Am J Transl Res 2022;14(9):6295-6302
www.ajtr.org /ISSN:1943-8141/AJTR0141934

Original Article

Clinical efficacy of high-dose intravenous gammaglobulin in acute Guillain-Barre syndrome and effect on serum concentration of inflammatory factors

Lifeng Lv*, Haijuan Xu*, Haining Zhang, Qinde Qi

*Department of Neurology, Ji'nan City People's Hospital, Ji'nan 271199, Shandong Province, China. *Equal contributors.*

Received January 22, 2022; Accepted May 19, 2022; Epub September 15, 2022; Published September 30, 2022

Abstract: Objective: To explore the clinical efficacy of high-dose intravenous gammaglobulin (IVIG) in acute Guillain-Barre syndrome (GBS) and its effect on serum concentrations of inflammatory factors. Methods: A total of 111 patients with acute GBS were enrolled in this retrospective study. They were admitted to Ji'nan City People's Hospital from January 2019 to December 2020. According to the treatment method, the patients were divided into a control group (n=53, received routine treatment) and an observation group (n=58, received high-dose IVIG in addition to routine treatment). The clinical efficacy, Barthel index for activities of daily living (ADL), serum concentrations of inflammatory factors (IL-6, TNF-α, NO) in peripheral blood, potential of electromyography signals, abnormal rates of motor and sensory conduction velocity, and F wave abnormality rate were compared. Also, the risk factors affecting IVIG treatment efficacy were analyzed. Results: The overall response rate, and Barthel index for ADL were higher, while serum concentrations of IL-6, TNF-α, and NO were lower in the observation group than the control group (all $P<0.05$). There were differences in spontaneous potential and motor potential before and after treatment in both groups (both $P<0.05$). The observation group showed lower abnormal rates of motor and sensory conduction velocity, F wave abnormality rate, and prolonged latency rate than the control group (all $P<0.05$). Concomitant lung infection, respiratory muscle involvement, and treatment with high-dose IVIG >2 weeks from onset were independent risk factors for treatment efficacy. Conclusion: High-dose IVIG has good clinical efficacy in treating acute GBS by reducing the serum concentrations of IL-6, TNF-α, and NO, improving patients' abnormal muscle electrical condition, and promoting recovery. It is recommended for use clinically at an early stage. At the same time, lung infection must be prevented.

Keywords: Acute Guillain-Barre syndrome, intravenous gammaglobulin, clinical response, inflammatory factors, electromyography, risk factors

Introduction

Guillain-Barre syndrome (GBS), also known as acute inflammatory demyelinating polyneuropathy, is a common disease in neurology and a major cause of acute flaccid paralysis [1-3]. GBS is an autoimmune disease with rapid onset, characterized by demyelinating of nerve roots and peripheral nerves, and inflammatory damage to lymphocytes and macrophages around small vessels [4, 5]. The clinical symptoms include limb paralysis, radicular pain, weakening or disappearance of tendon reflex, and respiratory dysfunction or even suffocation caused by respiratory muscular paralysis [6]. Thus, it is of great significance to treat GBS early. At present, the cause of GBS is not clear. Infection, hepatitis B surface antigen, vaccination, and organ transplantation can cause cellular and humoral immunity to trigger autoimmune response, leading to the occurrence of GBS [7]. Clinically, electrocardiogram monitoring and mechanical ventilation are used in symptomatic therapy. Due to the unknown cause of the disease, at present, there is no specific drug. A study has confirmed that immunoglobulin therapy is effective based on the changes in clinical muscle strength and electromyography, despite lack of serological indicators [8]. It has been reported that inflammatory

factors such as IL-6, TNF-α, and NO are abnormally expressed in the cerebrospinal fluid of neurological diseases [9]. These factors have been less studied in evaluating treatments for GBS. Moreover, due to the high price of gamma globulin, it is particularly important to analyze the risk factors influencing treatment efficacy. Therefore, in this study, we explored the clinical efficacy of high-dose IVIG on treatment for GBS, its effects on serum concentrations of inflammatory factors and electromyography changes, and the risk factors for treatment efficacy, with the aim of providing possible evaluation targets for the therapy of GBS.

Materials and methods

General data

A total of 111 patients with acute GBS were enrolled in this retrospective study. They were admitted to Ji'nan City People's Hospital from January 2019 to December 2020. According to treatment method, the patients were divided into a control group (n=53, received routine treatment) and an observation group (n=58, received high-dose IVIG in addition to the routine treatment). This study has been approved by the Ethics Committee of Ji'nan City People's Hospital.

