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Research Article

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Analysis of the Efficacy of mNGF Combined with ACDF Surgery in The Treatment of Cervical Spinal Cord Injury Without Fracture and Dislocation

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Abstract

Objective: *Analysis of the efficacy of mNGF combined with ACDF surgery for cervical spinal cord injury without fracture and dislocation compared to ACDF surgery alone for cervical spinal cord injury without fracture and dislocation.*

Methods: *50 patients of cervical spinal cord injury without fracture and dislocation admitted to the Department of Orthopaedics of the First Affiliated Hospital of Hebei North University from January 2019 to January 2021 were selected. The 27 patients treated with ACDF surgery were recorded as group A, and the 23 patients treated with mNGF combined with ACDF surgery were recorded as group B. JOA scores at admission, 1 month, 3 months, and 6 months after surgery, and ASIA grading at admission and at the end follow-up at 6 months after surgery were recorded for each group.*

Results: *There was no statistical difference between the admission JOA score and ASIA grading of patients in groups A and B at P > 0.05. At 1 month, 3 months and 6 months after surgery, the JOA scores and ASIA grading at the end follow-up at 6 months after surgery were compared between the two groups, P< 0.05, and there were statistical differences in JOA scores at 1 month, 3 months and 6 months after surgery and ASIA grading at 6 months after surgery between the two groups of patients in A and B.*

Conclusion: *The mNGF combined with ACDF surgery is safe, feasible and effective in the treatment of cervical spinal cord injury without fracture and dislocation. The combination of the two accelerates surgical recovery and has better clinical outcomes.*

Keywords: Cervical spinal cord injury without fracture and dislocation, Mouse Nerve Growth Factor, ACDF surgery

Clinical effect with the advent of an aging society and the rapid development of the transportation industry in China, the incidence of cervical spondylosis and cervical trauma is increasing year by year. Some studies have reported that about 33.3% -50% of patients with cervical spinal cord injury have no fracture and dislocation on imaging, but have obvious spinal cord injury, which is clinically called CSCIWOFD [1]. The treatment methods are divided into drug therapy, cell therapy, and surgery. Choosing the right treatment can improve the prognosis and quality of life of patients to a great extent [2, 3].

Currently, there is still more controversy on whether patients with CSCIWOFD should receive surgical treatment [4]. Although there are numerous reports in the literature that patients' neurological function can be satisfactorily restored after regular conservative treatment, surgical treatment is still necessary if patients have significant spinal cord edema, ligamentous injury, and potential risk of cervical spine instability [5]. And anterior surgery has obvious advantages in restoring and maintaining the physiological curvature of the cervical spine [6]. However, the current efficacy of single surgery is not satisfactory, and there is still a high rate of disability.

In our 2017 Expert Consensus on Assessment, Treatment and Rehabilitation of Traumatic Spinal Cord Injury, it is stated that nerve growth and neuroprotective drugs can be used as appropriate for patients with cervical spinal cord injury [7]. In recent years, Mouse Nerve Growth Factor (mNGF) is commercially available and widely used in the clinical treatment of peripheral nerve injury, which has a neurotrophic and synaptic regenerative effect and plays an

important role in regulating the growth, development and re-differentiation of nerve cells, and is an important substance involved in the regeneration and repair of injured nerves [8]. There are few research reports on the application of murine nerve growth factor in the treatment of cervical spinal cord injury without fracture dislocation at home and abroad. In this study, we retrospectively analyzed the clinical data of 50 patients with non-fracture-dislocation type cervical spinal cord injury who met the inclusion criteria and were admitted to the First Affiliated Hospital of Hebei North University from January 2019 to January 2021. To study the efficacy of murine growth factor combined with ACDF surgery in the treatment of non-fracture-dislocated cervical spinal cord injury. To find a safe and effective treatment option for patients with non-fracture-dislocated cervical spinal cord injury.

