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기 초

Pre-injury Treatment of Methylprednisolone in Experimental Spinal Cord Injury

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= Abstract =

The purpose of this study was to establish whether pre-injury administration of the methylprednisolone sodium succinate(MP) is effective for the treatment of acute spinal cord injury in rat, as it has been demonstrated that high dose of MP is effective in the treatment of acute spinal cord injury. Spinal cord injury was made by dropping a rod weighing 10 gm from a height of 1.25, 2.5, and 5.0cm onto the rat spinal cord at T-10, which had been exposed via laminectomy.

In oder to determine the effectivness, single dose of 5, 15 and 30mg/kg of MP was administrated at 10 minute before injury. The primary outcome was 24-hour spinal cord lesion volume estimated from spinal cord Na^+ and K^+ shifts.

Surprisingly, we failed to find any statistically significant preventive effect compare to control vehicle. Until this result is clearified, we recommend that acute pre-injury MP therapy be cautiously applied in operating room. The possible causes of this unexpected result are discussed.

KEY WORDS : Methylprednisolne · Spinal cord injury · Pre-injury treatment · Rat.

Introduction

The synthetic glucocorticoid, methylprednisolone sodium succinate(MP), has been extensively studied in models of spinal cord injury[1)2)3)4)5)7)8)9)10)11)13)14)16)17)21)22)26)30)33)36)40)]. MP is the first treatment shown to improve recovery in human spinal cord injury and remains the only form of management shown emeirically in a Phase 3 trial to have efficacy in treating this injury[4)35)]. Therefore MP is regarded as the standard against which all further treatments should be compared[4)30)].

In a number of previous studies, it has been demonstrated that intravenous doses of MP in the 30 mg/kg can have the most profound beneficial effect on the spinal cord injury[7)8)10)14)16)21)].

It prevent post-traumatic spinal cord ischemia and improves blood flow in the cord tissue and also improves tissue metabolism, restore extracellar calcium, lipid peroxidation, and improve neuronal conduction. A primary action of MP in the injured spinal cord is believed to be its ability to inhibit lipid peroxidation and to preserve the structural and functional integrity of biological membranes[3)6)17)16)18)19)20)21)30)39)43)]. The second National Spinal Cord Injury Study(NASCIS 2) studies clearly indicated that MP improves motor and sensory recovery only when given high dose and within 8 hours after spinal cord injury and this 8-hour period was simply the median treatment time which conveniently segregated the patient population into equal groups of early and late treatments for analysis[4)35)]. Therefore, the optimal therapeutic time for methylprednisolone in human spinal cord injury is likely to be shorter than 8 hours.

In cats, methylprednisolone has been shown to be effective when given as late as 45 minutes after injury[30)31)33)].

Our recent experiment, however, suggest that the therapeutic time window for methylprednisolone is less than 30 minutes after contusion in rat[18)]. Therefore, it has been suggested that MP should be initiated as soon as possible.

There have also been reports of high dose of MP being

used prophylactically during surgical procedures where the spinal cord is at risk of iatrogenic injury[3].

Since this short therapeutic time window for MP, many neurosurgeon routinely give patients a bolus dose of MP before major spinal surgery to expect that MP would protect intraoperative cord damage. But, data are very limited in regard to the pretreatment effect of MP in spinal cord injury[2]. This study was designed to determine the effectiveness of pre-injury treatment of MP in acute spinal cord injury in rats.

In order to determine the effectivness of pre-treatment for optimal neuroprotection[5][15], and 30mg/kg of MP was administered at 10 minutes before injury. Spinal cord contusions were induced and measured by means of a New York University weight-drop device. We quantified lesion volumes from shifts in Na^+ and K^+ levels[13][24]. We therefore compared each treatment groups on spinal cord lesion volume at 24 hours after injury in rats. These experiments yielded surprising findings. We failed to find any statistically significance preventive effect compare to control vehicle.