Inclusion criteria: (1) Patients' clinical manifestations, electrophysiological measurement results and cerebrospinal fluid (CSF) examination results met the criteria for GBS [10]. (2) Patients had a history of the prodromal period of infection. (3) Patients' condition worsened progressively and peaked within two weeks. (4) Patients had symmetrical muscle weakness with or without respiratory muscle weakness. (5) Patients had paresthesia or autonomic dysfunction. (6) CSF biochemical assays presented signs of protein-cell isolation.

Exclusion criteria: (1) Patients died during the treatment. (2) Patients had other autoimmune diseases. (3) Patients had hepatic and renal insufficiency. (4) Patients had IVIG allergy or contraindications. (5) Patients had malignant tumors or cachexia.

Methods

Treatments: After admission, patients in the control group received conventional nutritional neurotherapy (intramuscular injection of Methylcobalamin, 500 μg/time, 3 times/d; vitamins B1 and B6 oral, both 10 mg/time, 3 times/d). At the same time, assisted mechanical ventilation, and anti-infection treatment were implemented. Patients in the observation group were given IVIG based on conventional nutritional neurotherapy. IVIG was commonly used at a dose of 0.2 g/(kg.d), and the maximum dose was up to 0.4 g/(kg.d). In this study, IVIG at a dose of 0.4 g/(kg.d) was adopted with intravenous infusion, once a day, continuously for 5-7 days. After treatment, the clinical efficacy was recorded.

Determination of clinical efficacy: The clinical response rate was determined based on the patient's muscle strength recovery. Muscle strength that returned to level IV with the disappearance of muscle paralysis was regarded as full recovery. Muscle strength returning to level IV with a significant improvement in muscle paralysis was considered very effective. Muscle strength returning to level 1 with an improvement in respiratory muscle paralysis was regarded as effective. No improvement, or even worsening in muscle and respiratory paralysis was called ineffective [11]. Overall response rate = (Case of full recovery + very effective + effective)/total number of cases *100%.

Electromyography detection: Electromyography/evoked potential instrument (KEYPOINT, Denmark) was adopted for measuring muscle potential before and after treatment. A surface electrode was used to measure motor and sensory conduction velocity, distal latency, and changes in F wave.

Detection of serum concentrations of IL-6, TNF-α, and NO: Before and after treatment, 3-5 mL of peripheral venous blood was collected from patients. The blood sample was centrifuged (Sigma 3-30K, Germany) and stored. ELISA was used to detect the serum concentrations of IL-6, TNF-α, and NO. The reagents were from Shanghai Ricky Biotechnology Co., Ltd., China.

Evaluation of activities of daily living (ADL) by Barthel index: The Barthel index (maximum score: 100 points) was adopted for ADL evaluation, such as turning over, standing and sitting, using the restroom, walking, and climbing the stairs. Between 26-100 points, higher scores indicate a better athletic ability. Less than 25 points was defined as complete incapacitation [12].

Table 1. Comparison of general data

Group	Observation group (n=58)	Control group (n=53)	t/χ^2	P
Sex (male/female)	27/21	24/29	0.813	0.367
Age (years)	35.8±11.5	36.1±9.8	0.148	0.882
Disease course (days)	5.06±0.89	4.97±0.92	0.523	0.602
Site of infection				
Gastrointestinal tract	29	32	0.882	0.365
Respiratory tract	29	21		

Statistical analysis

SPSS 23.0 software was adopted for statistical analysis. Measured data were expressed as mean ± standard deviation ($\bar{x}$ ± sd). Independent t-test was carried out for comparison between groups. The counted data were tested by χ^2. One-way logistic regression analysis was carried out on each risk factor respectively. Stepwise logistic regression was done for *P* value, OR value, and 95% CI. P<0.05 was considered a significant difference.

Results

Comparison of general data

No statistical significance in terms of age, sex, disease course, or site of infection were found in the two groups. The baseline data were comparable. See **Table 1**.

Comparison of clinical efficacy

The observation group revealed a higher overall response rate than the control group. See **Table 2**.

Comparison of potential of electromyography parameters before and after treatment

There were no differences in spontaneous and motor potentials between the two groups before treatment. After treatment, the score of motor potential in the observation group was higher than that in the control group (P<0.001). See **Table 3**.