Information And Methods

Inclusion Criteria

(i) clear history of trauma to the neck; (ii) no fracture or dislocation was found by means of X-ray and CT examination after the injury; (iii) no sensory and motor dysfunction of the extremities before the injury and showing sensory and motor dysfunction of the extremities after the injury; (iv) cervical MRI examination of the neck after the injury showed signal changes in the cervical medulla, suggesting cervical spinal cord injury; (v) no previous neurological or psychiatric diseases in the patients; (vi) no recent history of neck surgery in the patients.

Exclusion Criteria

(i) combined cranial or other sites of nerve damage resulting in impaired cervical medullary nerve function evaluation; (ii) severe multiple injuries and eventual death due to injuries in other sites; (iii) those who were lost during follow-up; (iv) those who died during hospitalization or during follow-up.

General Information

The clinical data of 50 patients without fracture-dislocation type cervical spinal cord injury who met the inclusion and exclusion criteria and were admitted to the Department of Orthopedics of the First Affiliated Hospital of Hebei North University from January 2019 to January 2021 were selected. The 27 patients treated with ACDF surgery were recorded as group A. There were 20 males and 7 females, aged 25-51 years. The mean age was (36.19±1.496) years. The 23 patients treated with murine growth factor combined with ACDF surgery were recorded as group B, 16 males and 7 females, aged 23-55 years. The mean age was (37.35±1.965) years. The surgery was performed by the same chief physician team in both groups. All patients were followed up successfully, and there were no cases of loss of follow-up or death. Postoperative loosening, breakage and dislodgement of the fixed titanium plates and screws were not observed in any of the patients in both groups. P=0.6346>0.05 for the comparison of age between the two groups, and the difference was not statistically significant. There was no difference in the age of the patients in the two groups. Patients had different degrees of spinal cord and neurological dysfunction on admission, according to ASIA classification, group A admission: 3 cases of grade A, 6 cases of grade B, 13 cases of grade C, 5 cases of grade D, and 0 cases of grade E. Group B preoperative: 2 cases of grade A, 5 cases of grade B, 10 cases of grade C, 6 cases of grade D, and 0 cases of grade E. Admission JOA score [12]: group A: 7.21±2.98, group B: 7.12±3.12. P>0.05 for comparison of admission scores between the two groups, the difference was not statistically significant, and there was no difference in admission scores between the two groups [9-11].

Drug name: Rat nerve growth factor for injection; dosage: dissolve each bottle with 2ml sodium chloride injection before use, inject intramuscularly, 30μg daily, once a day; manufacturer: Sutexam (Beijing) Biopharmaceutical Co.

Treatment

Admission treatment All patients were given a cervical brace immobilization brake after admission, and all were treated with glucocorticoids and mannitol for symptomatic support. The MP protocol recommended by the Second National Acute Spinal Cord Injury Study Society (NASCIS-II) [13] in 1990 was used: for patients within 3 hours of injury, the first dose of 30 mg/kg was administered intravenously over 15min as a rapid shock. After an interval of 45min, the dose was followed by 5.4mg/(kg•h) for 23h. If the duration of injury was between 3-8h, the dose was continued for 24h, for a total of 48h. The patient was actively prevented from complications, and was treated with ambulatory cardiac monitoring and oxygenation. Patients in group B were treated with rat nerve growth factor 30μg/d intramuscularly upon admission.

Surgical Method

Anterior cervical discectomy fusion (ACDF) surgery was performed with the patient under general anesthesia in the supine position with a pillow under the shoulder, and a sterile surgical towel was routinely disinfected. The skin and subcutaneous tissues were incised layer by layer, the flap was free subconsciously, the broad cervical muscle was incised, the thyrohyoid muscle was ligated and cut, the cervical vascular sheath was entered along the medial side, the responsible vertebra was bluntly separated and exposed, the anterior cervical muscle was incised and exposed, after accurate positioning, the responsible vertebra was inserted into the positioning nail and propped open, the intervertebral disc was removed, and after satisfactory trial modeling, the bone taken from the iliac bone was placed into the intervertebral fusion device. The anterior cervical titanium locking nail plate and screws were placed in front of the adjacent vertebrae selected across the responsible vertebrae, and the "C" arm observation of the plate and fusion device position was satisfactory, the wound was irrigated, the instrument gauze was counted correctly, one negative pressure suction tube was placed and fixed, and the suture was closed layer by layer. The neck was fixed with a neck brace. The operation time was 90-130 min, mean (102.15±7.51) min, and the bleeding volume was 45-80ml, mean (55.24±5.12) ml.