Materials and Methods

1. Experimental procedures

All animal protocols were reviewed and approved by NYU Medical Center Institutional Animal Care and Use Committee. A total of 130 adult male Long-Evans hooded rats weighing 400–500gm were anesthetized with pentobarbital(60mg/Kg intraperitoneally). A catheter was placed in femoral vein, tunneled subcutaneously to the middosum where it exited the skin and another catheter was in tail artery to monitor blood pressure and gases. Rectal temperatures were maintained at 37±0.5℃ with heating pad during surgery. The spinal cord was exposed via laminectomy T 10 and a 10-gm rod was dropped 1.25(12.5 gcm), 2.50(25.0gcm), or 5.00(50.0gcm) cm directly onto the cord. The impactor has a diameter of 3.00 mm and care was taken to ensure that it did not contact bone during its descent. The impact device consisted of a vertical rod linked to digital optical potentiometers which precisely monitored rod and vertical column movements. Impact velocities were estimated from the rod trajectory during the 2 msec. period before impact. Relative movements of the rod and vertebral column give the maximum depth (Cd) and time(Ct) of cord compression. The ratio Cd/Ct represents the mean compression rate of the spinal cord and is the best predictor of 24-hour lesion volumes in contused spinal cord. Blood pressure was monitored from a catheterized tail artery. Blood gases, PH, and bicarbonate values were checked before injury.

The rats received MP or the equivalent volume of saline intravenously as treatment protocol at 10 minutes before injury. The rats were divided into 4 groups : one vehicle treated group(Group A) and three MP treated group (Group B : 5mg/kg, Group C : 15mg/kg, Group D : 30mg/kg).

At 24 hours after injury, the rats were anesthetized 60mg/Kg(intraperitoneally), the rats were decapitated. The spinal cord were rapidly removed, frozen, and cut into five 4mm segments from the site of impact, one piece was centered on the impact site, two from proximal cord(P1 and P2), two from neighboring distal cord(D1 and D2) One another cord simple was obtained from the T-1 spinal cord level. The samples were weighed to obtain wet weight, then dried overnight in a vacuum chamber at 100℃ and reweighed to obtain dry weight. We analyzed these samples for Na^+ and K^+ by air-acetylene flame atomic absorption spectroscopy as described previously[13][24]. In addition, we collected blood from the inferior vena cava into test-tubes coated with Na-free heparin to prevent clotting. The blood was centrifused to obtain plasma. Both whole blood and plasma were analyzed by atomic absorption analysis for Na^+ and K^+. We divided tissue Na^+ and K^+ contents by wet weight to obtain concentration units of mmoles/g of wet tissue([Na]w and [K]w). Tissue water concentrations were calculated from the formular : (wet weight-dry weight)/wet weight. Since wet weight-dry weight represents the weight of water in the tissue and 1 ml of water weighs 1 gm, water concentrations are given in ml/gm of wet tissue so that ionic and water concentration units are consistent. Units of blood([Na]b and [k]b) and plasma([Na]p and [K]p) concentrations are expressed as mol/gm of blood and mol/ml(or mM of plasma, respectively.

To correct for bound or sequestered ions in the tissue, we normalized spinal cord [Na]w and [K]w to plasma levels by multiplying with([Na]p and [K]p)/([Na]w and [K]w) to obtain [Na]t and [K]t in units of mM. This correction assumes that tissue fluids are isotonic with plasma. In most cases, values of [Na]t and [K]t were 5% to 6% lower than [Na]w and [K]w, suggesting that a fraction of [Na]t and [K]t may be bound or sequestered. We used [Na]t and [K]t , as well as [Na]w and [K]w, to assess spinal cord damage. Because [Na]t and [K]t more accurately

represent soluble tissue Na and K concentrations, we used lesion volumes calculated from [Na]t and [K]t.

2. Cell volume fraction determinations

Fluids in different tissue compartments are isotonic because small differences in osmolarity across membranes can produce high pressures. For example, according to the Van Hoff't equation, 1mM of ionic osmolarity difference will generate 19.7mm Hg of pressure. because Na, K, and associated anions exert greater than 95 % of tissue fluid osmolarity, sums of Na and K concentrations should be approximately equal in intracellular([Na]i and [K]i) and extracellular([Na]e and [K]e) fluids. Likewise, since macromolecules in plasma compensate for blood pressure differences, sums of Na and K concentrations should be similar in plasma and extracellular fluids. Therefore, isotonicity can be expressed by the fellowing equation :