Comparison of motor and sensory conduction velocity before and after treatment

Motor conduction velocity was measured for 111 patients, including a total of 256 nerves, such as median nerve, ulnar nerve, common peroneal nerve, and tibia nerve. Among them, 134 nerves were detected in the control group and 122 in the observation group. 96 sensory nerves were detected, 46 in the control group and 50 in the observation group. Before treatment, no differences in motor or sensory conduction velocity abnormality were found between the two groups. After treatment, the observation group revealed lower abnormality rates than the control group (both P<0.001). See **Table 4**.

Comparison of F wave abnormality rate and prolonged latency rate before and after treatment

F wave were detected from 222 nerves in 111 cases. Among them, 106 nerves in the control group and 116 nerves in the observation group were detected. As a result, 24 were not ejected, 78 had prolonged latency, and 34 had a reduced incidence of F wave. Before treatment, the F wave abnormality and prolonged latency rates showed no significant differences between the two groups. After treatment, the F wave abnormality and prolonged latency rates in the observation group were lower than those of the control group (both P<0.001). See **Table 5**.

Comparison of serum concentrations of inflammatory factors before and after treatment

Compared to before treatment, serum concentrations of inflammatory factors (IL-6, TNF-α, and NO) were lower after treatment (all P< 0.001). See **Figures 1**-**3**.

Comparison of the Barthel index for ADL before and after treatment

After treatment, the observation group had better the Barthel index for ADL than the control group (P<0.001). See **Figure 4**.

Univariate logistic regression analysis of risk factors for treatment efficacy

The results revealed that concomitant lung infection, respiratory muscle involvement, and IVIG treatment after two weeks from onset were all the risk factors influencing the effect of IVIG treatment. At the same time, the above factors were taken as the independent variable, and the IVIG treatment efficacy was taken

Table 2. Comparison of clinical efficacy

Group	Case (n)	Very effective (n)	Effective (n)	Ineffective (n)	Overall response rate (%)
Control group	53	26	1	26	27/53
Observation group	58	35	6	17	41/58
χ^2			4.550		
P			0.033		

Table 3. Comparison of potential of electromyography parameters before and after treatment (n, %)

Potential	Before treatment		After treatment	
	Control group	Observation group	Control group	Observation group
Spontaneous potential	49	51	24	12
Motor potential	4	7	29	46
χ^2	0.665		0.010	
P	0.415		6.563	

Note: Comparison of the incidence between groups was detected by χ^2 test.

Table 4. Comparison of motor and sensory conduction velocity before and after treatment (n, %)

Item	Slow motor conduction velocity	Lost motor conduction velocity	Slow sensory conduction velocity	Lost sensory conduction velocity
Before treatment				
Control group	110	24	32	14
Observation group	109	13	35	15
χ^2	2.163		0.031	
P	0.141		0.860	
After treatment				
Control group	56	12	20	9
Observation group	39	6	9	4
χ^2	4.430		11.896	
P	0.035		0.001	

Note: Comparison of the incidence between groups was detected by χ^2 test.

Table 5. Comparison of the rates of abnormality in F wave and prolonged latency before and after treatment (n, %)

Abnormal F wave	Before treatment		After treatment	
	Control group	Observation group	Control group	Observation group
Not ejected	13	11	8	3
A reduced incidence	34	44	31	18
Prolonged latency	17	17	11	8
In total	64	72[a]	50	29[b]

Note: Compared to before treatment, [a]P>0.05. Compared to control group, [b]P<0.05.

as the dependent variable (1= poor treatment efficacy; 0= good treatment efficacy) in the logistic regression model for analysis. As a result, lung infection, respiratory muscle involvement, and IVIG treatment after two weeks from the onset were adverse factors. See **Tables 6-8**.

Discussion

GBS is a peripheral neuropathy caused by autoimmune diseases with a high disability rate. It is mainly manifest as peripheral nerve monocyte and lymphocyte infiltration, phased demyelination and axial mutation pathologically. This

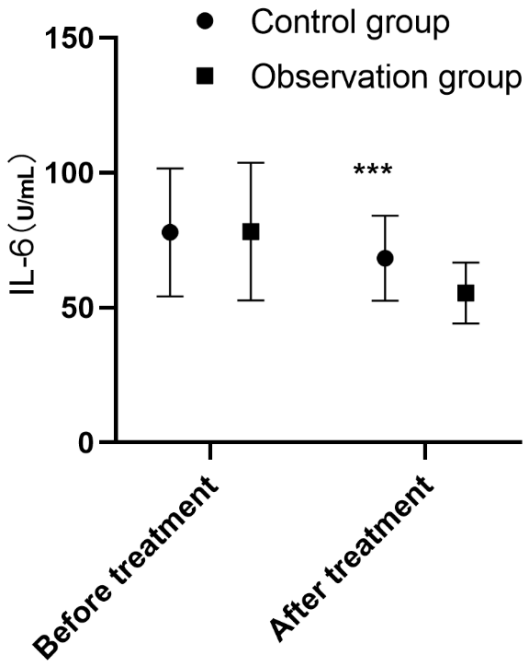

Figure 1. Comparison of serum concentrations of IL-6 before and after treatment. Compared to the observation group after treatment, ***P<0.001.

