Clinical efficacy of γ-globulin combined with dexamethasone and methylprednisolone, respectively, in the treatment of acute transverse myelitis and its effects on immune function and quality of life

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Abstract. Effects of γ-globulin combined with dexamethasone or methylprednisolone in the treatment of acute transverse myelitis (ATM) were investigated. A retrospective analysis of medical records from 136 ATM patients admitted to Linzi District People's Hospital from July 2014 to September 2017 was performed. Patients treated with dexamethasone combined with γ-globulin were in group A (66 cases), and patients treated with methylprednisolone combined with γ-globulin were in group B (70 cases). Clinical efficacy, recovery time of bone marrow function and incidence rate of adverse reactions were analyzed and compared between the two groups. T-lymphocyte subsets in peripheral blood of both groups were detected by Flow cytometry. Quality of life of patients was assessed by the Quality of Life Scale (SF-36) developed by the American Institute of Medicine. Time of sensory recovery, self-walking, improving muscle strength at two levels and urination recovery after treatment in group B were significantly shorter than those in group A ($P<0.001$); effective rate of treatment in group B was significantly higher than that in group A ($P<0.05$); incidence rate of adverse reactions in group B was significantly lower than that in group A ($P<0.05$); ratios of $CD3^+$, $CD4^+$, $CD8^+$ cells and $CD4^+/CD8^+$ in peripheral blood of group A and group B after treatment were significantly higher than those before treatment ($P<0.05$); scores of general health (GH), physical function (PF), role physical (RP), body pain (BP), social function (SF), role emotional (RE), mental health (MH) and vitality (VT) in group B after treatment were significantly higher than those in group A ($P<0.05$). In conclusion, clinical efficacy of γ-globulin combined with methylprednisolone in the treatment of ATM patients shows definitely fewer adverse reactions, which can improve their immune function and quality of life.

Introduction

Acute transverse myelitis (ATM) is a myelopathy characterized by acute or subacute movement, sensory, and autonomic neurospinal dysfunction, with one to four new cases per million people per year (1). The pathological and physiological mechanisms of ATM have not yet been elucidated, but it may be caused by ascending and descending spinal tracts of specific levels of bone marrow (2). Symptoms and signs of motor, sensory and autonomic nerve dysfunction in ATM patients may occur simultaneously, mainly depending on the level of the spinal cord involved (3). One-third of patients with ATM can fully recover, another third have moderate residual neurological deficits, and the remaining third show clinically severe residual neurological deficits. ATM patients with poor prognosis have spinal shock and high disability (4-6).

Currently, the first-line therapy for clinical treatment of ATM is glucocorticoid treatment, such as dexamethasone and methylprednisolone. Traditional dexamethasone treatment has slower onset, longer treatment time and more adverse reactions, often leaving serious neurological dysfunction (7,8). However, methylprednisolone can produce non-specific immunosuppressive responses to the nerve center, play a role in anti-inflammatory and anti-edema, improve the blood circulation of nerves, and reduce spinal cord inflammation (9). γ-globulin is an IgG obtained from thousands of human plasma, which can rapidly supplement antibodies in patients, inhibit the mononuclear phagocytic system, and it has good efficacy in both autoimmune and inflammatory diseases (10). At present, the pathogenesis of ATM has not been clearly clarified, and immune dysfunction may be one of its pathogenesis (11). Although there have been many studies on the application of glucocorticoids and γ-globulin in ATM (12-14), there are few studies on effects of γ-globulin combined with dexamethasone and methylprednisolone, respectively, on immune function and quality of life.

In this study, γ-globulin was combined with dexamethasone or methylprednisolone to treat patients with ATM. Clinical

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efficacy of the two treatment schemes and their effects on immune function and quality of life were compared.

Patients and methods

General data. A retrospective analysis of medical records from 136 ATM patients admitted to the hospital from July 2014 to September 2017 was performed. Patients treated with dexamethasone combined with γ-globulin were enrolled in group A (66 cases), and those treated with methylprednisolone combined with γ-globulin were included in group B (70 cases). In group A, there were 40 males and 26 females, aged 24 to 49 years, with a mean age of 34.7±5.9; in group B, there were 39 males and 31 females, aged 23 to 50 years, with a mean age of 35.9±6.4. All patients were informed and signed an informed consent. This study was approved by the Ethics Committee of Linzi District People's Hospital (Zibo, China).