$$[Na]i+[K]i=[Na]e+[K]e=[Na]p+[K]p \quad (1)$$

If so, transmembrane Na and K gradient(G) values also should be equal ; that is,

$$G=[Na]i - [Na]e=[K]e - [K]i \quad (2)$$

By definition, tissue ionic contents equal sums of intracellular and extracellular ionic contents,

$$[Na]t\ Vt=[Na]i\ Vi+[Na]e\ Ve \quad (3)$$

and

$$[K]t\ Vt=[K]i\ Vi+[K]e\ Ve \quad (4)$$

where Vt, Vi and Ve are tissue intracellular and extracellular volumes respectively. Subtracting Equation 4 from Equation 3 yields :

$$[Na]t-[K]t)\ Vt=([Na]e-[K]e)\ Ve+([Na]i-[K]i)\ Vi \quad (5)$$

Since [Na]i=G+[Na]e and [K]i=[K]e-G, substitution into Equation 5 gives :

$$([Na]t-[K]t0Vt=([Na]e-[K]e)\ \ Ve+([Na]e-[K]e+2G)\ Vi \quad (6)$$

Rearranging terms gives :

$$[Na]t-[K]t=([Na]e-[K]e)(Vi+Ve)/Vt+2G\ Vi/Vt \quad (7)$$

Since Vt=Vi+Ve, the equation simethylprednisolonelifies to :

$$[Na]t-[K]t=[Na]e-[K]e+2G\ Vi/Vt \quad (8)$$

Equation 8 states that [Na]t-[K]t is linearly related to Vi/Vt with a slop of twice the gradient and a y intercept of [Na]e-[K]e. The ratio of cell to tissue volume(Vi/Vt) is equivalent to the cell volume fraction(CVF) of the tissue. To calculate Vi/Vt from [Na]t - [K]t, we assumed that [Na]e-[K]e=[Na]p-[K]p and that G=-120mM. Ion-selective microelectrode recordings have shown that [Na]e and [K]e approach [Na]p and [K]p within 30minutes of injury. calculated Vi/Vt values are expressed as percentages.

3. Lesion volume assessment

The change in Vi/Vt(Δ Vi/Vt) reflects the volume of cells that have lost their ionic gradients as a result of injury. To eatimate Δ Vi/Vt, we subtracted a normal CVF value of 0.70 from the calculated Vi/Vt of each cord sample. since 1 μl of tissue weighs about 1 mg, multipling Δ Vi/Vt by the tissue wet weight in milligrams gives the cell volume lost(Δ V) in microliters. The sum of the Δ V in P2, P1, site of impact, D1, and D2 tissue samples represents microliters of cells lost within 1 cm of the impact center. we refer to summed Δ V values as the ionic lesion volume.

Ionic lesion volumes thus depend on three variables : [Na]t-[K]t, [Na]p-[K]p, and wet weight. The calculations assume that [Na]e-[K]e=[Na]p-[K]p and that G=-120mM. Concentration of [Na]p-[K]p closely approximate [Na]e-[K]e at 24 hours after injury. Small inaccuracies of the assumed gradient value will not invalidate treatment effects as long as the gradient values are similar in all the treatment groups. To rule out general effects of treatment or injury on transmembrane ionic gradients, we estimated gradient values in blood samples by linear regression of [Na]b-[k]b and hematocrit. Since hematocrit is essentially the CVF of blood, [Na]b-[K]b should correlate linearly with hematocrit, and the slope of the relationship should equal twice the gradient value while the y intercept should be close to [Na]p-[K]p.

4. Statistical analysis

All data were entered and initially calculated on a spreadsheet program and then transfered to a statistics program(Stat view 4.02, Super Anova 1.1 by Abacus Concepts, Berkeley, CA) for statistical analyses on Macintosh computers.

We compared individual groups pre-treated with MP and vehicle control group using analysis of covarience (ANCOVA) with Cr as the linear covariate. To identify groups that differed significantly from vehicle control group, we used the Fisher LSD *post hoc* test. ANCOVA and ANOVA were performed with commercially available statistics programs superANOVA 1.1 and StatView 4.

01(Abacus Concepts, Berkeley, CA). Regression plots were generated with StatView. All measured data are expressed below in means±standard error of the means unless otherwise indicated. The criterion for significance was $p < 0.05$.