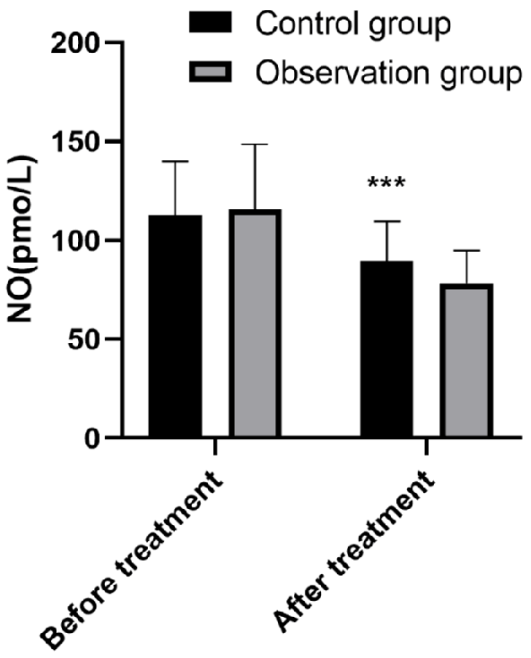

Figure 2. Comparison of serum concentrations of NO before and after treatment. Compared to the observation group after treatment, ***P<0.001.

may cause nervous system damage, especially for peripheral nerves and nerves connecting respiratory muscle [13]. Effective treatment is

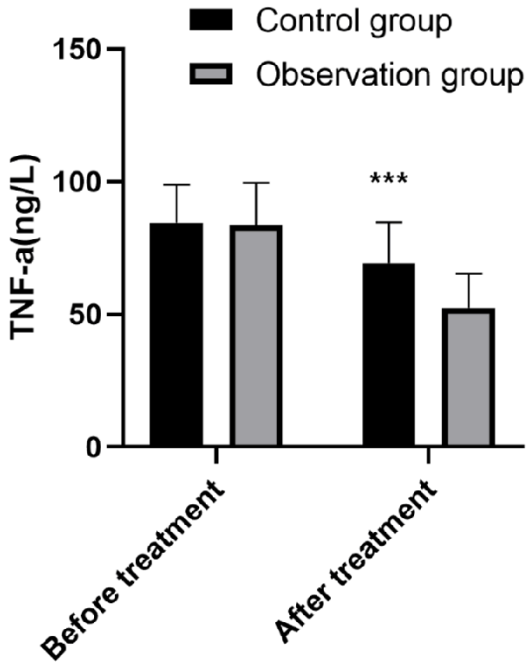

Figure 3. Comparison of serum concentrations of TNF-a before and after treatment. Compared to the observation group after treatment, ***P<0.001.

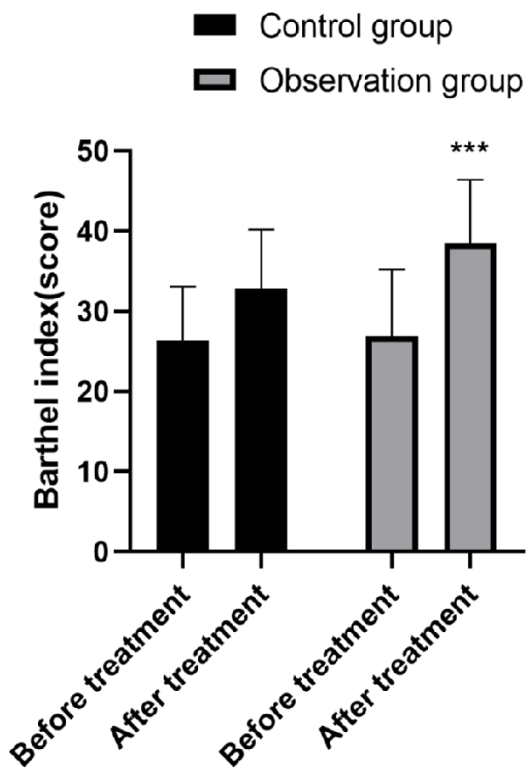

Figure 4. Comparison of the Barthel index for activities of daily living before and after treatment. Compared to the control group after treatment, ***P<0.001.