Inclusion and exclusion criteria. Inclusion criteria were as follows: patients complied with the diagnostic criteria of ATM in the International Collaboration Group of Acute Myelitis (TMCWG) (15); the protein of the lumbar puncture cerebrospinal fluid increased, and the diagnosis was confirmed by imaging MRI; patients bilaterally asymmetric, with symmetric nervous system signs and symptoms; the level of muscular strength of double lower limbs of people was from 0 to 3, with sensory plane barriers and sphincter dysfunction; patients with complete clinical data; patients with drug contraindications in this treatment, and anti-inflammatory, immunosuppressive drugs used in the past month. Exclusion criteria were as follows: Patients with myelitis caused by vascular, metabolic, radioactive and oppressive factors; patients with other neurological deficits, peripheral nerve damage, central nervous system diseases, severe liver and kidney dysfunction, severe infections, malignant tumors, systemic immune diseases, cardiovascular and cerebrovascular disease, hypertension, diabetes and inflammation; patients with cognitive dysfunction and mental illness.

Treatment methods. Altogether 0.3-0.5 mg/(kg•day) of dexamethasone (Shandong Chenxin Pharmaceutical Co., Ltd., batch no. H37021969) was given by intravenous drip to patients in group A; at the same time, 200-400 mg/(kg•day) of γ-globulin (Beijing Tiantan Biological Products Co., Ltd., batch no. S20023026) was given by intravenous drip; after continuous use for five to seven days, prednisone tablets (Zhejiang Xianyi Pharmaceutical Co., Ltd., batch no. H33021207) were administered orally once a day, with an oral dose of 60 mg and a reduction of 5 mg per three days. Patients in group B were given high-dose methylprednisolone (Belgium PFIZER SA, batch no. H20130302) 1,000 mg mixed with 500 ml of 10% glucose injection combined with intravenous drip; 200-400 mg/(kg•day) of γ-globulin was given by intravenous drip at the same time, and then changed to take prednisone tablets orally. The usage and dosage were consistent with those in group A. During the treatment, antacids, antibiotics, and neurotrophins were normally used, and other immunosuppressants were prohibited. Both groups were treated for four weeks.

Efficacy evaluation and observation indicators. Indicators of spinal cord function were observed, including time of sensory recovery, self-walking, improving muscle strength at two levels and urination recovery. Efficacy of patients was assessed four weeks after treatment. Efficacy of the two groups was evaluated according to the recovery of sensory disturbance, dyskinesia, and autonomic nerve dysfunction, as shown in Table I. Quality of life of patients after admission and at two months was assessed in conjunction with the Quality of Life Scale (SF-36) developed by the American Institute of Medicine (16). The assessment included general health (GH), physical function (PF), role physical (RP), body pain (BP), social function (SF), role emotional (RE), Mental Health (MH) and vitality (VT) eight dimensions, and each dimension was divided into 100 points; the higher the score, the better the quality of life.

Detection of T-lymphocyte subsets. Ratios of $CD3^+$, $CD4^+$ and $CD8^+$ as well as $CD4^+/CD8^+$ in peripheral blood were measured by Attune NxT flow cytometry (Shanghai Thermo Fisher Technology Co., Ltd.) on admission and after treatment. In total, 100 μl of anticoagulated blood was placed in the TruCOUNT tube, and then 20 μl of fluorescein isothiocyanate (FITC) fluorescently labeled monoclonal antibody CD3-PC5, CD4-PE and CD8-ECD (Shanghai Kemin Biotechnology Co., Ltd., item no. 6607010, DXT-130-109-451, 737659) were added to the tube. Then mixed evenly, and placed at room temperature for 20 min; 500 μl of hemolysin was added to lyse the cells, and the solution was placed at room temperature for 15 min; 500 μl PBS buffer solution was added; mixed well, and then placed at room temperature for 10 min. Samples were tested on a flow cytometer, and data of $CD3^+$, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ were read.

Statistical analysis. SPSS 22.0 (Beijing Boao Yijie Technology Co., Ltd.) was used for the statistical analysis of the data; GraphPad 7 was used to draw the illustrations; normal distribution data were represented as mean ± standard deviation (SD); independent sample t-test was used for comparison between groups, and paired t-test was used for comparison of the same group before and after treatment; the counting data were represented by [n(%)] and those between groups were tested by the Chi-square. When the theoretical frequency in the Chi-square test was less than five, continuous correction Chi-square test was adopted. $P<0.05$ was considered statistically significant.

Results

General data of the two groups. There was no significant difference in general clinical data including sex, body mass index (BMI), course of disease, age, history of upper respiratory tract, history of drinking, history of smoking, location of spinal lesions, cerebrospinal fluid pressure, protein level of cerebrospinal fluid, quadriplegia, paraplegia, or place of residence between group A and B ($P>0.05$) (Table II).

