Clinical Efficacy of Ganglioside Combined with Methylprednisolone in the Treatment of Spinal Cord Injury and Its Effect on Inflammatory Response and Oxidative Stress Factors

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ABSTRACT

Objective: To determine the clinical efficacy of monosialotetrahexosylganglioside (GM1) combined with methylprednisolone in the treatment of spinal cord injury (SCI).

Study Design: An observational study.

Place and Duration of the Study: Department of Orthopaedics, Baoding No.1 Central Hospital, Baoding, Hebei, China, from January 2018 to June 2021.

Methodology: A total of 80 patients with SCI were divided into control and observation groups according to treatment methods, the control group receiving methylprednisolone treatment and the observation group receiving methylprednisolone combined with GM1. The effective rate of treatment, time of normal muscle strength recovery, walk on the ground, and hospital stay were compared. The changes in the American Spinal Injury Association (ASIA) score, activity of daily living (ADL), serum inflammatory factors, oxidative stress factor levels, and adverse reactions were recorded.

Results: The effective rate of clinical efficacy of the observation group was 92.50%, surpassing the control group's which was 75.00% ($\chi^2 = 4.501$, $p = 0.034$). The observation group had a shorter recovery time for muscle strength, walking time, and hospital stay compared to the control group ($p < 0.05$). After treatment, the ADL scores of both groups were higher than before treatment, and the degree of increase in the observation group was higher than the control group ($p < 0.05$). The levels of serum tumour necrosis factor-α (TNF-α) and interleukin-8 (IL-8) for all patients were significantly reduced, with the observation group showing a more significant decrease ($p < 0.05$). There was a notable increase in glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) levels in both groups, while the levels of malondialdehyde (MDA) decreased significantly. GSH-Px, SOD, and MDA levels were significantly greater in the observation group ($p < 0.05$).

Conclusion: The combination of methylprednisolone and MG1 treatment of SCI can significantly reduce the inflammatory response and improve clinical efficacy.

Key Words: *Spinal cord injury, Ganglioside, Methylprednisolone, Inflammatory indicators, Oxidative stress.*

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INTRODUCTION

Spinal cord injury (SCI) is a common critical illness in orthopaedics.[1] Currently, the incidence of SCI has increased, SCI patients often experience varying degrees of sensory and motor function loss, which can lead to severe cases such as limb paralysis, loss of labour ability, and even death, causing serious physiological and psychological burdens to patients.[2]

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There are two main types of SCI injuries: Primary and secondary. Primary injury is mainly caused by bleeding and compression, while secondary injury is mainly caused by neuronal apoptosis, oxidative stress, and inflammatory response. After SCI occurs, active surgical haemostasis and relief of spinal cord compression can play a key role, while active antioxidant and anti-inflammatory treatments are equally important. Not only it can protect neuronal cells, but it can also promote spinal cord function recovery.[3] How to correct inflammation and oxidative stress levels, promote neurological recovery, and reduce mortality after SCI is currently a key and challenging issue in the treatment of SCI.

Methylprednisolone is a commonly used treatment for SCI, however, there are adverse reactions. Monosialotetrahexosylganglioside (MG1) is composed of sialic oligosaccharides and ceramides and has good lipophilicity. It can penetrate the blood-

brain barrier, activate cell-membrane enzymes / regulate the concentration of second messenger Ca^{2+}, enhance the effect of nerve growth factors, regulate gene expression, reduce the neurotoxicity of free radicals and excitatory amino acids, protect nerve cells, and promote the remodelling and regeneration of damaged nerve cells.[4] There are few reports on the combination of ganglioside and methylprednisolone in the treatment of SCI. Based on the above facts, the aim of this study was to determine the clinical efficacy of MG1 combined with methylprednisolone in the treatment of SCI.

METHODOLOGY

The study was a retrospective review of 80 patients with lumbar SCI carried out in the Baoding No.1 Central Hospital, Hebei, China, from January 2018 to June 2021. The individuals were assigned to the observation group (n = 40) and the control group (n = 40) according to treatment methods. The Ethics Committee of the Hospital approved the study, and all participants provided written informed consent.

Patients with diagnostic criteria for SCI established by the American Spinal Injury Association (ASIA) with grades C and D, confirmed by imaging, having complete clinical data, without other spinal diseases or other serious injuries prior to SCI, informed and signed consent forms, were included. Patients with combined-limb disabilities and neurological disorders, individuals with combined-psychiatric disorders who were unable to cooperate with treatment, with severe heart, liver, kidney and other functional impairments, pregnant or lactating women, and incomplete clinical data were excluded.

