

# Clinical study of ganglioside (GM) combined with methylprednisolone (MP) for early acute spinal injury

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**Abstract:** This paper aims to make an analysis of the effects of ganglioside (GM) combined with methylprednisolone (MP) in early acute spinal injury. Fifty-three patients with acute spinal cord injury were included in this study and they were randomly divided into experimental and control group. Twenty-seven patients in the control group were treated with MP, while the rest 26 patients received more GM based on that. By observing and comparing the clinical responses from patients and recovery time of all indexes, results came out: the curative rates in the experimental and control group were 50.0%, 40.7% respectively, and the total effective rates were 92.3%, 85.2% respectively. There was a remarkable difference between the two groups ( $P < 0.05$ ). Patients in the experimental group took  $6.2 \pm 1.9$ d to restore their sphincter function,  $11.2 \pm 2.8$ d to recover their muscle forces to over grade II, and  $13.8 \pm 3.9$ d to return general activity, while the patients in the other group clearly spent longer time on recovery, that were  $12.1 \pm 3.2$ ,  $19.2 \pm 4.6$  and  $23.9 \pm 5.6$  respectively. The distinct difference between the two groups was of statistical significance ( $P < 0.05$ ). We conclude that GM has better curative effects than MP, for it is able to promote the recovery of nerve function for patients and greatly improve the prognosis.

**Keywords:** Acute spinal cord injury, MP, GM.

## INTRODUCTION

Acute spinal cord injury (ASCI) is one of the common clinical diseases (Xiaobing *et al.*, 2013), which is always attributed to traffic, violence, downfall and exercises. It mainly occurs in the young and adults. ASCI places a heavy burden on the patients family and society with its extremely high disability and mortality rate. ASCI is nowadays considered to be global problem and the secondary injury brought by ASCI often leads to a disaster. Therefore, it is of utmost importance to seek an effective remedy to improve the prognosis, low the disability and mortality rate as well (Yufei *et al.*, 2010). Effective remedy can improve the fate and function of uninjured nervous tissues around the primary injury, as well as unlink the chain of vicious circle, alleviate the sequelae of spinal injury, prolong the life of patients with spinal injury and improve their lives (Guobing *et al.*, 2010). From these, it can be seen that any possible measures to alleviate the loss of neurons is appealing to us. There are a number of studies, which have proved that the MP is one of the top choices with curative effects. And they suggest that its activation mechanism lies in its inhibition of oxygen radical and its effect of anti-lipid per oxidation (Shuo and Yangbing, 2011; Aomar M *et al.*, 2011). However, whether the related hormone will protect the neuron or not still remains a dispute. There were reports in recent years that the application of MP could not improve the dead issues in the early stage of ASCI. Although GM can greatly promote the nerve regeneration, the scientist Gatte Walker, found in his further study that

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both Nerve Growth Factor (NGF) and GS were the necessary matters in the regeneration of brain nerves. The NGF is activated many times by the mediation of GM and then a new large neural network will be formed, which will restore and promote the regeneration of brain nerves (Na and Naihong, 2009; Linkun and Yincheng, 2010). This paper included 53 patients with ASCI for study objects and made an analysis of the effects of GM combined with MP in the early treatment of ASCI.

## MATERIALS AND METHODS

### General materials

Fifty-three patients with ASCI were randomly included for study objects. All patients have been checked by CT and MRI on admission and all received treatment within 8 hours. According to the American Spinal Injury Association (ASIA) scale, seven patients were assessed to be A (13.2%), 12 were B (22.6%), 13 were C (24.5%) and 21 were D (24.5%). And then they were randomly divided into an experiment and a control group. There were 26 patients in the experiment group, including 15 males and 11 females, ranging in age from 16 to 63 years (mean  $35.1 \pm 1.8$  years). There were 27 patients in the control group, including 16 males and 11 females, ranging in age from 17 to 62 years (mean  $36.2 \pm 2.1$  years). There was no remarkable difference between the two groups in sex, age and ASIA scale ( $P > 0.05$ ) and they were comparable. Besides the patients who needed surgical fixation and decompression due to spinal cord compression caused by the difference in the spinal stability and patients with

Hematological diseases, others all had a idea of the study goal and were all willing to take part.