Spinal cord function indicators after treatment in the two groups. Time of sensory recovery, self-walking, improving muscle strength at two levels and urination recovery after

Table I. Criteria of clinical efficacy.

Efficacy	Sensory disturbance	Dyskinesia	Autonomic nerve dysfunction
Recovery	Back to normal	Normal walking ability	Normal excretion function
Significantly effective	Subtle abnormalities	Able to walk by holding on to something	Basically normal excretion function with subtle barriers
Effective	Some abnormalities	Unable to walk, but muscle function has improved	Unable to relieve oneself, but bladder function has improved
Ineffective	Clinical symptoms and signs were not changed or even deteriorated		

Total effective rate = (Recovery + significantly effective + effective)/all cases x100%.

Table II. General data of group A and group B [n (%), mean ± SD].

Category	Group A (n=66)	Group B (n=70)	t/χ^2 value	P-value
Sex			0.334	0.563
Male	40 (60.61)	39 (55.71)		
Female	26 (39.39)	31 (44.29)		
BMI (kg/m^2)	22.75±2.68	22.57±2.76	0.386	0.700
Course of disease (days)	6.6±1.3	6.4±1.2	0.933	0.352
Age (years)	34.7±5.9	35.9±6.4	1.135	0.258
History of upper respiratory tract			0.053	0.818
Yes	27 (40.91)	30 (42.86)		
No	39 (59.09)	40 (57.14)		
History of drinking			0.293	0.588
Yes	29 (43.94)	34 (48.57)		
No	37 (56.06)	36 (51.43)		
History of smoking			0.576	0.448
Yes	25 (37.88)	31 (44.29)		
No	41 (62.12)	39 (55.71)		
Location of spinal lesions			0.724	0.867
Limited to the cervical spine	13 (19.70)	14 (20.00)		
Limited to the chest spine	35 (53.03)	40 (57.14)		
Union of chest and neck	14 (21.21)	11 (15.72)		
Lumbar spinal cord involved	4 (6.06)	5 (7.14)		
Cerebrospinal fluid pressure (mmH$_2$O)	157.39±46.58	162.37±49.75	0.602	0.548
Protein level of cerebrospinal fluid (g/l)	0.41±0.22	0.43±0.24	0.506	0.614
Quadriplegia			0.033	0.855
Yes	17 (25.76)	19 (27.14)		
No	49 (74.24)	51 (72.86)		
Paraplegia			0.319	0.572
Yes	39 (59.09)	38 (54.29)		
No	27 (40.91)	32 (45.71)		
Place of residence			0.102	0.749
City	46 (69.70)	47 (67.14)		
Country	20 (30.30)	23 (32.86)		

treatment were significantly shorter in group B than those in group A (P<0.001) (Table III).

Effects of treatment in the two groups. After treatment, there were 14 cases (21.21%) recovered, 31 cases

Table III. Comparison of spinal cord function indicators after treatment in group A and group B (mean ± SD, days).

Indicators	Group A (n=66)	Group B (n=70)	t value	P-value
Sensory recovery time	8.61±3.52	5.94±2.28	5.280	<0.001
Self-walking time	21.73±8.75	17.32±5.39	3.561	<0.001
Time of improving muscle strength at two levels	13.49±4.68	9.45±3.52	5.710	<0.001
Urination recovery time	11.36±3.74	7.97±2.86	5.958	<0.001

Table IV. Comparison of effective rates between group A and group B [n (%)].

Groups	n	Recovery	Significantly effective	Effective	Ineffective	Effective rate (%)
Group A	66	14 (21.21)	31 (46.97)	10 (15.15)	11 (16.67)	83.33
Group B	70	21 (30.00)	30 (42.86)	15 (21.43)	4 (5.71)	94.29
χ^2 value	-	1.373	0.232	0.892	4.153	4.153
P-value	-	0.241	0.630	0.345	0.042	0.042

Table V. Incidence rate of adverse reactions in group A and group B [n (%)].

Groups	n	Nausea and vomiting	Rash	Bellyache	Elevated blood glucose	Incidence rate (%)
Group A	66	6 (9.09)	3 (4.55)	4 (6.06)	5 (7.58)	27.27
Group B	70	4 (5.71)	0 (0.00)	1 (1.43)	4 (5.71)	12.86
χ^2 value	-	0.569	1.488	0.958	0.190	4.437
P-value	-	0.451	0.223	0.328	0.662	0.035

(46.97%) significantly effective, 10 cases (15.15%) effective, 11 cases (16.67%) ineffective in group A, and the effective rate was 83.33%; there were 21 cases (30.00%) recovered, 30 cases (42.86%) significantly effective, 15 cases (21.43%) effective, and 4 cases (5.71%) ineffective in group B, and the effective rate was 94.29%. Effective rates of treatment in group B were significantly higher than those in group A (P<0.05). More details were shown in Table IV.