Postoperative Management

Postoperatively, patients were given primary monitoring, dynamic electrocardiographic monitoring, continuous low-flow oxygen, pain relief, fluid replacement and other symptomatic treatments.

The patient was given nebulized inhalation to reduce the production of airway secretions. The antibiotics used for prophylaxis were stopped within 24h after surgery. Daily dressing changes were performed for 3d after surgery, and the drainage tube was removed according to the drainage flow. Patients in group B continued the preoperative murine nerve growth factor treatment regimen (intramuscular injection of 30μg once a day for 6 weeks) on the second postoperative day.

Statistical Methods

JOA scores at admission, 1 month, 3 months and 6 months after surgery, and ASIA classification at admission and at the end follow-up at 6 months after surgery were collected for each group of patients. The statistically obtained data were categorized, tabulated, entered and organized, and then processed by applying the statistical software SPSS 21.0.

Results

2.1 Results of JOA scores of patients in groups A and B at admission and at 1 month, 3 months and 6 months after surgery.

JOA score at admission for patients in group A: 7.21±2.98, JOA score at admission for patients in group B: 7.12±3.12, P=0.0531>0.05 for comparison of JOA scores at admission for patients in both groups, and there was no statistical difference between JOA scores at admission for patients in groups A and B. At 1 month, 3 months, and 6 months after surgery, P< 0.05 for the comparison of JOA scores between the two groups, and there was a statistical difference between the JOA scores of patients in groups A and B at 1 month, 3 months, and 6 months after surgery (Table 1).

Table 1: JOA scores of patients in groups A and B at admission and 1 month, 3 months and 6 months after surgery ($x \pm s$)

Time	A group (n=27)	B group (n=23)	t
Hospitalization	7.21±2.98	7.12±3.12	0.672*
1 month after surgery	9.13±2.85	9.39±2.78	2.085**
3 months after surgery	10.38±3.21	11.25±2.12	2.112***
6 months after surgery	12.01±3.02	13.23±3.05	2.351****
*P=0.531>0.05, **P=0.043<0.05, ***P=0.039<0.05, ****P=0.028<0.05			

2.2 Results of ASIA grading of patients in groups A and B at admission and at the end follow-up of 6 months after surgery.

The preoperative and 6-month postoperative final follow-up ASIA grading of patients in both groups B was performed by Mann-Whitney U rank sum test. comparison of ASIA grading of patients in groups A and B on admission: Z=-0508, P=0.611>0.05, statistical difference in ASIA grading between groups A and B on admission. Comparison of the two groups A and B at the end follow-up 6 months after surgery: Z=-2.286, P=0.022<0.05, indicating a statistical difference in ASIA grading between groups A and B at the end follow-up 6 months after surgery (Table 2).

Table 2: preoperative and final 6-month postoperative follow-up ASIA classification of patients in groups A and B

Group	Hospitalization*					6 months after surgery**				
	A	B	C	D	E	A	B	C	D	E
A	3	6	13	5	0	0	3	13	6	5
B	2	5	10	6	0	0	2	3	9	9
*: Z=-.0508, P=0.611>0.05, **:Z=-2.286, P=0.022<0.05										

Discussion

Applicability of murine nerve growth factor for the treatment of CSCIWOFD

Mouse Nerve Growth Factor is a class of growth factors extracted from the submaxillary gland of male mice and isolated and purified. Since its structure is highly homologous to human nerve growth factor, it has approximately the same efficacy as human nerve growth factor and has a very low rejection reaction. Its mechanism of action is divided into: murine nerve growth factor can act on certain central cholinergic neurons, which can repair damaged nerves and promote neuronal axon regeneration. Protect and maintain the normal function of neurons [14].