Result

1. Contusion parameters

Spinal cord contusion parameters were very consistent across treatment groups. Fig. 1 shows a scatterplot of impact velocity and spinal cord compression rate(Cd/Ct). Table 1 lists the mean impact velocities in the 12.5, 25.0, and 50.0gm-cm injury groups. ANOVA indicated no significant differences in mean velocities and compression rate among treatment groups($p > 0.05$). Impact velocities linearly predicted spinal cord compression rates(Cd/Ct), with a correlation coefficient of 0.92.

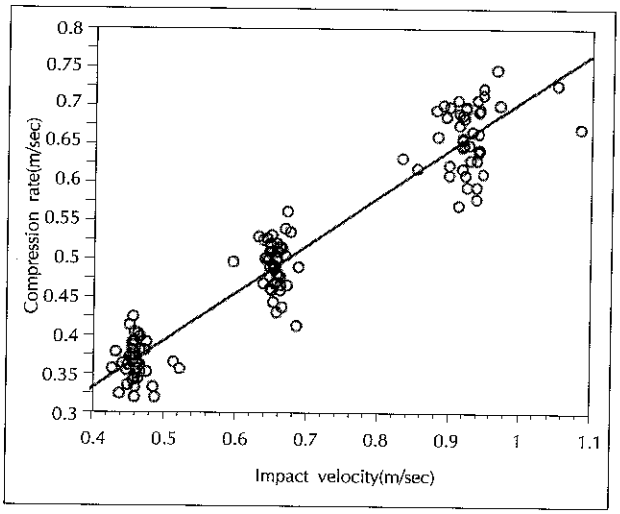

Fig. 1. Scatterplots of compression rate versus impact velocity.

Table 1. Contusion parameters in spine-injured rats

Weight drop (gcm)	No. of rats	Impact velocity (m/sec)	Rate of cord compression (m/sec)
12.5	43	0.466±0.026	0.364±0.038
25.0	43	0.660±0.023	0.491±0.049
50.0	44	0.930±0.062	0.663±0.065

Means are expressed±standard error of contusion parameters in all rats subjected to spinal cord injury and analyzed for spinal cord ionic changes.

In extense previous study, we have found that compression rate is generally the most linear accurate predictor of spinal cord lesion volumes. Thus, all groups received very similar mechanical contusions.

2. Pre-injury blood gases and systolic arterial pressure

ANOVA indicated some significant differences in PO_2(P =0.0029), PCO_2(0.0032), and O_2 saturation(P, 0.0001) value among each groups . Table 2 lists means of blood gas value. However, regression analysis showed no significant correlation between ionic lesion volumes and PO ₂(correlation coefficienct of 0.002), PCO_2(0.001), O_2 saturation(0.002). We could not find any statistical significance in pre-injury , injury, and post-injury systolic and diastolic blood pressure among treatment groups compared to vehicle control group.

3. Systemic variables

All groups lost body weight after injury with mean values ranging from 4.5±0.24%. Mean blood hematocrits ranged from 38.0±0.49%(Table 3).

ANOVA of the lost body weight and hematocrit showed significant difference between each group(lost body weight p=0.0308, hematocrit p=0.0368). Group D significantly lost its weight compare to control vehicle(P=0. 0372). Hematocrit of Group D are statistically decreased compare to contol group(P=0.0066).

The majority of the rats had gross hematuria 24 hours after injury.

Mean sample wet weights were elevated at the impact site and decreased in the surrounding cord(Table 4). Additionally, wet weights increased distally toward the lumbar enlargement. MP pre-treatment did not decreased tis-

Table 2. Means of blood gas values

Group	PH	PO_2	PCO_2	HCO_3	Base excess	O_2 saturation
A	7.36±0.007	71.49±2.65	42.09±0.87	23.21±0.32	−1.32±0.39	92.00±0.92
B	7.38±0.010	82.67±2.27	36.53±1.26	22.87±0.63	−2.28±0.88	95.45±0.43
C	7.37±0.007	79.52±1.95	40.72±1.27	23.07±0.36	−1.52±0.52	94.87±0.42
D	7.36±0.006	72.37±2.53	40.66±0.89	22.87±0.33	−1.90±0.41	92.40±0.72
Total	7.37±0.003	76.21±1.26	40.07±0.56	23.00±0.21	−1.75±0.28	93.58±0.32