Incidence rates of adverse reactions in the two groups. During treatment, there were six cases with nausea and vomiting (9.09%), three cases with rash (4.55%), four cases with belly-ache (6.06%), five cases with elevated blood glucose (7.58%) in group A, and the incidence rate of adverse reactions was 27.27%. During treatment, there were four cases (5.71%) with nausea and vomiting, one case (1.43%) with bellyache, four cases (5.71%) with elevated blood glucose in group B, and the incidence rate of adverse reactions were 12.86%. Incidence rate of adverse reactions in group B was significantly lower than that in group A (P<0.05) (Table V).

Results of T-lymphocyte subsets in peripheral blood in the two groups. There were no significant differences in ratios of CD3+, CD4+ and CD8+ cells or CD4+/CD8+ in peripheral blood between group A and group B before or after treatment (P>0.05); ratios of CD3+, CD4+ and CD8+ cells and CD4+/CD8+ in peripheral blood between group A and group B

after treatment were significantly higher than those before treatment (P<0.05) (Fig. 1).

Comparison of results of quality of life before and after treatment in the two groups. There were no significant differences in scores of GH, PF, RP, BP, SF, RE, MH and VT between group A and group B before treatment (P>0.05); scores of GH, PF, RP, BP, SF, RE, MH and VT in group A and group B after treatment were significantly higher than those before treatment (P<0.05); scores of GH, PF, RP, RE and MH in group B after treatment were significantly higher than those in group A (P<0.05) (Fig. 2).