The pharmacological treatment options for non-fracture-dislocated cervical spinal cord injuries are currently controversial. Glucocorticosteroids are commonly used anti-inflammatory drugs, but their use in the treatment of patients with spinal cord injury is associated with the risk of side effects. Long-term use of glucocorticoids increases the risk of infection in patients and increases the risk of gastrointestinal stress ulcers [15-17]. Gangliosides can also be used to treat cervical spinal cord injury, but Geisler FH found that although gangliosides were beneficial for the recovery of neurological function in patients with spinal cord injury, the difference was not statistically significant compared to the control group [18]. And clinical studies of gangliosides have shown that their use increases the risk of Guillain-Barré syndrome [19]. In the

2017 Expert Consensus on Assessment, Treatment and Rehabilitation of Traumatic Spinal Cord Injury, it was pointed out that nerve growth and neuroprotective drugs can be used as appropriate for patients with cervical spinal cord injury [7]. Therefore, in view of the effectiveness and safety of rats nerve growth factor in the treatment of spinal cord injury, rats nerve growth factor can be used as a therapeutic drug for spinal cord injury.

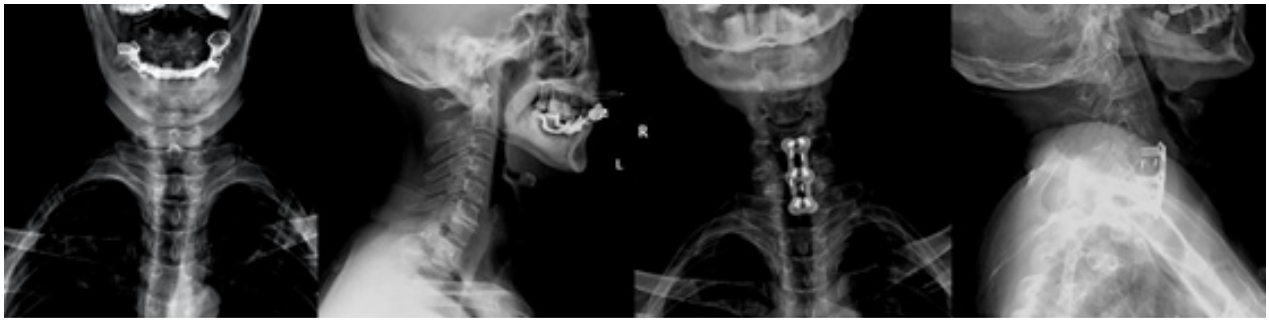

Figure 1: Group A patient without fracture dislocation type of cervical spinal cord injury were imaged before and after ACDF surgery,-no obvious fracture dislocation was seen on preoperative cervical spine X-ray,and good position of plate screws was seen on postoperative X-ray

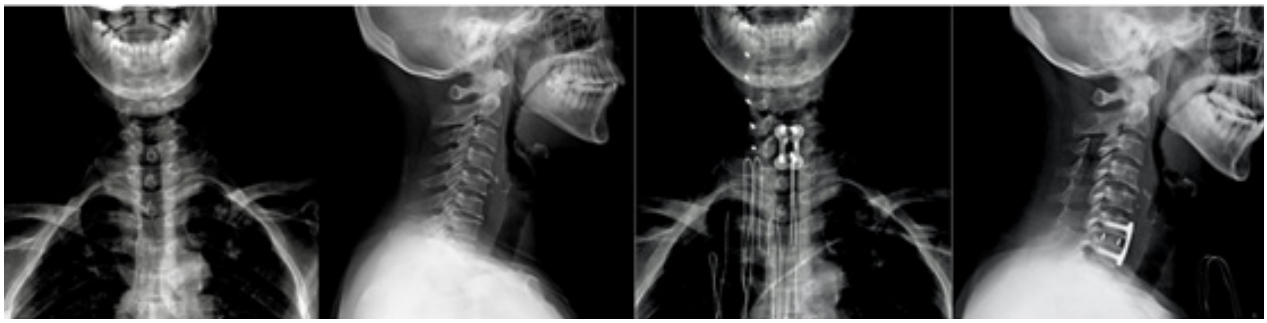

Figure 2: Group B patient without fracture dislocation type of cervical spinal cord injury were imaged before and after ACDF surgery,-no obvious fracture dislocation was seen on preoperative cervical spine X-ray,and good position of plate screws was seen on postoperative X-ray,no significant difference compared to group A patients.