Group A : received control vehicle, Group B : 5mg/kg of MP,
Group C : 15mg/kg of MP, Group D : 30mg/kg of MP

Table 3. Effect of injury and treatment on body weight, hematocrit

Group	Preinury weight	Postinjury weight	Δ W(%)	Hct(%)
A	437.15±12.80	419.26±13.09	−4.3±0.38	39.5±0.91
B	441.63± 6.15	425.77± 7.17	−3.7±0.48	38.5±0.99
C	449.17± 5.77	430.17± 6.39	−4.3±0.52	38.1±1.00
D	431.67± 6.02	407.97± 6.92	−5.6±0.47	35.7±0.92
Total	439.44± 4.21	420.15± 4.52	−4.5±0.24	38.0±0.49

Group A : received control vehicle, Group B : 5mg/kg of MP,

Table 4. Effect of injury and treatment on wet weight, water concentration, tissue Na, K(1)

	P2	P1	Imp	D1	D2
Wet weight	26.26±0.22	28.75±0.24	32.99±0.33	31.47±0.26	32.42±0.29
Water concentration	0.68±0.009	0.70±0.001	0.76±0.009	0.71±0.009	0.70±0.009
Naw	67.15±0.25	76.23±0.48	104.50±0.43	71.87±0.37	64.13±0.23
Kw	83.93±0.27	73.94±0.52	44.86±0.45	76.22±0.39	83.76±0.24
Naw-Kw	−16.78±0.41	2.29±0.96	59.64±0.83	−4.35±12.16	−19.63±0.38
Naw+Kw	151.08±0.31	150.18±0.30	149.36±0.28	148.09±0.27	147.89±0.28

Imp : impact site, P1, P2 : proximal cord D1, D2 : distal cord
Naw : Total tissue sodium concentration Kw : Total tissue potassium concentration

Table 5. Effect of injury and treatment on wet weight, water concentration, tissue Na, K(2)

Group	Wet W	Water C	Naw	Kw	Naw-Kw	Naw+Kw
A	30.51±0.36	0.71±0.002	76.26±1.16	72.71±1.22	3.55±2.35	148.97±0.34
B	30.69±0.30	0.71±0.003	75.00±1.28	72.30±1.26	2.69±2.51	147.30±0.34
C	30.69±0.30	0.70±0.003	75.19±1.29	71.52±1.25	3.65±2.51	146.69±0.39
D	29.73±0.28	0.71±0.003	77.78±1.15	71.85±1.16	5.93±2.29	149.63±0.36

Wet W : tissue wet weight, Water C : tissue water concentration
Naw : Total tissue sodium concentration Kw : Total tissue potassium concentration
Group A : received control vehicle, Group B : 5 mg/kg of MP,
Group C : 15 mg/kg of MP, Group D : 30 mg/kg of MP

sue wet weights at all group(Table 5). To evaluate the effect of MP on edema, tissue water concentration was calculated from 'Wet weight-Dry weight/wet weight'. Impact site water concentrations were greater than surrounding cord. Pre-injury treatment with MP had some effect on spinal cord water concentration($P=0.0208$). Group C had decreased water concentration compare to control vehicle($P=0.0494$)(Fig. 2). But, other treatment group did not show any statistically significance. Wet weight (ANOVA, $p<0.0001$) and tissue water concentration (ANOVA, $p=0.0298$) were increased with injury severity.

[Na]w($p=0.0003$) and [K]w($p<0.0001$) changes correlate with increasing injury severity. Injury caused a large rise in spinal cord [Na]w and a marked depletion in spinal cord [K]w. But pre-injury MP treatment had no affect on tissue [Na]w and [K]w.

The [Na]w−[K]w increased with injury severity($p=0.0001$), but we can not find any statistical difference between each MP treatment group and control vehicle.