Discussion

The onset and progress of ATM are relatively rapid. If it is not treated in time, functional disorders in sensory, motor and autonomic nerves may occur, and even death in severe cases (17,18). In our study, the combination of γ-globulin and methylprednisolone in the treatment of ATM has better clinical symptoms, which can effectively improve the clinical symptoms of patients with fewer adverse reactions, and improve their immune function and quality of life.

Clinically, γ-globulin is mostly used for the treatment of infectious diseases, and can deliver antibodies to patients, so that they can achieve immune protection from low immunity or no immunity, and promote their recovery (19). Dexamethasone
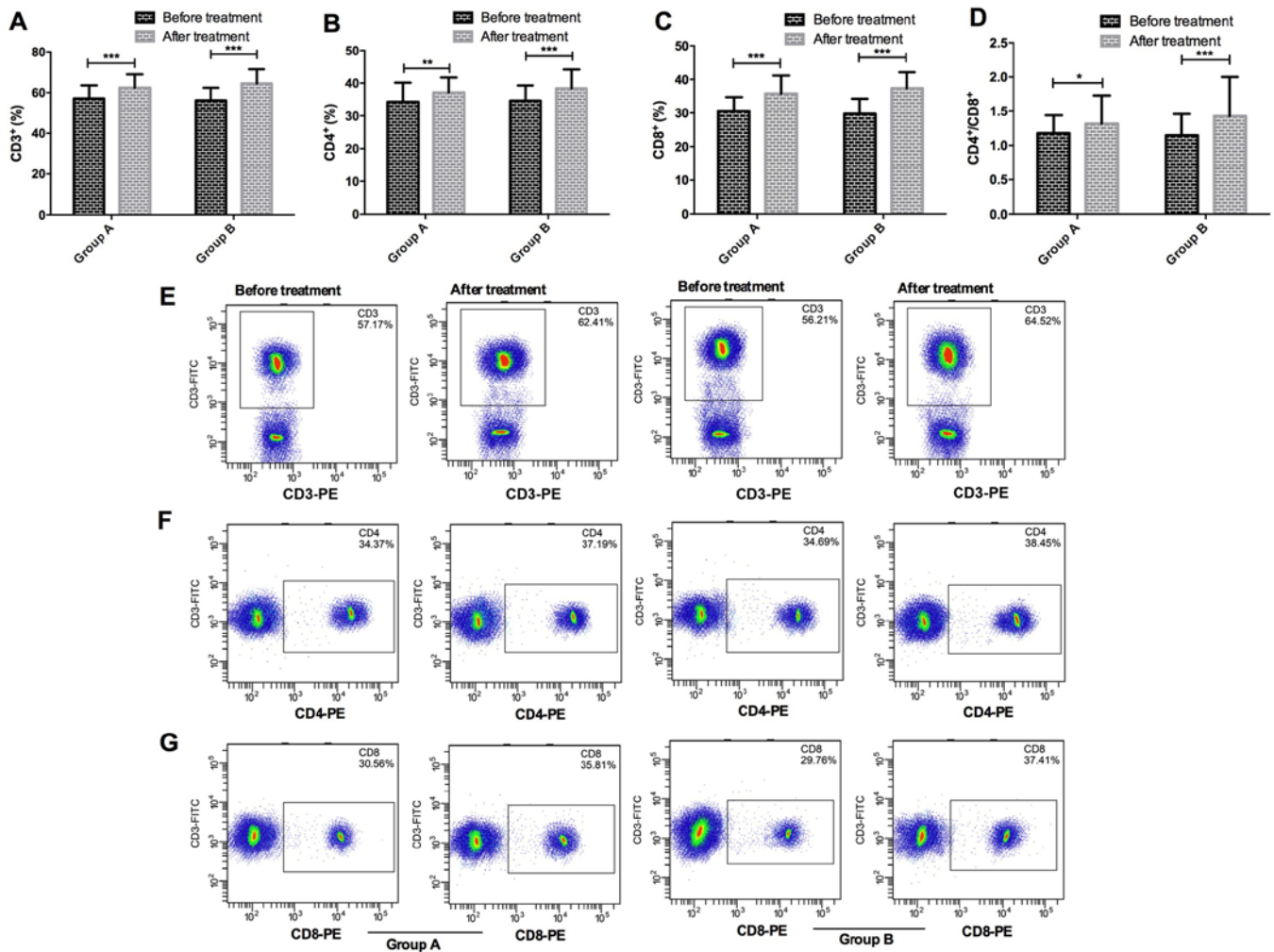
Figure 1. Comparison of T-lymphocyte subsets in peripheral blood before and after treatment in group A and group B. (A) Comparison of ratios of CD3+ cells in peripheral blood before and after treatment in group A and group B; (B) comparison of ratios of CD4+ cells in peripheral blood before and after treatment in group A and group B; (C) ratios of CD8+ cells in peripheral blood before and after treatment in group A and group B were compared; (D) ratios of CD4+/CD8+ in peripheral blood before and after treatment in group A and group B were compared; (E) flow cytometry of CD3+ ratio in peripheral blood; (F) flow cytometry of CD4+ ratio in peripheral blood; (G) flow cytometry of CD8+ ratio in peripheral blood. *P<0.05; **P<0.01; ***P<0.001.

