 15 minutes of reperfusion. The volume of blood withdrawn was replaced by an equal volume of intravenous normal saline.

Using the operating microscope, we made a midline ventral neck incision and isolated the right common carotid artery (CCA), external carotid artery (ECA), and internal carotid artery (ICA). The occipital and superior thyroid branches of the ECA were coagulated and divided and the ECA was ligated with two No. 6-0 silk sutures placed distal to the latter branch. The pterygopalatine artery was ligated close to its origin at the ICA. The CCA and ICA were temporarily occluded using microvascular clips, and the ligated ECA was cannulated with a 22-gauge catheter, whose tip was advanced close to the carotid bifurcation and secured there. Following removal of the clips, MgSO4 or vehicle was infused via the catheter and the catheter was removed. A monofilament nylon suture, 250 μm in diameter with a rounded and polished tip, was advanced via the ECA 19 to 21 mm into the ICA from the CCA to the ICA was visually confirmed by means of the operating microscope. After establishing the reperfusion, the rats were returned to their cages for 24 hours, at which time they were evaluated neurologically in the manner described by Bederson, et al., and then killed.

To confirm the correct positioning of the occluding suture, 2 ml/kg of 2% Evans blue dye was injected intravenously and allowed to circulate for 50 minutes. This dye stains the vessel along the path of the suture and shows the position of the suture in the MCA.11

Sham-operated animals were subjected to a similar operative procedure; however, the occluding filament was advanced and then immediately withdrawn.

Experimental Groups

Sixty-five rats were subjected to 1.5 hours (42 animals) or 2 hours (23 animals) of reversible MCA occlusion. Before surgery, the animals were randomly assigned to receive equal volumes (0.2 ml) of MgSO4, vehicle (5% dextrose in water), or normal saline prior to occlusion. The results in animals given vehicle were not significantly different from those in animals infused with saline and the two groups were later pooled into a single control group. Thus, three treatment groups were used. Twenty-four rats received a 5% solution of MgSO4 (to a dose of 30 mg/kg), 18 animals were given a 15% solution of MgSO4 (90-mg/kg dose), and 23 control animals were injected with the same volume of vehicle or saline. Because the rapid intravenous injection of magnesium salts may induce a cardiodepressant effect and hypotension, MgSO4 or vehicle was infused over a 10-minute period at a rate of 0.02 ml/minute. The rate of intracarotid infusion of the drug was chosen on the basis of pilot experiments in our laboratory that demonstrated no hypotensive effects. The doses of MgSO4 were chosen to correspond to those used in clinical practice, in which loading doses of 30 and 90 mg/kg have been reported to be effective in the treatment of preeclampsia.12

Measurements of infarct size, histopathology, and neurological outcome were performed by an individual blind to the animal’s group. Animals with subarachnoid hemorrhage due to vessel injury by the suture and/or animals that died within 24 hours were discarded from this analysis. Fifty-seven rats developed full infarctions involving both the cortex and the striatum; the remaining eight rats, six of which were in the 90-mg/kg treatment group, had only striatal infarction or no infarction on staining, despite a correctly positioned intraluminal suture. Only animals with full infarction (57 animals) were used for data analysis in this study, although this may have underestimated the efficacy of MgSO4 as a neuroprotective agent. Five rats underwent sham operations and were processed for histological examination.

Measurement of Infarction

Animals were killed while under halothane anesthesia by intracardiac injection of hyperosmolar KCl solution. The brains were removed rapidly and sectioned in a rodent brain matrix into five, 2-mm-thick coronal sections, starting at 3 mm from the frontal pole. Sampling encompassed the entire span of the lesion, with the exception of a small portion extending into the frontal pole. The sections were incubated for 30 minutes at 37°C in a 2% solution of 2,3,5′-triphenyl-2H-tetrazolium chloride (TTC) to stain for mitochondrial dehydrogenase activity.26 The unstained area in each section was traced and quantified using a video digitizer and a computerized image analysis system (Image 1.55; National Institutes of Health, Rockville, MD) as the total right and left hemispheric areas. The total infarction volume was then calculated by multiplying the area of infarct in each slice by the slice thickness. The extent of infarction was expressed as a percentage of the whole measured brain volume. Cortex and basal ganglia were outlined separately. Brain edema that contributed to the infarction volume was expressed as a percentage of the difference between both hemispheric volumes and the whole measured brain volume.27 After the infarction, TTC measurements were obtained, the slices were stored in a 10% formalin solution until histological evaluation was performed.