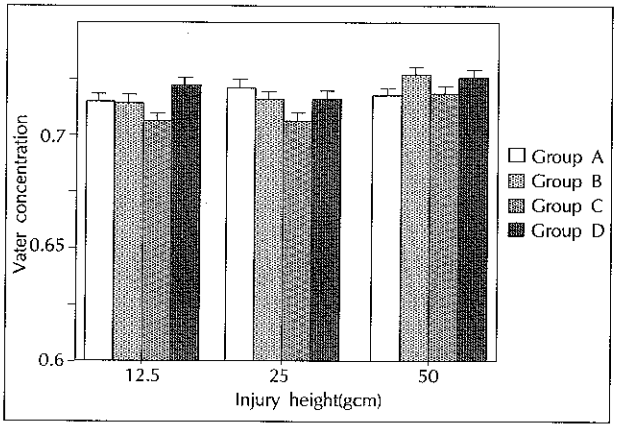

Fig. 2. Mean water concentrations of different injury in pre-injury treatment groups. Significant difference from vehicle control (Group A) was only found in Group C($P=0.0494$). The errors bar represent standard error of the means.

The sum of [Na]w and [K]w represents tissue ionic osmolarity. [Na]w+[K]w was reduced at the impact site and improved in adjacent segments, perhaps related to changes in tissue water concentrations. Total tissue [Na]w

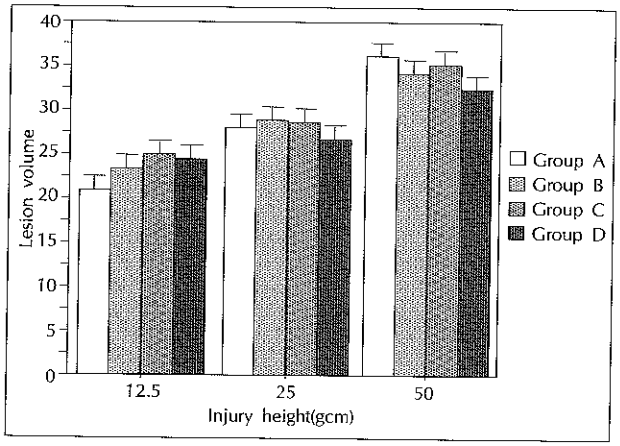

Fig. 3. Mean lesion volumes of different injury in pre-injury treatment groups. preventive treatment of Methylprednisolone had no significant effect on lesion volume. The error bars represent standard error of the means.

+ [K]w was significantly elevated in group B($P=0.0011$) and group C($P<0.0001$) compare to control group.

Drop height had very large effects on wet weight($p<0.0001$), tissue water concentration($p=0.0298$), [Na]w($p=0.0003$), [K]w($p<0.0001$), [Na]w - [K]w($p<0.0001$), but not [Na]w+[K]w($p=0.0298$).

4. Lesion volume assessment

All pre-injury treatment with MP had no significant protective effect on lesion volume compared to the control group(Fig. 3). Although lesion volume in group D appeared to be decreased compare to control vehicle, it did not reach significance compare to control.

Discussion

We had originally thought that giving MP 10 minutes before injury would be the most beneficial. However, our results showed that pretreatment with MP at 10 minutes did not reduced 24- hour lesion volumes. This is very unexpected and puzzing finding. If conformed, this result suggest that the timing of MP treatment is more critical than previously thought.

We will first discuss some local and systemic effect of pre-injury MP treatment and then discuss possible causes of this unexpected result.

Pre-injury MP treatment had no effect on overall spinal cord wet weight and water concentration except group C (15mg/kg of MP). Group C had significantly decreased water concentration compare to control. But this finding did not affect tissue lesion volume. Tissue wet weight are generally believed to reflect swelling of the tissue and water concentrations of the tissue appear to suggest tissue edema[24)25)] . These finding suggest that methylprednisolone had little effect on spinal cord swelling after cord injury. Lewin et al found that edema formation in acutely injured spinal cord is not significantly affected by glucocorticoid administration, despite an improved functional recovery[25)] and we have previously shown that tissue water concentration and edema do not correlate with injury severity but correlate net ionic shifts[24)34)43)44)45)].

Spinal cord contusions caused a large rise in spinal cord [Na]w and marked depletion in tissue [K]w[12)24)43)] and methylprednisolone was well known to reduce the accumulation of sodium at the lesion site in cat spinal cord injured model[30)31)34)36)]. But, we failed to demonstrate that pre-injury MP treatment had statistically significant effect on tissue [Na]w and [K]w. In moderate to severe injured case, group D, which given 30mg/kg of MP, seems to have less lesion volume compare to control, but it did not rearch statistically significance because it had adverse effect in mild injured case. Therefore, we could not find any preventive effect on each group.