is a commonly used glucocorticoid therapy drug for ATM, with anti-allergic and anti-toxic effects. However, its onset time is relatively slow, and some patients may suffer from dizziness, limb movement disorder, mental retardation and other complications (20). Methylprednisolone is a synthetic glucocorticoid, which can promote the synthesis of a variety of enzyme proteins, thus playing an anti-inflammatory and immunosuppressive role and promoting the recovery of nerve function (21). In recent years, there have been many studies on the application of methylprednisolone used in ATM patients. Defresne et al (22) reported that effects of high-dose methylprednisolone were better than not using hormone or low-dose methylprednisolone in the treatment of children with severe ATM; time of bladder function recovery, walking and muscle strength of children was significantly improved. Kovacs et al (23) verified that methylprednisolone combined with cyclophosphamide in the treatment of ATM patients was significantly better than cyclophosphamide alone. In this study, time of recovery, self-walking, improving muscle strength at two levels and urination recovery of group B was significantly shorter than that of group A, and effective rates of group B were significantly higher than those

of group A. Thus indicating that γ-globulin combined with methylprednisolone was effective in the treatment of ATM, which could promote the recovery of spinal cord function with fewer adverse reactions. Further research found that the incidence rate of adverse reactions in group B was significantly lower than that in group A, indicating that there were fewer adverse reactions in combination of the two. Although some adverse reactions occurred during the treatment, all patients recovered completely without special treatment, so this is in line with expectations. Pavlou et al (24) confirmed that a patient with ATM was treated with high-dose methylprednisolone, and the condition was not effectively controlled. There were still aggravated limb paralysis and respiratory muscles paralysis, followed by intravenous γ-globulin. Patients' neurological function began to recover with no apparent complications, which was similar to our study. Changes in T-lymphocyte subsets reflect the status of immune system function, and they are classified into CD3+, CD4+ and CD8+ cells according to their functions and surface markers (25), in which CD3+ is positively correlated with T-lymphocyte immune function, while the increase and decrease of ratios of CD4+ and CD8+
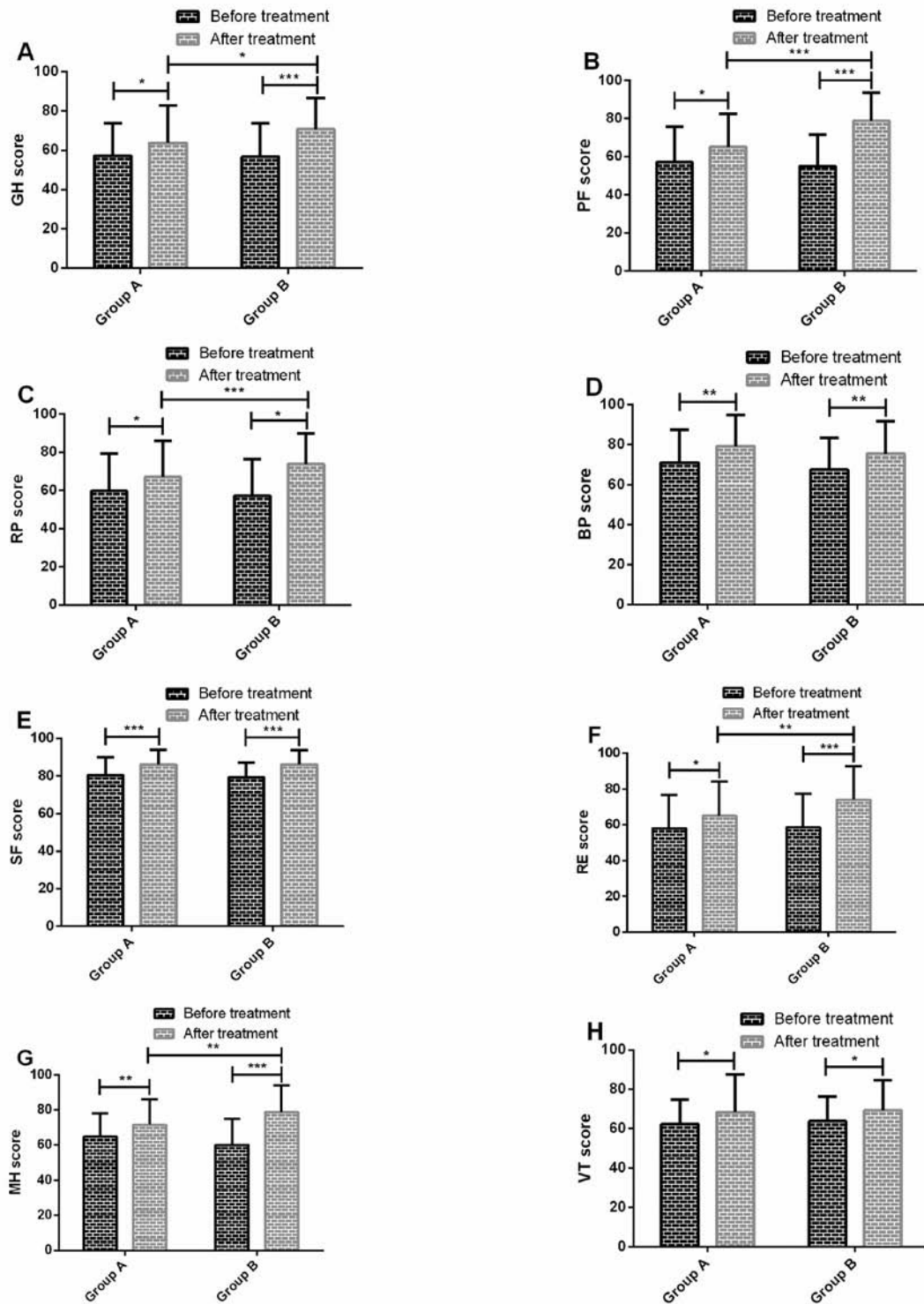
Figure 2. Comparison of results of quality of life before and after treatment in group A and group B. (A) Comparison of GH scores before and after treatment between group A and group B; (B) comparison of PF scores before and after treatment between group A and group B; (C) comparison of RP scores before and after treatment between group A and group B; (D) comparison of BP scores before and after treatment between group A and group B; (E) comparison of SF scores before and after treatment between group A and group B; (F) comparison of RE scores before and after treatment between group A and group B; (G) comparison of MH scores before and after treatment between group A and group B; (H) comparison of VT scores before and after treatment between group A and group B. *P<0.05; **P<0.01; ***P<0.001.