Methylprednisolone was administered to patients in the control group: Within eight hours of SCI occurrence, methylprednisolone 30 mg/(kg/h) was administered intravenously for 15 minutes, then changed to 5.4 mg/(kg/h) for 23 hours. After shock therapy, 160 mg/d was administered intravenously in four doses, and after three days, it was changed to twice a day. The medication was discontinued after three days. The observation group was given an intravenous infusion of 100 mg/d MG1 sodium, once a day. After 20 days of treatment, the medication was stopped for 10 days as one cycle and continued to be used for 2 cycles. The usage of methylprednisolone was the same as that in the control group.

Total effective rate of treatment was evaluated according to the standards of clinical spinal surgery which was divided into cure (clinical symptoms of SCI completely disappear, sensorymotor function restored), significant effect (significant improvement in clinical symptoms, effective control of complications, and no new additions), effective (reduced clinical symptoms of spinal cord injury), and ineffective (clinical symptoms not improved or even worsened). The total effective rate was calculated as (cure rate + significant effect rate + effective rate) × 100%.[5] The recovery effect of two groups of patients, including the time for muscle strength to return to normal, the time for walking on the ground, and the length of hospital stay were noted. The ASIA criteria for assessing spinal cord injury neurological function recovery were used to calculate the motor, pain, and tactile function scores of each patient. The maximum score for motor function was 100 points, and the total score for pain and tactile was 112 points. The higher the score, the better the neurological function. A comparison of activity of daily living (ADL) was calculated as the scores of 10 items including eating, dressing, bowel control, walking on flat ground, and going up and downstairs between the two groups of patients before and after treatment. Higher score indicates better daily living ability. Enzyme-linked immunosorbent assay (ELISA) was used to measure malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), interleukin-8 (IL-8), and tumour necrosis factor-α (TNF-α) from 2ml of fasting venous blood before and after treatment. The occurrence of adverse reactions in the patients during treatment was recorded and compared.

Data were collected retrospectively from the medical records at baseline and at the end of treatment. Follow-up was done with the patient through phone, outpatient, and other means one month after the end of treatment.

Statistical analysis was performed using the SPSS version 22.0 software. Continuous variables were measured as mean and standard deviation and categorical variables were reported as frequencies and percentages. T-test was used to compare means of continuous variables and Chi-square test was applied for the comparison of categorical variables. A p-value of <0.05 was taken as significant.

RESULTS

The observation group's total efficiency rate was 92.50%, surpassing the 75.00% rate of the control group ($p<0.05$). The recovery time of muscle strength, walking time, and hospital stay in the observation group was shorter than the control group ($p<0.05$, Table I).

The daily living ability scores of both groups of patients were higher before the treatment ($p<0.05$). The degree of improvement of the observation group was higher than the control group ($p<0.05$). The motor, pain, and tactile function scores of the patients of both groups were significantly improved compared to their scores before treatment ($p<0.05$), with the observation group having a higher degree of elevation than the control group ($p<0.05$, Table II).

The levels of IL-8, TNF-α, and MDA in the patients of both groups were significantly reduced compared to before treatment, the observation group had a higher degree of decrease than the control group ($p<0.05$). While the levels of GSH Px and SOD significantly increased after treatment, the observation group had a higher degree of increase than the control group ($p<0.05$, Table III).

The total incidence of complications in the observation group was 32.50% and 37.50% in the control group ($p>0.05$).

Table I: Comparison of clinical efficacy and recovery effect between the two groups ($\bar{x}\pm s$).

Group	Total effective rate (n, %)	Time for muscle strength to return to normal (d)	Time to walk on the ground (d)	Length of hospital stay (d)
Observation group	37 (92.50)	10.93 ± 1.49	9.45 ± 1.15	20.23 ±1.23
Control group	30 (75.00)	19.18 ± 1.69	14.15 ± 1.74	25.20 ± 1.24
t	4.501	23.125	15.155	17.985
p	0.034*	<0.001$^{\triangle}$	<0.001$^{\triangle}$	<0.001$^{\triangle}$

*Notes: *χ^2 test, $^{\triangle}$independent sample t-test.*

Table II: Comparison of scores of daily living ability, motor, pain, and tactile functions between the two groups before and after treatment ($\bar{x}\pm s$).

Group	Daily living ability		Motor function		Pain function		Tactile function	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Observation group	69.50 ± 6.61	83.08 ± 6.09*	63.33 ± 7.19	77.58 ± 5.06*	72.70 ± 5.96	91.35 ± 5.51*	74.90 ± 9.21	90.78 ± 6.42*
Control group	68.90 ± 8.53	74.75 ± 7.96*	62.53 ± 7.22	73.83 ± 5.31*	72.08 ± 8.01	82.00 ± 7.74*	74.55 ± 8.78	86.83 ± 5.97*
t	0.352	5.254	0.497	3.236	0.396	6.227	0.174	2.849
p$^{\triangle}$	0.726	<0.001	0.621	0.002	0.693	<0.001	0.862	0.006

Notes: $^{\triangle}$independent sample t-test.