Advantages of ACDF surgery for patients with CSCIWOFD

There is still controversy as to whether patients with CSCIWOFD need to receive surgical treatment. Although there are numerous reports in the literature that patients' neurological function can be satisfactorily restored after regular conservative treatment, surgical treatment is still necessary if patients have significant spinal edema, ligamentous injury, and potential risk of cervical instability. Kiwerski et al. showed that complete decompression is an advantage of anterior surgery, which can adequately reconstruct spinal stability, has a wide range of decompression characteristics, alleviate spinal cord injury, and facilitate early recovery of neurological function [20-21].

The advantages of ACDF surgery: (1) since most of the injuries in patients with CSCIWOFD cause damage and compression to the anterior part of the spinal cord, ACDF surgery can more directly remove the disc to relieve spinal cord compression; (2) the excessive stretching injury to the spinal cord during posterior surgery can be avoided in ACDF surgery; (3) ACDF surgery can effectively avoid postoperative cervical deformity caused by posterior surgery; (4) the anterior approach surgery is divided into anterior cervical discectomy decompression fusion (ACDF) and anterior cervical subtotal discectomy decompression fusion (ACCF) surgery, with the former having a better safety profile than the latter [22].

Therefore, adequate relief of edematous spinal cord compression and reconstruction of spinal stability are key factors in the prognosis of patients with CSCIWOFD, so surgery is an important treatment method for patients with CSCIWOFD. Because of the safety of ACDF surgery and the direct and complete decompression, ACDF surgery is chosen as the treatment option for cervical spinal cord injury without fracture dislocation.

Efficacy of murine nerve growth factor combined with ACDF surgery for non-fracture dislocation type cervical spinal cord injury

The comparison of JOA scores at 1 month, 3 months, and 6 months after surgery in groups A and B (Table 1) showed that there was a difference in recovery between the two groups ($P=0.043<0.05$ at 1 month, $P=0.039<0.05$ at 3 months, and $P=0.028<0.05$ at 6 months after surgery). There was a difference in recovery status at 1 month of discharge compared with patients in group A treated with single ACDF surgery, but it was not significant. The difference was more significant at 3 and 6 months after discharge in group B than in group A. The comparative status of ASIA classification at the end follow-up at 6 months after surgery in groups A and B (see Table 2) showed that there was a significant difference in the recovery status of patients in groups A and B at 6 months after surgery ($Z=-2.286$, $P=0.022< 0.05$), and there was a significant difference in the recovery status of patients in group B compared with patients in group A at 1 month after surgery. There was a difference but not

significant at 1 month postoperatively between patients in group B and group A. The recovery status of patients in group B was better than that of patients in group A at 3 months and 6 months after discharge.

Summary

In conclusion, the combination of murine nerve growth factor and ACDF surgery is safe, feasible and effective in the treatment of non-fracture-dislocated cervical spinal cord injury. The anterior approach is more advantageous than the posterior approach in restoring and maintaining the physiological curvature of the cervical spine, and can more visually relieve the anterior spinal cord compression. Mouse nerve growth factor is neurotrophic and promotes synaptic regeneration, and is an important substance involved in the regeneration and repair of injured nerves. It has fewer adverse effects and is safer, so it can be used as a drug treatment option for patients with non-fracture-dislocated cervical spinal cord injury. The combination of the two has a better clinical effect by accelerating surgical rehabilitation. However, the number of cases in this study is relatively small, the follow-up time is short, and the long-term efficacy needs further observation.

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