can cause the ratios to become imbalanced, which leads to abnormal immune function (26). The present study showed that ratios of CD3$^+$, CD4$^+$, CD8$^+$ and CD4$^+$/CD8$^+$ in peripheral blood of group A and group B were significantly higher than those before treatment, but there were no significant differences between the groups. γ-globulin combined with dexamethasone and methylprednisolone, respectively, can improve the immune status of patients and improve their immunity. Larroche et al (27) reported that γ-globulin was an important drug for the treatment of various autoimmune and

neurological diseases, and one of its mechanisms was to immunomodulate patients. It may be that γ-globulin exerts enhancing immunity (28), while glucocorticoid drugs can alleviate the damage of peroxide to spinal cord tissue (29). Combination of these two drugs can eliminate the abnormal immune function of ATM patients, reduce the damage of immune responses to spinal cord, thereby promoting the recovery of spinal cord function. Gelfand (30) reported that γ-globulin could be used as clinical immunomodulatory therapy to treat a variety of immune diseases, such as Guillain-Barré syndrome, myasthenia gravis, Kawasaki disease, and in kidney transplant. However, γ-globulin is a mixed blood product, which is relatively expensive. Therefore, the application of γ-globulin may be accompanied by cost-effectiveness considerations. Finally, SF-36 was adopted to assess patients' quality of life. The results revealed that scores of GH, PF, RP, BP, SF, RE, MH and VT in group A and group B after treatment were significantly higher than those before treatment, and scores of GH, PF, RP, RE and MH after treatment in group B were significantly higher than those in group A, which indicated that γ-globulin combined with methylprednisolone also had a certain improvement effect on patients' quality of life. This may be because the γ-globulin combined with methylprednisolone has better efficacy and can improve the clinical symptoms and signs of patients, thereby improving their quality of life.

This study confirmed the clinical efficacy of γ-globulin combined with methylprednisolone in the treatment of ATM. However, the long-term quality of life of ATM patients was not observed and the influencing factors of the efficacy remain to be analyzed.

In conclusion, γ-globulin combined with methylprednisolone in the treatment of ATM patients has definite clinical efficacy and fewer adverse reactions, which can improve their immune function and quality of life.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

PW conceived the study and wrote the manuscript. SZ analyzed and interpreted the patient general data. HLv and GQ performed flow cytometry. XZ, HLi and LZ were responsible for the analysis of the observation indicators. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Linzi District People's Hospital (Zibo, China). Patients who participated in this study had complete clinical data. Signed informed consents were obtained from the patients and/or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. He H, Jin L, Ju M, Tu G and Luo Z: Acute transverse myelitis of the cervical spine secondary to psoas abscess. BMC Infect Dis 16: 579, 2016.
2. Frohman EM and Wingerchuk DM: Clinical practice. Transverse myelitis. N Engl J Med 363: 564-572, 2010.
3. The Lancet Infectious Diseases: Enterovirus D68: The unexpected guest. Lancet Infect Dis 14: 1023, 2014.
4. Holm-Hansen CC, Midgley SE and Fischer TK: Global emergence of enterovirus D68: A systematic review. Lancet Infect Dis 16: e64-e75, 2016.
5. Huh Y, Park EJ, Jung JW, Oh S and Choi SC: Clinical insights for early detection of acute transverse myelitis in the emergency department. Clin Exp Emerg Med 2: 44-50, 2015.
6. Chen L, Li J, Guo Z, Liao S and Jiang L: Prognostic indicators of acute transverse myelitis in 39 children. Pediatr Neurol 49: 397-400, 2013.
7. Kuo SC, Cho WH, Shih HI and Tu YF: Idiopathic acute transverse myelitis in children: A retrospective series. Neuropediatrics 46: 307-312, 2015.
8. Li J, Zhou J and Zhan QS: Comparative observation of Methylprednisolone and gamma globulin in the treatment of acute myelitis. Chin J Biochem Pharm 37: 163-164, 2017.
9. Nelson GR, Bonkowsky JL, Doll E, Green M, Hedlund GL, Moore KR and Bale JF Jr: Recognition and management of acute flaccid myelitis in children. Pediatr Neurol 55: 17-21, 2016.
10. Branch DR: Serologic problems associated with administration of intravenous immune globulin (IVIg). Immunohematology 35: 13-15, 2019.
11. Greenberg BM and Frohman EM: Immune-mediated myelopathies. Continuum (Minneap Minn) 21 (1 Spinal Cord Disorders): 121-131, 2015.
12. Patel V, Griffith NC, Blackwood E, Dias M and Cordato DJ: Spectrum disorder of neuromyelitis optica in a patient presenting with intractable vomiting and hiccups, transverse myelitis and acute encephalopathy. J Clin Neurosci 19: 1576-1578, 2012.
13. Hurlbert RJ: Methylprednisolone for the treatment of acute spinal cord injury: Point. Neurosurgery 61 (Suppl 1): 32-35, 2014.
14. Torisu H, Kira R, Ishizaki Y, Sanefuji M, Yamaguchi Y, Yasumoto S, Murakami Y, Shimono M, Nagamitsu S, Masuzaki M, *et al*: Clinical study of childhood acute disseminated encephalomyelitis, multiple sclerosis, and acute transverse myelitis in Fukuoka Prefecture, Japan. Brain Dev 32: 454-462, 2010.
15. West TW: Transverse myelitis - a review of the presentation, diagnosis, and initial management. Discov Med 16: 167-177, 2013.
16. Yarlas A, Bayliss M, Cappelleri JC, Maher S, Bushmakin AG, Chen LA, Manuchehri A and Healey P: Psychometric validation of the SF-36® Health Survey in ulcerative colitis: Results from a systematic literature review. Qual Life Res 27: 273-290, 2018.
17. Annunziata P, Masi G, Cioni C, Gastaldi M, Marchioni E, D'amico E, Patti F, Laroni A, Mancardi G, Vitetta F, *et al*: Clinical, laboratory features, and prognostic factors in adult acute transverse myelitis: An Italian multicenter study. Neurol Sci 40: 1383-1391, 2019.
18. West TW, Hess C and Cree BAC: Acute transverse myelitis: Demyelinating, inflammatory, and infectious myelopathies. Semin Neurol 32: 97-113, 2012.
19. Dhandha MM, Siegfried EC and Knutsen AP: Treatment of selective antibody deficiency with IVIG resulting in decreased frequency of streptococcal infection and improvement of guttate psoriasis. Dermatol Online J 23: 23, 2017.