Histopathological Examination

Thirty brains were processed for evaluation of the effects of treatment on ischemic cell damage after reversible MCA (five in the sham-operated group, 15 in the 1.5-hour MCA occlusion group, and 10 in the 2-hour MCA occlusion group). Histological sections stained with hematoxylin and eosin and with acid fuscian were obtained from the frontal surface of the 2-mm-thick paraffin block corresponding to section No. 2 of the TTC examination (5–7 mm from the frontal pole). This region was consistently centered in the infarcted tissue. The level of the anterior commissure (stereotactic level A 7470 μm) was used for additional histological examination.34 Direct counting of histologically intact neurons was performed in 40 nonoverlapping fields in the infarct border zone (dorsolateral neocortex) and in the homotopic area of the contralateral, nonischemic hemisphere. We applied our previously described light microscopic criteria for evaluation of acute ischemic neuronal damage.31 Morphological features, such as pyknosis/eosinophilia and loss of hematoxylin affinity, were interpreted as indicators of irreversible cell damage.32 Results from cell counting were presented as the percentage of histologically intact neurons in the ischemic hemisphere compared to intact neurons in homotopic regions of the nonischemic hemisphere. Corresponding data from counts in the sham-operated rats were given as a right-to-left hemisphere ratio in percent.
Magnesium sulfate in reversible cerebral ischemia

**Results**

The physiological variables did not differ significantly between vehicle and treatment groups (Table 1). Moderate hyperglycemia was noted in all groups. A trend toward increased glucose levels after MCA occlusion was observed, although this did not reach statistical significance. Intracarotid MgSO₄ infusion did not induce significant hemodynamic effects (mean arterial blood pressure (MABP) reduction < 10% of baseline), although a transient reduction in heart rate was noted at the start of MgSO₄ infusion. The 30-mg/kg MgSO₄ dose produced a short-lasting (<1 hour) elevation in plasma Mg²⁺ levels from 0.76 ± 0.11 mmol/L to 1.08 ± 0.13 mmol/L. In the 90-mg/kg MgSO₄ group, the plasma Mg²⁺ concentration increased from 0.74 ± 0.09 mmol/L to 1.49 ± 0.18 mmol/L and the hypermagnesemia lasted for more than 1 hour (Fig. 1).

Fifty-seven rats developed full infarctions involving both the cortex and the striatum. All animals subjected to 2 hours of MCA occlusion and 11 of 12 animals in both the vehicle and 30-mg/kg MgSO₄ groups subjected to 1.5 hours of MCA occlusion developed full infarctions. However, only 12 of 18 rats with 90 mg/kg MgSO₄ and 1.5 hours of occlusion developed full infarctions. This was significantly different from the vehicle and the 30-mg/kg MgSO₄ groups (p < 0.05). The effect of MgSO₄ on infarct size, as well as on brain edema, is summarized in Table 2. Infarct volume was significantly decreased in treatment groups when compared to controls. Attenuation of edema was pronounced in the 1.5-hour MCA occlusion–90-mg/kg MgSO₄ rats. This group also displayed a significantly lower neurological deficit score (Table 3).

The cerebroprotective effect of MgSO₄ in the 2-hour ischemia group resulted from sparing the cortex (Fig. 2 upper), whereas the rats subjected to 1.5-hour MCA occlusion demonstrated protection of both cortex and basal ganglia (Fig. 2 lower). The mean infarct size was not significantly different between the 1.5- and 2-hour control

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**Tables and Figures**

**Table 1**

<table>
<thead>
<tr>
<th>Group &amp; Time</th>
<th>MABP (mm Hg)</th>
<th>Arterial pH</th>
<th>PaCO₂ (mm Hg)</th>
<th>PaO₂ (mm Hg)</th>
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<td>pre</td>
<td>103.7 ± 5.3</td>
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<tr>
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<tr>
<td>pre</td>
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<td>119.3 ± 9.9</td>
<td>193.5 ± 23.3</td>
<td>37.6 ± 0.3</td>
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*Each group was composed of four rats. Values are expressed as mean ± standard deviation. Abbreviations: MABP = mean arterial blood pressure; MCA = middle cerebral artery; post = 45 minutes after treatment and onset of ischemia; pre = 15 minutes before MCA occlusion and treatment; temp = temperature.

