The Effects of Methylprednisolone on Prevention of Brain Edema after Experimental Moderate Diffuse Brain Injury in Rats

—Comparison between Dosage, Injection Time, and Treatment Methods—

Chong Oon Park

Our study was designed to determine whether methylprednisolone exerts a beneficial effect after experimental moderate diffuse brain injury and whether this possible beneficial effect is affected by the dosage, the timing of administration, and the methods of treatment. A total of 200 anesthetized adult rats were injured utilizing a weight-drop device through a Plexiglas guide tube. These rats were divided into eight groups: Group 1 (n=35) was assigned to receive no methylprednisolone after impact (control group), Group 2 (n=25) received an initial intraperitoneal administration of methylprednisolone with a dose of 5 mg/kg at 1 hour after cranial impact, followed by administration with a maintenance dose of 5 mg/kg/4 hours. Group 3 (n=25), group 5 (n=25), and group 7 (n=20) received an initial 30 mg/kg at 1 hour, 4 hours, and 8 hours, respectively without a maintenance dose. Group 4 (n=25), group 6 (n=25), and group 8 (n=20) received an initial 30 mg/kg at 1 hour, 4 hours, and 8 hours after impact, with a maintenance dose of 15 mg/kg/4 hours. Measured water content of brain tissue expressed the amount of water as the difference between fresh and dry weight. At 48 hours after impact, the water content in group 4 and 6 were significantly lower than group 1. Mean±SD was 61.4±0.37% in group 4 (p<0.03), 61.5±0.34% in group 6 (p<0.001), and 63.6±0.48% in group 1. Compared to group 1, the difference was not statistically significant in group 2 (p>0.1), group 3 (p>0.5), group 5 (p>0.6), group 7 (p>0.1), and group 8 (p>0.5). Groups treated with mega dose before 4 hours after head impact, including maintenance dose, showed beneficial effects. Our study suggests that the efficacy of methylprednisolone in head injury was related to the dosage, the timing of administration, and method of treatment.

Key Words: Moderate diffuse brain injury, mega dose, methylprednisolone, brain edema, weight-drop device

Received September 5, 1997
Accepted August 29, 1998

Department of Neurosurgery, Inha Hospital, College of Medicine, Inha University, Sung Nam City, Korea
This work was partly supported by Faculty Funds of Inha University, College of Medicine for 1997.
Address reprint request to Dr. C.O. Park, Department of Neurosurgery, Inha hospital, College of Medicine, Inha University, 3309-327, Tae Pyung Dong, Su Jung Ku, Sung Nam City, Kyung Gi Do 461-192, Korea. Tel: 0342-720-5836, Fax: 0342-755-2812

Since Galicich and French demonstrated the benefits of glucocorticoids in the management of cerebral edema resulting from a tumor, it has been hoped that glucocorticoids might be able to reduce edema and thus improve the outcome in patients with cerebral trauma (Galicich and French, 1961). Clinical trials have been instituted in an attempt to show a reduction in morbidity and mortality in head-injured patients treated with adrenal corticosteroids. Guterman and Shenkin and Alexander had denied any bene-
ficial effect from the administration of the conventional doses of dexamethasone phosphate (16 mg/day)(Alexander, 1972; Guttermann and Shenkin, 1972). Gobiet et al. and Faupel et al., in their studies of head injury, could not detect any significant beneficial effect with conventional doses of dexamethasone (16 mg/day)(Faupel et al. 1976; Gobiet et al. 1976). However, following administration of a high dose (48 mg initially, and a total dose of 96 mg during the first day), they achieved a significant reduction in mortality, in the complication rate, and in the frequency with which intracranial pressure (ICP) rose. However, Cooper et al. and Braakman et al. were unable to document improvement in outcome in head injured patients using a variety of steroid preparations (Cooper et al. 1979; Braakman et al. 1983). Evidence for or against the efficacy of steroids in head injury has been clouded by a lack of agreement regarding the drug of choice, the dosage, and the time of administration.

We considered it important that this controversy will be resolved. Our goal was to design a preliminary study to assess the effects of large doses of methylprednisolone on the outcome of patients suffering from moderate blunt brain injury.