Table 6. Univariate logistic regression analysis of risk factors for treatment efficacy (n)

Group	Case	Age of onset >40 years old	Respiratory muscle involvement	Cranial nerve involvement	Concomitant lung infection	IVIG treatment > two weeks from onset	Isolation pretreatment on cerebrospinal fluid protein
Valid	41	23	3	25	4	8	27
Invalid	17	9	6	11	10	10	11
χ^2		0.001	5.200	0.010	12.34	10.074	0.002
P		0.980	0.023	0.975	0.000	0.002	0.966

Note: IVIG, intravenous gammaglobulin.

Table 7. Assignment for independent variable

Independent variable	Assignment	
	1	0
Concomitant lung infection	Yes	No
Respiratory muscle involvement	Yes	No
IVIG treatment > two weeks from onset	Yes	No

Note: IVIG, intravenous gammaglobulin.

the main intervention to save the patient's life and athletic ability. Based on the pathogenesis of GBS, the current guidelines recommend the use of immunotherapy, including plasma exchange, hormone therapy, and high-dose IVIG therapy [14, 15]. IVIG has become a recognized treatment for GBS with good therapeutic effect, due to multiple complications and unsatisfactory clinical treatment outcomes of hormone therapy with a high cost and many contraindications of plasma exchange. Besides, guidelines for GBS treatment suggests that high-dose IVIG showed better clinical efficacy when compared to different doses of IVIG [16]. In this study, the observation group showed better clinical efficacy than the control group, which is similar to the data provided in the previous study [17]. This further consolidated the conclusion of the study on the efficacy of IVIG in the treatment of GBS.

Electrophysiological testing is the main non-invasive means for GBS and the main auxiliary method for assessing the patient's condition. It has been confirmed that motor and sensory conduction velocity, and changes in electromyography and F waves were the main manifestations in electrophysiologic detection of GBS [18]. In this study, slow and lost motor and sensory conduction velocity, and F wave abnormality were observed in 111 cases. After treatment, the above-mentioned detected nerves were restored to varying degrees in the two groups, and the observation group showed better results than the control group. The possible mechanisms are as follows. IVIG activates complement and effectively removes immune complexes; a large amount of IVIG binds to macrophage-related receptors, blocking their antigen presentation function, thereby blocking the immune response. Besides, IVIG plays a competitive site-binding role to antagonize the binding of autoantibodies, usually inhibiting macrophage function to produce antibodies and directly repairing the myelin function of nerve cells, ultimately improving the clinical symptoms of patients. This is supported by the conclusions from previous research [19, 20].

Inflammatory factors, such as IL-6 and TNF-α, have biologic effects in multiple systems of the body, and participate in immune regulation and mediate inflammatory response. IL-6 is a cytokine necessary for B cells to terminally differentiate and produce antibodies. It promotes myelin destruction and loss by boosting B cell differentiation and producing antibodies against peripheral nerve myelin sheaths. TNF-α can not only increase the permeability of the blood nerve barrier, and induce the expression of NO to cause damage to the myelin sheath and axon of the peripheral nerves, but also directly mediate the loss of the myelin sheath. NO, as a non-classical neurotransmitter, a regulator of cell function or a messenger, also participates in the biologic functions of many systems, and directly damage Schwann cells and myelin sheaths [21-23]. The overexpressions of IL-6, TNF-α and NO in patients with GBS have been confirmed in the latest study [24]. In this study, IL-6, TNF-α and NO were decreased to varying degrees after treatment in the two groups, and were lower in the observation group than those of the control group, confirming the anti-inflammatory and NO inhibitory function of IVIG, which is similar to previous reports [24, 25].

This study explored whether IVIG improves patients' athletic ability. Results revealed that

Table 8. Logistic regression analysis of IVIG treatment efficacy

Indicator	Standardized β	SE	Wald χ^2	OR	95% CI	P
Concomitant lung infection	2.172	1.76	6.93	8.776	3.768-18.776	0.001
IVIG treatment > two weeks from onset	1.844	1.53	4.71	6.321	2.338-21.330	0.002
Respiratory muscle involvement	1.268	1.44	2.35	3.553	1.12-2.97	0.041

Note: IVIG, intravenous gammaglobulin.

the patients' motor ability improved significantly after treatment in both groups, and the observation group had higher scores than the control group. This was associated with IVIG improving immune status and anti-IL-6/ TNF-α /NO. This suggests that the direct nerve injury effect of TNF-α, the effect of IL-6-related lymphocytes, and the demyelinating injury of NO were reduced, which supports the conclusion of a past study [26].