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**Figure 1**

Chart displaying the time course of the Mg²⁺ plasma levels (normal 0.66–0.95 mmol/L) in both MgSO₄ groups subjected to 1.5 hours of middle cerebral artery occlusion. Six animals were in each treatment group. Values are presented as mean ± standard deviation. ***p < 0.001 vs. pretreatment baseline in the 30- and 90-mg/kg MgSO₄ groups, respectively.
groups. The protection provided by 30 mg/kg MgSO₄ was greater in the group of rats that had 1.5 hours of occlusion (28.4% reduction compared to vehicle, p < 0.001) than in the group that had 2 hours of occlusion (19.3% volume reduction, p < 0.05). A clear dose–response effect was documented for MgSO₄ in that the 90-mg/kg dose decreased infarct volume 59.8% compared to controls (p < 0.001) and 43.1% compared to the 30-mg/kg MgSO₄ group (p < 0.001). The reduction in the total infarct volume in the 2-hour occlusion group was evident in the caudal sections, whereas in the 1.5-hour ischemia group, the protection was apparent both as attenuation of the infarct area in individual slices as well as in its rostrocaudal extent (Fig. 3).

Analysis of variance confirmed a statistically significant effect of MgSO₄ treatment on infarct volume across all groups (F = 22.95, p < 0.0001). However, the study was not powerful enough to determine the relationship between length of ischemia and infarct volume (F = 2.08, power 0.29). There was no interaction between length of ischemia and MgSO₄ dose.

The percentage of histologically intact neurons in the infarct border was greater in MgSO₄-treated rats. Surprisingly, the difference was statistically significant only for the 30-mg/kg group (Fig. 4). We believe that this is due to a less sharply demarcated border zone in the 90-mg/kg–treated rats because of a larger transitional area adjacent to a smaller infarct core in this group.

Discussion

The data presented here demonstrate that significant neuroprotection, measured as a reduction in infarct size, has been achieved with preischemic, intraarterial administration of MgSO₄ in a rat model of reversible focal ischemia. Animals that were subjected to 1.5 hours of MCA occlusion after receiving 90 mg/kg MgSO₄ had the smallest infarct volume and demonstrated significantly decreased cerebral edema formation compared to other groups. This supports the concept that cerebral edema in focal ischemia is related to infarct size, as recently suggested by Slivka, et al.⁵⁰

Previous reports have shown that magnesium improves
blood flow to ischemic cortex and attenuates infarct size in focal cerebral ischemia in rats.9,21 However, those studies evaluated permanent MCA occlusion models and are not as applicable as the present study to the clinical setting of cerebrovascular surgery. In addition, the present study used a unique treatment regimen of preischemic, intrarterial administration of a single-bolus, clinically applicable dose of drug administered to the same side as the ischemia. We think this model is relevant to the clinical situation that may occur during cerebrovascular procedures when one wishes to deliver a potentially cytoprotective agent to a vascular territory that is to be rendered transiently ischemic.

Our data demonstrate that the cytoprotective effects of MgSO4 are dose dependent for the two doses studied. However, even at the 90-mg/kg dose the plasma magnesium concentration was considerably lower than that found after systemic administration of magnesium in most previous reports on the effects of magnesium salts.7,9,21,36,49,52,57 We do not know the concentration of magnesium in the brain following intraarterial administration. However, the neuroprotection we were able to demonstrate was more prominent than that specified in previous studies of the cytoprotective effects of magnesium and we suspect that this efficacy may be due to the intraarterial method of administration used in our experimental protocol.