Table III: Comparison of the levels of inflammatory and oxidative stress factors before and after treatment between the two groups ($\bar{x}\pm s$).

Group	TNF-α (μg/L)		IL-8 (μg/L)		GSH-Px (mg/L)		SOD (u/ml)		MDA (u/ml)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Observation group	45.62 ± 3.62	20.0 ± 3.34*	2.27 ± 0.76	1.11 ± 0.24*	6.37 ± 3.14	13.64 ± 3.67*	60.53 ± 4.28	126.63 ± 3.85*	7.30 ± 1.80	4.13 ± 1.67*
Control group	45.74 ± 4.99	22.50 ± 4.04*	2.30 ± 0.42	1.49 ± 0.30*	6.31 ± 5.54	11.50 ± 2.87*	60.38 ± 4.09	113.93 ± 4.32*	7.12 ± 0.46	4.89 ± 1.13*
t	0.126	2.937	0.218	6.366	0.082	2.896	0.160	13.869	0.597	2.361
p$^{\triangle}$	0.900	0.004	0.828	<0.001	0.935	0.005	0.873	<0.001	0.552	0.021

Notes: $^{\triangle}$independent sample t-test.

DISCUSSION

SCI has a high disability and mortality rate, which seriously affects the quality of life of patients.[6] At present, there is no specific treatment plan for SCI.[7] Therefore, how to improve the clinical treatment effect of SCI is currently challenging. Methylprednisolone is currently the preferred medicine for the treatment of SCI.[8] It can stimulate neural excitability and conductivity and stabilises cell ion channels.[9] Injection of MG1 can protect cell membranes, reduce neuro-oedema, improve nerve conduction, and restore neural enzyme activity.[10] Internationally, it has been confirmed through multicentre clinical observations that it has a therapeutic effect on SCI.[11,12] This study showed that the total effective rate in the observation group was significantly higher than the control group, and the time for muscle strength recovery, walking time, and hospital stay in the observation group were shorter than the control group, and improvement in daily living ability score was higher than the control group ($p < 0.05$). However, there was no significant difference in treatment complications between the two groups ($p > 0.05$), indicating that combined use of gangliosides and methylprednisolone can effectively promote the recovery of neurological function in SCI patients and improve prognosis without increasing the incidence of adverse reactions.

The literature shows that the most important pathological process of secondary injury in SCI is the inflammatory response.[13] Therefore, controlling the inflammatory response is crucial in the treatment of SCI.[14] Oxidative stress response is also one of the main mechanisms of secondary injury in SCI.[15] Studies have shown that oxidative stress response in SCI can reduce the activity of GSH Px and SOD.[16] MDA can induce the formation of free radicals and increase the degree of secondary damage.[17] This study showed that the levels of inflammatory factors in both groups decreased significantly after treatment, and the degree of decrease in the observation group was significantly higher than the control group ($p > 0.05$). The levels of GSH Px and SOD were significantly increased after treatment, while MDA levels were significantly reduced, and the degree of change in the observation group was more significant ($p > 0.05$). Meanwhile, this study showed that the motor, pain, and tactile function scores of patients of both groups were significantly improved, and the observation group had a more significant improvement ($p > 0.05$). It indicated that combined use of gangliosides and methylprednisolone can reduce the occurrence of inflammatory and oxidative stress reactions after SCI, reduce secondary injury, effectively restore the function of damaged nerves, improve patient prognosis, and enhance patients' quality of life.

The current study has limitations as the sample was small and there was no long-term follow-up of interventions to assess the sustainability of treatment effects. Future studies should focus on long-term follow-up of interventions with larger sample sizes.

CONCLUSION

Methylprednisolone combined with ganglioside is a satisfactory treatment regimen for SCI, boasting a variety of benefits such as reducing inflammatory response, elevating oxidative stress levels, and promoting neurological recovery.

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ETHICAL APPROVAL:
Ethical approval from the Institutional Ethical Review Committee (ERC No: 2020-084; dated: November 4, 2020) was obtained before commencing the research work.

PATIENTS' CONSENT:
Informed and written consent was obtained from the patients.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
DR, HL: Concept of the study, design, data collection, drafting of the manuscript, and data interpretation.
XL: Concept of the study, data collection, and critical analysis.
MW: Data collection, critical analysis, and manuscript review.
All authors approved the final version of the manuscript to be published.

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