**MATERIALS AND METHODS**

We used the trauma device introduced by Marma-roiu and colleagues (1994)(Fig. 1). The trauma device consists of a column of brass weights falling freely onto a metallic helmet fixed by dental acrylic to the skull vertex of a rat. For the purpose of obtaining high acceleration upon impact, the head was lightly supported allowing rapid displacement after impact. The brass weights, each 50 gm, were threaded so that they could be connected to produce a falling weight ranging from 50 to 500 gm. From a designated height, the weight fell through 2-m and 1-m vertical sections of a transparent Plexiglas tube held in place with a ring stand. The helmet consisted of a stainless-steel disc, 10 mm in diameter and 3 mm in thickness. Previously, we reported that 400 gm-2 m impact was considered to be the upper limit for producing severe head trauma. The weight-height combination determined a mortality rate of approximately 50% in nonventilated animals. In order to induce a moderate head injury, the energy delivery was decreased to 50% by reducing the height to 1 m.

A total of 200 adult Sprague-Dawley rats, each weighing 300 to 350 gm, were anesthetized with intraperitoneal injection of Nembutal (pentobarbital, 35 mg/kg). The animals were allowed to breathe spontaneously without tracheal intubation. A midline scalp incision was performed followed by periosteal elevation to expose the central area of the skull vault between the coronal and lambdoid sutures. A stream of air was used to keep the area dry. A stainless-steel disc, 1 cm in diameter, was firmly fixed by dental acrylic to this exposed area of the skull vault.

**Fig. 1. Diagram of the head-injury device. The upper weight is attached to a string and the segmented brass weights elevated to the desired height. Brass weight is made of 50-gm segments, 18 mm in diameter. The bottom opening of the Plexiglas cylinder is positioned in close proximity to the head of the rat and centered for mass to strike directly upon the helmet. The helmet consists of a stainless-steel disc, 10 mm in diameter and 3 mm in thickness, cemented to the calvaria with a thin layer of dental acrylic. The foam (of known spring consistency) is cut to fit in the Plexiglas frame without being compressed. After release of the weight and contact, the Plexiglas frame is removed rapidly to prevent a second impact.**
The animal was placed in a prone position on a foam bed with the disc centered directly under the lower end of the Plexiglas tube of the trauma device. Two belts were fastened around the trunk of the rat to prevent it from falling off the foam bed after trauma induction. The weight was allowed to drop freely from the predetermined height through the Plexiglas tube onto the disc. Rebound impact was prevented simply by sliding the Plexiglas box (foam bed) containing the animal away from the tube immediately following the initial impact. The scalp was sutured and the rat was allowed to recover from anesthesia. Rats which died on impact and those with skull fractures were excluded from this study. Animals in the control group (n=35) were subjected to the head trauma, but were not treated with methylprednisolone. One hundred and sixty-five animals were subdivided into 7 groups according to methods of treatment (Table 1).

To investigate the effect of diffuse head trauma on animals without respiratory assistance, five animals from Group 1 and 5 animals from Group 4 were decapitated for microscopic pathological examination at 48 hours after head trauma. The fixative used was 10% formaldehyde in 0.1 M sodium phosphate buffer for light microscopy. The brains were coronally sectioned before being embedded in paraffin. Sections of 4 μm thickness were cut with a rotatory microtome and stained with hematoxylin and eosin (H & E).

All animals were decapitated and their brains were removed for the measurement of water content depending on times (4, 8, 12, 16, 24, and 48 hrs after head injury). These were placed in preweighed aluminum foil and reweighed on a microanalytical balance. The specimens were desiccated at 104°C for 24 hours. By subtracting the measured dry weight of the tissue from the wet weight, the water content of the brain was obtained. Water content was determined as a percentage of wet weight according to the following formula (Ferszt et al. 1980):

\[
\text{Water content} = \frac{\text{wet weight} - \text{dry weight}}{\text{wet weight}} \times 100
\]

\text{STATISTICS}

For the comparison of water contents, Mann-Whitney Rank test by SigmaStat® software was used. A p-value of 0.05 was taken to indicate statistical significance.