### Methods

Patients in the two groups all received regular treatment such as giving the nutrition support, strengthening the warmth, keeping the skin clean and respiratory tract fluent. Patients with uroschesis just kept their catheter which would let out every 3 or 5 hours. And their bladders were douched by the 0.1% furacilin (SFDA Approval NO.H13024101 from Tangshan Jichuan Pharmaceutical Factory Likang Pharmaceutical Co., Ltd.) once or twice a day. In the control group, patients received intravenous administration of MP (from Wuhan Hong Rui Kang Reagent Co., Ltd.) 30mg/kg within 8 hours of injury, and then they were treated by a 23-hour continuous infusion in 5.4mg/kg per hour. After the continuous treatment, they were injected by 40mg MP with 250ml 5% glucose solution four times a day and after 3 days of continuous infusion, it turned 2 times a day and kept on 3 days.  $\alpha$ In the experiment group, patients received intravenous administration of 100g GM (SFDA Approval No. H20056782 from Qilu Pharmaceutical Co., Ltd.) with 250ml 5% glucose solution once a day, 10d were cycle. The therapeutic effects of the two groups were observed.

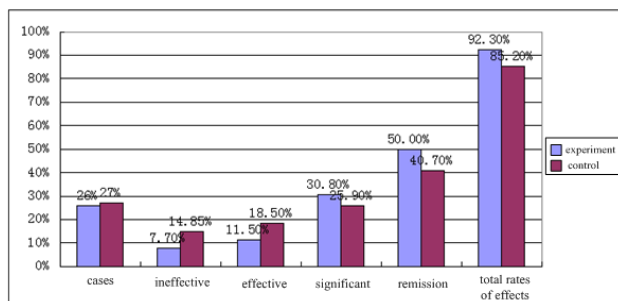


Fig. 1: The comparison of curative effects in the two groups

### Observation indexes

The effective clinical curative rates of patients in the two groups, including ineffective, effective, significant and complete remission rate. The total rates of effects are the effective plus significant plus complete remission rate. The time when clinical indexes disappear, including the recovery time of sphincter functions, the time when limb muscle force recovers to grade II and time for general activities.

### Elevation methods

Complete remission: basic body senses, limb muscle forces and sphincter functions can be restored. Some complications can be cured and patients can live by their own. Significant: the basic body senses, limb muscle forces and sphincter functions for patients can be greatly improved. Besides, some complications can be effectively controlled. Effective: There are some improvements in the basic body senses, limb muscle forces and sphincter

functions. Ineffective: There is no a clinical improvement or even aggravation for patients.

### STATISTICAL ANALYSIS

All data were analyzed by the SPSS17.0 software. The measurement data were expressed by means  $\pm$ variance, and compared with t-test. The enumeration data were shown in percentage (%) and inspected by  $\chi^2$ .  $P < 0.05$  means that the difference is of statistical significance.

### RESULTS

There were two clinical patients in the two groups who were treated ineffectively. The remission rates and total rates of effects in the experiment group (50.0% and 92.3% respectively) were both higher than those in the control group (40.7% and 85.2% respectively). There was a marked difference between the two groups ( $P < 0.05$ ) and it was of statistic significance. (As shown in table 1). The comparison of effects in the two groups is shown in the fig. 1.

By comparing the clinical indexes disappearing time for patients in the two groups, it was found that the patients in the experiment group spent less time on the restoration of muscle forces and sphincter functions than the other group. The difference between the two groups was remarkable and of great statistic importance. (As shown in table 2)

### DISCUSSION

According to the report from the American National Acute Spinal Cord Injury Association (Nerve Injury Team in Trauma Branch of Chinese Medical Association (CMA), 2010), a high dose of MP is quite beneficial to the recovery of spinal functions and it can be the first choice for the remedy. A number of studies have confirmed the continuous application of high dose of MP quite effective (Shaoping, 2012; Chaopin and Jianhua, 2012; Yongjun and Hua, 2012). Its mechanisms may be like this: (1) Refrain the metabolism and aggregation of catecholamine within the tissues after injury. (2) Enhance the stimulation and conductivity of nerves, promote the reflex transmission of spinal synapses and polysynapses.  $\beta$  Inhibit the transfer of calcium ion and stabilize the pathway of cells and ions.  $\chi$  regulate the blood flow in the spinal cord, directly expand the small vessels and prevent the contraction of vessels from the 5-HT, NE and some other biogenic amines. GM is a kind of extract from cell - membrane in pig brain, which a necessary matter in the development of brain nerves. Quite a number of clinical studies find that GM is able to promote the regeneration of nerves (Shuangming and Weixin, 2012; Nerve Injury Team in Trauma Branch of Chinese Medical Association