20. Tomietto P, D'Agostini S, Annese V, De Vita S and Ferraccioli G: Mycophenolate mofetil and intravenous dexamethasone in the treatment of persistent lupus myelitis. J Rheumatol 34: 588-591, 2007.
21. Costa DD, Beghi E, Carignano P, Pagliacci C, Faccioli F, Pupillo E, Messina P, Gorio A and Redaelli T: Tolerability and efficacy of erythropoietin (EPO) treatment in traumatic spinal cord injury: A preliminary randomized comparative trial vs. methylprednisolone (MP). Neurol Sci 36: 1567-1574, 2015.
22. Defresne P, Meyer L, Tardieu M, Scalais E, Nuttin C, De Bont B, Loftus G, Landrieu P, Kadhim H and Sébire G: Efficacy of high dose steroid therapy in children with severe acute transverse myelitis. J Neurol Neurosurg Psychiatry 71: 272-274, 2001.
23. Kovacs B, Lafferty TL, Brent LH and DeHoratius RJ: Transverse myelopathy in systemic lupus erythematosus: An analysis of 14 cases and review of the literature. Ann Rheum Dis 59: 120-124, 2000.
24. Pavlou E, Gkampeta A, Kouskouras K, Evangeliou A and Athanasiadou-Piperopoulou F: Idiopathic acute transverse myelitis: Complete recovery after intravenous immunoglobulin. Hippokratia 16: 283-285, 2012.
25. den Otter I, Willems LN, van Schadewijk A, van Wijngaarden S, Janssen K, de Jeu RC, Sont JK, Sterk PJ and Hiemstra PS: Lung function decline in asthma patients with elevated bronchial CD8, CD4 and CD3 cells. Eur Respir J 48: 393-402, 2016.
26. Zhao Z, Liao H and Ju Y: Effect of compound Kushen injection on T-cell subgroups and natural killer cells in patients with locally advanced non-small-cell lung cancer treated with concomitant radiochemotherapy. J Tradit Chin Med 36: 14-18, 2016.
27. Larroche C, Chanseaud Y, Garcia de la Pena-Lefebvre P and Mouthon L: Mechanisms of intravenous immunoglobulin action in the treatment of autoimmune disorders. BioDrugs 16: 47-55, 2002.
28. Ballow M: The IgG molecule as a biological immune response modifier: Mechanisms of action of intravenous immune serum globulin in autoimmune and inflammatory disorders. J Allergy Clin Immunol 127: 315-323, quiz 324-325, 2011.
29. Esposito E, Bruscoli S, Mazzon E, Paterniti I, Coppo M, Velardi E, Cuzzocrea S and Riccardi C: Glucocorticoid-induced leucine zipper (GILZ) over-expression in T lymphocytes inhibits inflammation and tissue damage in spinal cord injury. Neurotherapeutics 9: 210-225, 2012.
30. Gelfand EW: Intravenous immune globulin in autoimmune and inflammatory diseases. N Engl J Med 367: 2015-2025, 2012.