\text{RESULTS}

Four hundred gm-1 m impact (moderate head trauma) caused no mortality and no skull fracture in all animals. Although 28 animals impacted at 400 gm-1 m level experienced a brief (5- to 10-second) apneic period, they rapidly recovered to control respiratory rates. In moderate head trauma, apart from a mild subarachnoid hemorrhage (SAH) in basal cisterns, the brains looked normal without contusion or focal lesions. The central portion of the area involved was located under the site of the metallic disc. In sections prepared with H & E stain, “pink shrunken neurons” associated with perineuronal va-

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Table 1. Experimental groups} & \\
\hline
Group 1 (35): No treatment (control) & \\
Group 2 (25): 5 mg/kg/4 hr from 1hr after head injury & \\
Group 3 (25): 30 mg/kg at 1 hr after head injury & \\
Group 4 (25): 30 mg/kg at 1 hr after head injury with maintenance dose (15 mg/kg/4 hr) & \\
Group 5 (25): 30 mg/kg at 4 hr after head injury & \\
Group 6 (25): 30 mg/kg at 4 hr after head injury with maintenance dose (15 mg/kg/4 hr) & \\
Group 7 (20): 30 mg/kg at 8 hr after head injury & \\
Group 8 (20): 30 mg/kg at 8 hr after head injury with maintenance dose (15 mg/kg/4 hr) & \\
\hline
\end{tabular}
\end{table}

(n) means the number of experimental animals
cuolation could be observed in these areas. In addition, dark contracted neurons with "cork-screw like processes", and capillaries congested with red blood cells and associated with pericapillary astrocytic swelling were observed in the same sections. But comparing the group without treatment to the groups with treatment, the differences in microscopic changes were not significant. However, there were differences in microscopic findings between the severely and moderately injured brains (Fig. 2).

The water contents of brain tissue that was taken from the injured brain in both the treated and un-

![Image](image_url)

**Fig. 2. High magnification of histopathology (H & E stain, ×400).** a) no traumatic brain, which shows no specific pathological findings. b) moderately injured brain, which shows perineuronal vacuolation (arrow), erythrocyte congestion (arrowhead), and cork-screw shape axon (empty arrow). c) severely injured brain, which shows the same findings, but more severe than moderately injured brain.

<table>
<thead>
<tr>
<th>Group</th>
<th>0 hr</th>
<th>4 hr</th>
<th>8 hr</th>
<th>12 hr</th>
<th>16 hr</th>
<th>24 hr</th>
<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>61.6 ± 1.78</td>
<td>71 ± 0.42</td>
<td>69.4 ± 0.66</td>
<td>68 ± 0.69</td>
<td>66 ± 0.48</td>
<td>65.2 ± 0.61</td>
<td>63.6 ± 0.48</td>
</tr>
<tr>
<td>Group 2</td>
<td>70.5 ± 0.76</td>
<td>69.7 ± 0.54</td>
<td>68 ± 0.47</td>
<td>64.5 ± 0.35</td>
<td>63.6 ± 0.35</td>
<td>61.4 ± 0.37</td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>69.4 ± 0.87</td>
<td>67.4 ± 1.02</td>
<td>66.4 ± 0.45</td>
<td>64.3 ± 0.33</td>
<td>63.2 ± 0.31</td>
<td>61.4 ± 0.37</td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td>69.1 ± 0.52</td>
<td>67.3 ± 0.34</td>
<td>64.5 ± 0.28</td>
<td>63.6 ± 0.35</td>
<td>61.4 ± 0.37</td>
<td>60.5 ± 0.34</td>
<td></td>
</tr>
<tr>
<td>Group 5</td>
<td>69.1 ± 0.32</td>
<td>67.4 ± 0.36</td>
<td>66.8 ± 0.40</td>
<td>65.5 ± 0.31</td>
<td>63.8 ± 0.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 6</td>
<td>69 ± 0.46</td>
<td>66.3 ± 0.37</td>
<td>65 ± 0.32</td>
<td>64 ± 0.39</td>
<td>61.5 ± 0.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 7</td>
<td>68 ± 0.63</td>
<td>66.7 ± 0.42</td>
<td>65.8 ± 0.48</td>
<td>64.4 ± 0.41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 8</td>
<td>68.3 ± 0.37</td>
<td>66.1 ± 0.35</td>
<td>64.8 ± 0.42</td>
<td>63.7 ± 0.38</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Maximal beneficial effect of methylprednisolone was noted at around 8 hours after administration. In comparison with group 1, there was more reduction of water content in brain tissue particularly in group 4 and group 6. Above data are mean ± standard deviation. Horizontal line: the decapitated time for water content of brain tissue. hr: hour.
The Effects of Mega-Dose Steroid on Experimental Brain Edema