There are several possible explanations for the capability of MgSO4 to ameliorate ischemic injury when given intraarterially before inducing ischemia. When administered intravenously in high concentrations, magnesium is transported into the cerebrospinal fluid.39,53 It is well documented that elevated parenchymal concentrations of magnesium exert a cytoprotective effect during ischemia. In vitro experiments using superfused rat hippocampal slices23,45 and isolated rabbit retina,3 in which minimal diffusional barriers exist and high magnesium concentrations can be achieved, have unequivocally demonstrated the protective action of magnesium against anoxic neuronal damage. When administered directly to the hippocampus, magnesium salts have also been effective in limiting ischemic damage to CA1 pyramidal cells, even when given up to 24 hours after the ischemic episode.34 In vivo studies have shown the benefits of systemically administered magnesium in experimental models of permanent focal cerebral ischemia,9,21 spinal cord ischemia,35 traumatic brain injury,30 topically induced quinolinate hippocampal neurodegeneration,57 perinatal postasphyxial brain damage,52 and delayed cerebral vasospasm after subarachnoid hemorrhage.46 More recently Nishiki, et al.,36 reported that MgSO4 administered intraperitoneally prior to ischemia and 60 minutes thereafter is capable of reducing cortical infarct in neonatal rats subjected to transient global ischemia. Data demonstrating magnesium to be a potent neuroprotective agent in vivo are consistent with the active transportation of magnesium into the brain after systemic administration. A recent report by Sjostrom and Wester49 confirmed that such a transport occurs.

Although many of the underlying mechanisms of the

<table>
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<th>Treatment Group (no. of animals)</th>
<th>Grade of Neurological Deficit</th>
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<tr>
<td>30 mg/kg MgSO4 (12)</td>
<td>— 8 2 2</td>
<td>2.50 ± 0.80</td>
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* Outcome based on Bederson, et al.5 Abbreviations: MCA = middle cerebral artery; — = not applicable.
† Values are expressed as means ± standard deviation.
‡ p < 0.05, 30 mg/kg MgSO4 vs. 90 mg/kg MgSO4.
§ p < 0.01, vehicle vs. 90 mg/kg MgSO4 (Mann–Whitney U analysis).
artery occlusion in various treatment groups. The data are ex-
age in the infarct border 24 hours after temporary middle cerebral
treated group.

Neuroprotective mechanisms of MgSO4 probably in-
clude blockade of calcium channels, inhibition of excit-
atory neurotransmitter release, and/or blockade of the
NMDA–glutamate receptor. Rothman42 showed that by inhibiting excitatory neurotransmitters with high concen-
trations of magnesium or specific glutamate antagonists,
anoxic neuronal death could be prevented in neuronal cell
 cultura. The importance of inhibition of excitatory synap-
tic transmission for preventing hypoxic neuronal injury
was further confirmed in hippocampal slice preparations.
In this model, high concentrations of magnesium reduced
the vulnerability of neurons by blocking the persistent
phase of anoxia-induced depolarization and by enhancing
postischemic recovery of high-energy phosphates.23,45

Another mechanism by which magnesium may de-
crease the size of brain infarct is cerebral vasodilation. Altura and Altura36 infused MgSO4 into the carotid arteries
of adult rats and showed a dose-dependent vasodilatation
of intracranial arterioles and venules. The drug also reversed
delayed vasospasm after experimental subarachnoid hem-
orrhage in rats41 and increased cerebral blood flow after
parenteral administration in rat ischemia models. In con-
cious rats, MgSO4 antagonizes carotid artery vasocon-
striction that is caused by endothelin-I, angiotensin II, and
neuropeptide Y.24 In isolated human cerebral arteries, it
inhibits both serotonin- and prostaglandin-elicted con-
striction and relaxes prostaglandin-preconstricted arteries.1 Extracellular magnesium affects smooth-muscle
contraction by its action on membrane permeability to cal-
cium ions and blocks both L- and N-type voltage–operat-
ed calcium channels.20 Recently Huang and colleagues19
produced evidence indicating that magnesium may also
modulate hypoxic–ischemic events by blocking local
excitatory amino acid–induced spasm and rupture of pial
microvasculature; a transcranial Doppler ultrasound study
in preeclampsia patients by Belfort and Moise6 also
showed that intravenously administered MgSO4 dilates
small intracranial arterial vessels distal to the MCA.