**Table 1:** The comparison of clinical curative effects of patients in the two groups [N(%)]

Group	Cases	Ineffective	Effective	Significant	Remission	Total rates of effects
Experiment	26	2(7.7)	3(11.5)	8(30.8)	13(50.0)*	24(92.3)*
Control	27	4(14.8)	5(18.5)	7(25.9)	11(40.7)	23(85.2)
$\chi^2$		3.043	2.768	2.183	0.112	3.452

**Table 2:** The comparison of clinical indexes disappearing time for patients in the two groups

Group	Time for restoring sphincter functions (d)	Time for restoring muscle forces to grade II (d)	Time for general activities (d)
Experiment (n=26)	6.2±1.9*	11.2±2.8*	13.8±3.9*
Control (n=27)	12.1±3.2	19.2±4.6	23.9±5.6
T	7.089	6.644	6.619
P	<0.05	<0.05	<0.05

Note: \*means  $P < 0.05$ , compared with the control group

(CMA), 2010), axons and synapses, improve the conductivity of nerves, promote the recovery of neuroelectrophysiology indexes and different enzyme activities in cell-membrane, as well as prevent the damage of nerve cells. In the treatment of patients with acute osteomyelitis, based on a high dose of hormone, the combined GM is able to effectively relieve the damage of neuron cells. Besides the endogenous trophic factors can also help inhibit the peroxidation of diseased lipid and then further stabilize the structure and functions of cell-membrane.

Ganglioside (GM1) is a kind of sphingoglycolipid containing sialic acid and has quite abundant contents in the central nervous system. GM is able to protect the cell-membrane, relieve the nerve tissue edema and promote the axonal regeneration, while the GM can help remodel the nerves. Its main pharmacological effects lie in protecting the enzyme activity of  $\text{Na}^+/\text{K}^+$ -ATP and  $\text{Ca}^{2+}$ - $\text{Mg}^{2+}$ -ATP on the nerve cell-membrane; keeping the balance of the cell ions both inside and outside; Reducing the influx of intracellular  $\text{Ca}^{2+}$ ; Preventing intracellular  $\text{Ca}^{2+}$  from overload; guarding against free radicals; inhibiting lipid peroxidation; Blocking or mitigating the toxic effects of excitatory amino acids. It even plays a dual role in the protection, repair and regeneration of neurons (Nerve Injury Team in Trauma Branch of Chinese Medical Association (CMA), 2010; Lei and Juan, 2012). GM is a global medicine since MP, which has been confirmed to be effective in human spinal cord injuries after many year clinical observations

In this experiment, patients in the experiment group were treated with GM combined with MP in the early stage. The remission rates were 50.0% and the total rates of effects were 92.3%, which were obviously higher than those in the control group (40.7% and 85.2% respectively). It is shown in the table 2 that patients in the experiment group have restored their spinal cord functions better than the other. This result is consistent with Xie Jun (Jun, 2012). It can be proved that a simple

continuous high-dose of MP will positively recover the nerves functions for patients, and also help improve the prognosis. The combination of the two can effectively cut down the disability and mortality. However, it is quite hard to extract the GM and costs too much for clinical applications. Here, we want to claim the attention and efforts of researchers and drug manufacturers. We are looking forward the ideal alternative drugs in order to promote the recovery for more patients.

## CONCLUSION

Nowadays, Methylprednisolone (MP) is well-recognized to be one of the first choices in the treatment of early ASCI. But it still has no clear effects on the recovery of nerve functions for patients. Therefore, there lies a great defect in treating the early acute spinal injury with the only MP, and it is weak in preventing the complications. However, GM combined with MP has significant effects on early ASCI and can effectively facilitate the recovery of nerves functions and improve the prognosis for patients.

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