treated rats is shown in Table 2. In group 1, a large increase of edema fluid in brain tissue tended to occur at around 4 hours after head trauma (15.3% increase), but gradually resolved by 48 hours after head trauma (3.2% increase). The water content in group 2, which received 5 mg/kg/4 hours, was not significantly lower compared to group 1 (p>0.1, 64 ±0.32%). At 48 hours after impact, The water content in groups 4 and 6, which received an initial 30 mg/kg with a maintenance dose of 15 mg/kg/4 hours, were significantly lower compared to group 1. Mean ±SD was 61.4 ±0.37% in group 4 (p<0.003), 61.5 ±0.34% in group 6 (p<0.001), and 63.6 ±0.48% in group 1. However, the water con-

| Table 3. P-value between control group and other groups depending on time |
|---------------------------------|------|------|------|------|------|------|
|                                  | 4 hr | 8 hr | 12 hr| 16 hr| 24 hr| 48 hr|
| Group 2                          | 0.222 | 0.687 | 1    |      | 0.467 | 0.172 |
| Group 3                          | 0.032 | 0.021 | 0.002| 0.003| 0.082 | 0.583 |
| Group 4                          | 0.001 | 0.39  | 0.492| 0.07 | 0.533 | 0.681 |
| Group 5                          | 0.304 | 1.05  | 0.043|      | 0.002 | 0.001 |
| Group 6                          | 0.439 | 0.738 | 0.226|      |      |      |
| Group 7                          | 0.304 | 1.05  | 0.043|      | 0.002 | 0.001 |
| Group 8                          | 0.439 | 0.738 | 0.226|      |      |      |

Groups treated with megadose and maintenance dose showed less water content than without maintenance dose or with conventional dose. But when treated at around 8 hours after head trauma, there was no statistical significance.

![Graphs a, b, c, d](image)

**Fig. 3.** Comparison between the maintenance and no-maintenance dose treated groups at the time of first administration. Groups treated with maintenance dose were more effective than no-maintenance dose (a, b). But, when steroid was administered 8 hours after head trauma (c), there was no statistically significant difference. Groups 4 and 6 treated with mega dose showed less water content than group 1 treated with conventional dose (d). G1−G8: Group 1−8.
tent in group 8, which received mega dose at 8 hours after impact, was not statistically significant after impact (p > 0.8, 63.7 ± 0.38%). A decrease of water contents in groups 3, 5, and 7, which received an initial 30 mg/kg without maintenance dose, was not statistically significant compared to group 1 (p > 0.5, 63.2 ± 0.31%; p > 0.6, 63.8 ± 0.33%; p > 0.1, 64.4 ± 0.41%) (Table 3). These findings could mean that there is no beneficial effect with the administration of conventional doses of methylprednisolone (5 mg/kg/4 hr), but mega dose methylprednisolone (initial 30 mg/kg) reduced cerebral edema (a favorable dose-related effect). Treatment with maintenance dosage was more effective than without maintenance dosage (p < 0.003). The timing of administration, considered to be important in the treatment of head injury, showed more effectiveness the earlier it was made, especially until 4 hours after head trauma (p < 0.05) (Fig. 3).

DISCUSSION

Diffuse brain injured patients may suffer from widespread brain damage secondary to trauma in the absence of a focal lesion, which is not a consequence of herniation or perfusion failure. This type of brain injury has long been emphasized as the most common cause of a persistent vegetative state and severe disability after closed head injury. Adams et al. observed this type of brain injury in 13% to 28% of fatal head injuries and they introduced the term “diffuse axonal injury” to express its pathological nature (Adams et al. 1983). More recently, Marshall et al. found that 55% of patients with severe head injury in the Traumatic Coma Data Bank suffered from diffuse head injury, of whom 12.6% had an entirely normal computerized tomography (CT) scan (Marshall et al. 1991).