Back and colleagues4 have shown that the volume of
the ischemic penumbra is greater than the volume of the
densely ischemic core soon after the onset of focal isch-
emia. However, during the first hours of ischemia the
penumbra is subjected to progressive metabolic compro-
mise by repetitive waves of anoxic depolarization, proba-
bly due to glutamate efflux from the deteriorating isch-
emic core.16,18 As a result, infarct progresses over time by
incorporating tissue surrounding the ischemic core and,
by 3 to 4 hours, the core and the penumbra merge.13,22
Magnesium may exert its beneficial effect by selectively
antagonizing anoxic neuronal depolarization by blocking
NMDA receptors in the penumbra. It has also been sug-
gested that, because magnesium is intimately involved in
adenosine triphosphate (ATP) regeneration after ischemia,
its cerebroprotective action may be attributed to attenua-
tion of the ATP depletion during the periods of relative
hypoxia that occur with each depolarization.45

Studies of transient focal ischemia in rats have shown
that the window of opportunity for tissue salvage by reper-
fusion is between 1 and 2 hours.23,32,46 We saw no differ-
eence in infarct size in our control animals with 1.5 and 2.0
hours of occlusion. This indicates that in our model the
time window for salvage of tissue by reperfusion is less
than 90 minutes in untreated animals, which is similar
to the data published by Memezawa and coworkers22 in
1992. The effect of the duration of ischemia on infarct size
in MgSO4-treated animals is difficult to determine from
our data. It is possible that the magnesium dose alone
determined the infarct size in our study because the rela-
tionship between the duration of reversible ischemia and
the infarct volume did not reach statistical significance.
There was, however, a trend toward smaller infarct vol-
umes with shorter periods of MCA occlusion in MgSO4-
treated animals and we think this would have been sig-
nificant had the power of our analysis been greater.

It is known that hypermagnesemia may cause a reduc-
tion in plasma insulin levels, resulting in hyperglycemia.56
Hyperglycemia is known to aggravate the cerebral injury
that follows global ischemia27 and transient focal isch-
emia12,17,35 and it might limit the effectiveness of magne-
sium treatment for cerebral ischemia.21 The level of hyper-
glycemia was modest in our study and not significantly
increased after treatment. Although the increase in plasma

FIG. 4. Bar graph depicting a comparison of the neuronal dam-
age in the infarct border 24 hours after temporary middle cerebral
artery occlusion in various treatment groups. The data are ex-
pressed as mean ± standard deviation and represent the ratio (per-
cent) of histologically intact neurons counted in the infarct periph-
ery to intact neurons in a homotopic area in the contralateral,
nonischemic hemisphere (five animals in each group). Data for
sham-operated animals are given as a ratio of right-to-left hemi-
sphere in percent. *p < 0.05 for 30-mg/kg MgSO4 group vs. vehi-
cle-treated group.
Magnesium sulfate in reversible cerebral ischemia

glucose levels observed in our study was small, it may have decreased the efficacy of MgSO₄ and the use of insulin to control glucose levels might have potentiated the beneficial effects of the magnesium administration. However, because of difficulties inherent in adjusting the insulin dose appropriately and because of evidence that insulin itself may be cerebroprotective in rat transient focal ischemia, we have not used insulin to achieve tighter glucose control in our laboratory. Other magnesium salts, such as MgCl₂, appear to produce a greater hyperglycemic response than MgSO₄. Studies using MgSO₄ in concentrations much higher than were used in our study did not report problems with significant hyperglycemia. The anion associated with Mg²⁺ seems to be responsible for the differential effects on glucose metabolism, as demonstrated in a comparative study by Nishio, et al.³⁷

Conclusions

Preischemic, intracarotid infusion of MgSO₄ in rats subjected to transient focal cerebral ischemia had a beneficial effect when compared with vehicle-treated control animals. The neuroprotection was dose dependent and could be documented by improved neurological outcome, decreased volume of infarct, and diminished histological evidence of neuronal injury in the ischemic border zone. The cytoprotective effects of intraarterial MgSO₄ were similar in magnitude to those demonstrated in studies of competitive and noncompetitive excitatory amino-acid antagonist drugs. These results suggest that MgSO₄, a compound with a long history of clinical use, may prove to be a valuable neuroprotective agent if given intraarterially before inducing transient cerebral ischemia during microsurgical or endovascular procedures on the cerebral vessels.

References


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