Based on the pharmacodynamics of MP, in pre-injury normal cord, peak tissue concentration of MP were obtained 5 - 10 minutes after drug administration compare with 30 minutes to 1 hour in traumatized cord[8)]. A bolus dose of MP given 10 minutes before injury should achive maximal plasma levels and tissue levels at the time of injury. High levels of MP may be deterious and enhance tissue damage in several ways.

First, MP is well known to have vasodilatation effects both on peripheral and central vessels[1)16)19)20)22)23)27)37)38)39)42)]. Blood pressure falls with rapid injections of MP and we have previously shown that spinal cord blood flow may double within 10 minutes after 30mg/kg of MP[38)39)]. Central vasodilatation and increased blood flow at the impact site. Hemorrhage may paradoxically increase damage.

Second, the rise in blood flow after MP treatment is accompanied by an increase in extracellar calcium activity monitored with ion selective microelectrodes[15)28)29)32)41)44)].

Many designers of therapeutic protocols seldom consider the possibility that "secondary injury mechnisms" may serve protective[28)29)32)43)] clean-up, or recovery purpose. For example, lipid peroxidation and Ca^{++} activated phospholipase activity are likely to be important for rapid breakdown of moribund cells to release Ca^{++} binding substances that lower extracellular Ca^{++} and protect surviving

cells[28][29][32][39][41][45]. MP rapidly increases white matter blood flow in injured spinal cord[30][31][37][39][42] and also prevents the delayed fall of extracellular Ca^{++} at the injury site. This findings suggest that very high doses of methylprednisolone facilitate lipid peroxidation and thereby would be deleterious.

We had earlier proposed that the profound and prolonged depression of extracellar calcium activity protects surviving cells at the injury site[28][29]. MP treatment before the injury may well prevent the fall in extracellar calcium activity normally associated with injury and thereby paradixically enhance tissue damage.

Third, pretreatment with MP may completely inhibit other responses to the injury, responses that are beneficial. For example, injury causes activation of a number of genes including C-fos and C-jun, heat shock protein, and other responses. The function of these genes are not well understood. Some of their effects may be beneficial. It would be interest to determine and compare the effects of MP given 10 minutes before and 10 minutes after injury on these "early-early" gene responses and other injury responses.

We emphasize that our primary outcome measure in these experiments is ionic lesion volume estimated from the difference of total tissue Na and K concentrations at 24 houres after injury, It would be interest and important to confirm that the results histologically, physiologically, and behaviously.

Until these issures are resolved, we recommended that acute pre-injury MP therapy be cautiously applied in the operating room. It has come to our attention that many neurosurgeons routinely give patients a bolus doses of MP before spinal surgery. The beneficial effects of such treatments have not yet been established in animal or human studies.

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실험동물의 척수손상에서 손상전 MP 투여의 효과

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=국문초록=

저자들은 척수손상전에, methylprednisolone의 투여가 효과가 있는지를 알아보기 위하여 다음의 연구를 진행하였다. 5, 15 그리고 30mg/kg의 methylprednisolone을 정맥주사하고 10분 후에 쥐의 제 10 흉수부위에 10gm의 무게를 갖는 rod를 1.25, 2.5 그리고 5.0cm 높이에서 급성 척수손상을 가하였다. 손상 후 24시간 후에 쥐의 척수를 제거하여 손상부위의 Na, K의 변화 정도를 관찰하고 척수손상의 정도를 측정하였다. 저자들은 기대했던 것과는 다르게 손상전 methylprednisolone의 투여가 대조군에 비하여 아무런 예방효과가 없는 것을 발견 하였다. Methylprednisolone 은 많은 신경외과적 수술시에 척수손상의 예방목적으로 사용되고 있으나 이러한 치료가 과연 효과적인지에 대하여는 이전에 아무런 연구가 없었으며 이러한 저자들의 연구 결과로 볼 때 수술전 또는 수술시 사용되는 methylprednisolone에 대하여는 좀 더 신중을 기하여야 할 것으로 판단된다. 저자들은 이러한 실험결과의 원인에 대하여 의논하고자한다.