Over the past 20 years, numerous investigators have studied the response of rats to experimental closed head injury. Unfortunately, studying this type of diffuse brain injury in animals has been difficult since the currently available models of severe head trauma essentially produce a focal brain contusion more readily than a diffuse injury. In a study of head injury by Beckman and Bean readily, the heads of hand-held, nonanesthetized rats cushioned with a rubber sponge were impacted with a bolt (Beckman and Bean, 1969). In those animals, a contusion, subarachnoid hemorrhage, and subdural hemorrhage were frequently found in the brain. In other such models, including the widely used fluid-percussion injury models (Sullivan et al. 1976; Dixon et al. 1987; Cortez et al. 1989; McIntosh et al. 1989), these high-velocity impacts produced focal cortical contusions. Thus, due to the focal nature of lesions produced, the results derived from these models have been criticized because of their inability to faithfully replicate the range of diffuse brain injuries seen in man. A study of the effects on closed head injury in which mice were impacted with a sliding bolt striking the immobilized head was conducted by Nelson et al. Shapiro et al. introduced another model for closed head injury in rats using a weight-drop impact on the unprotected skull (Shapiro et al. 1988). This model produced a focal brain contusion or depressed skull fracture with focal brain contusion and/or laceration because there was no protection for skull fracture. Those models would be suitable for studying focal but not diffuse forms of brain injury.

Experimental diffuse brain injury identical to that occurring in man has been produced by subjecting the head of a monkey to angular acceleration (Ommaya and Gennarelli, 1974; Gennarelli et al. 1982; Jane et al. 1985), but this model has not been widely used. However, Marmarou et al. recently introduced a new model of diffuse brain injury in which an accelerated impact was designed to be directed to the skull of rats protected with a foam bed to allow freedom of movement and acceleration (Marmarou et al. 1994). They reported that this model had certain advantages over other models (Foda and Marmarou, 1994; Marmarou et al. 1994): 1) a lethal level of closed head injury can be achieved without predominant brain-stem damage as seen with direct dural impact; 2) the transient rise in blood pressure seen in closed head injury immediately after impact is milder than other models; 3) this model produces a pronounced diffuse axonal injury consistent with features of human diffuse axonal injury described by Adams et al. (1989); 4) posttraumatic ventriculomegaly is observed, which also mirrors the experience in human head injury. We used this model to produce experimental mod-
erate diffuse brain injury. We determined severe head injury to have a mortality rate of approximately 50% in nonventilated animals with a low incidence of skull fracture. We reduced the height to 1 m, decreasing the energy delivery by 50%, in order to induce a moderate head injury that caused no mortality and no skull fracture. Microscopically, moderate head injury developed neuronal, axonal, and microvascular abnormalities similar to, but less extensive than, those observed in severely injured rats.

Shapira et al. reported that brain edema was demonstrable as early as 15 min after severe head injury, was maximal at 18–48 hours, and was gradually resolved by 10 days after injury (Shapira et al. 1988). Neurologic function was maximally impaired immediately after injury and was gradually resolved to almost no residual deficit by 10 days after injury. Both forms of brain edema, cytotoxic and vasogenic edema, could be seen as early as 6 hours after severe head trauma, and appeared to reach a maximum after 24 hours at the light microscopic level. Thereafter, the edema was resolved in a few days. A recent report demonstrated the development of ischemia in the first 12 hours in severely head-injured patients (Bouma et al. 1991). In our moderate brain injury, a maximal increase of edema fluid in brain tissue was noted around 4 hours after impact. A large increase of brain edema was retained for 12–16 hours after trauma, but it was gradually resolved by 48 hours after head trauma. We thought that the time of maximal brain swelling and the resolution time in moderate head injury may be different from severe head trauma. We believe that it may be more effective in reducing brain edema if the medical treatment is started before 4 hours have passed after moderate brain injury.

Many actions of methylprednisolone in damaged and normal central nervous system tissue have been noted: 1) the protective effects on axonal integrity in the face of various degenerative influences by preservation of lysosomal integrity and membrane-bound enzymes (Beyer-Mears and Barnett, 1983); 2) the enhanced flow and preservation of microcirculatory pathways (Emerson and Brain, 1977; Anderson et al. 1982; Young and Flamm, 1982); 3) a decrease in thromboxane and prostaglandin production (Nelson et al. 1966; Gamache and Ellis, 1986); 4) a reduction in endothelial lipid peroxidation by enhancing synaptosomal (Na⁺+K⁺)-ATPase activity (Bangham et al. 1965; Nelson et al. 1966; Demopoulos et al. 1972); 5) the maintenance of capillary endothelial membranes (Laha et al. 1978; Gamache and Ellis, 1986); 6) a decrease in the permeability of the blood-brain barrier (Chan et al. 1984; Gamache and Ellis, 1986); 7) the inhibition of free radicals (Hall and Braughler, 1982; Cortez et al. 1989); and 8) anti-inflammatory effects (Giannotta et al. 1984; Kalayci et al. 1992). The assumption has been made that the beneficial effects of steroids in treating head injuries were related to the reduction of edema. This was based on observations made in patients with tumors who showed a dramatic reduction in the mass effect when given glucocorticoids (Gallicich and French, 1961). Korbine and Kempe were able to show reductions in the wet weight of the brain after experimental trauma using corticosteroid (Korbine and Kempe, 1975). However, other investigators have not been able to demonstrate a significant benefit using conventional doses of dexamethasone for traumatically-induced cerebral edema (Gutterman and Shenkin, 1972). After Braughler and Hall, Faden et al., Braughler et al., and Bracken et al. reported mega dose methylprednisolone to improve neurological outcome after spinal cord injury, mega dose methylprednisolone has been widely used in head-injured patients (Braughler and Hall, 1984; Faden et al. 1984; Braughler et al. 1987; Bracken et al. 1990). Faupel et al. reported a favorable dose-related effect on mortality, even in patients who had received treatment some 6 hours or more after an accident (Faupel et al. 1976). A number of investigators supported the use of methylprednisolone for treatment of head-injured patients. But Cooper et al., Braakman et al., Giannotta et al., and Shapira et al. reported that the administration of high-dose or low-dose corticosteroid in patients with severe head injury is not warranted (Cooper et al. 1979; Braakman et al. 1983; Giannotta et al. 1984; Shapira et al. 1992). One reason may be, as Cooper et al. suggested, that in severe injury, tissue destruction is so immediate and irreversible that any management modalities have little chance of improving neurological outcome (Cooper et al. 1979). We hypothesized that the efficacy of methylprednisolone in head injury was related to the dosage, the timing of administration, and method of treatment. Braughler
and Hall found that the optimal tissue level of methylprednisolone in a traumatized spinal cord is approximately 3 μg/g wet weight (Braughler and Hall, 1984). The tissue half-life of methylprednisolone suggests that a 3-hour dosing schedule may be more appropriate than the traditional 6-hour schedule (Braughler and Hall, 1982). We decided that the optimal dosage for methylprednisolone was in doses of 30 mg/kg, administered intraperitoneally 1 hour after impact, with a maintenance dose of 15 mg/kg every 4 hrs (a 4-hour dosing schedule). We demonstrated that methylprednisolone in conventional doses (5 mg/kg/4 hr) showed no statistically significant effect on brain edema, but in initial high doses (30 mg/kg at 1 hour after trauma) with maintenance doses (15 mg/kg/4 hr) for 48 hours it was associated with a statistically significant effect. Methylprednisolone treatment was not effective statistically when injected 8 hours after head trauma.

In summary, because a new model of diffuse brain injury induced by Marmarou et al. (1994) was very simple, cheap, and has been developed with several features similar to the experience in a clinical setting, we thought this was an ideal model in which to make an experimental diffuse brain injury. In moderate diffuse brain injury, brain edema developed early after injury, reaching a maximum at around 4 hours and maintained for 12-16 hours after trauma. Mega dose methylprednisolone treatment with maintenance dose was more effective on brain edema before 4 hours have passed after trauma, compared to its effectiveness 8 hours after trauma. A 4-hour dosing schedule seemed to be more appropriate than the traditional 6-hour dosing schedule.

REFERENCES


The Effects of Mega-Dose Steroid on Experimental Brain Edema

Shapira Y, Artru AA, Yadid G, Shoami E: Methylprednisolone does not decrease eicosanoid concentrations or edema in brain tissue or improve neurologic outcome after head trauma in rats. Anesth Analg 75: 238-244, 1992