Finally, the risk factors influencing the IVIG treatment efficacy were further analyzed. This indicated that concomitant lung infection, respiratory muscle involvement, and IVIG treatment after two weeks from onset (P=0.002, OR=6.321, 95% CI: 2.338-21.330) were independent influencing factors. The underlying mechanism is related to the persistence of immune responses mediated by autoantibodies, complement activation, the participation of a variety of immune cells and inflammatory mediators, and heavy damage to the nerve myelin sheath and axon 2 weeks after onset. The poor efficacy of IVIG therapy may be related to its mechanism, which is mainly directed at the body's immune response and has no effect on lung infections or respiratory muscle involvement [27, 28].

However, some limitations still exist in this study. This single-center retrospective study only included a small sample size. A multicenter prospective large-sample study is necessary to further confirm the clinical efficacy of IVIG. The mechanism for anti-inflammatory action of IVIG and NO pathways should be added to the conclusions of this study. In addition, this study adopted dosages of IVIG suggested by guidelines, so as to avoid lungdamage to the patients, so no regular dose groups were established. This reduced the reliability of the results to some extent.

In conclusion, high-dose IVIG has good clinical efficacy in the treatment of acute GBS, improves patients' abnormal muscle electrical condition, and promotes the life quality and athletic ability, which may be related to anti-autoimmunity and inflammation.

Disclosure of conflict of interest

None.

Address correspondence to: Qinde Qi, Department of Neurology, Ji'nan City People's Hospital, No. 001 Xuehu Avenue, Laiwu District, Ji'nan 271199, Shandong Province, China. Tel: +86-13863478506; E-mail: qqd1963@163.com

References

[1] Chung A and Deimling M. Guillain-Barré syndrome. Pediatr Rev 2018; 39: 53-54.
[2] Liu SA, Dong CL and Ubogu EE. Immunotherapy of Guillain-Barre syndrome. Hum Vaccin Immunother 2018; 14: 2568-2579.
[3] Kaida K. Guillain-Barré syndrome. Adv Exp Med Biol 2019; 1190: 323-331.
[4] Chevret S, Hughes RA and Annane D. Plasma exchange for Guillain-Barré syndrome. Cochrane Database Syst Rev 2017; 2: CD001798.
[5] Cherian A, Ajitha KC, Iype T and Divya KP. Neurotuberculosis: an update. Acta Neurol Belg 2021; 121: 11-21.
[6] Prada V, Massa F, Salerno A, Fregosi D, Beronio A, Serrati C, Mannironi A, Mancardi G, Schenone A and Benedetti L. Importance of intensive and prolonged rehabilitative treatment on the Guillain-Barre syndrome long-term outcome: a retrospective study. Neurol Sci 2020; 41: 321-327.
[7] Malek E and Salameh J. Guillain-Barre syndrome. Semin Neurol 2019; 39: 589-595.
[8] van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC and van Doorn PA. Guillain-Barre syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol 2014; 10: 469-482.
[9] Restrepo-Jimenez P, Rodriguez Y, Gonzalez P, Chang C, Gershwin ME and Anaya JM. The immunotherapy of Guillain-Barre syndrome. Expert Opin Biol Ther 2018; 18: 619-631.
[10] Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, Ferreira MLB, Cornblath DR, van

Doorn PA, Dourado ME, Hughes RAC, Islam B, Kusunoki S, Pardo CA, Reisin R, Sejvar JJ, Shahrizaila N, Soares C, Umapathi T, Wang Y, Yiu EM, Willison HJ and Jacobs BC. Diagnosis and management of Guillain-Barre syndrome in ten steps. Nat Rev Neurol 2019; 15: 671-683.

[11] Barohn RJ, Kissel JT, Warmolts JR and Mendell JR. Chronic inflammatory demyelinating polyradiculoneuropathy. Clinical characteristics, course, and recommendations for diagnostic criteria. Arch Neurol 1989; 46: 878-884.

[12] Fan Z, Liu BY, Zhang YL, Li M and Lu T. The effectiveness and safety of acupuncture therapy for Guillain-Barre syndrome: a systematic review and meta-analysis protocol. Medicine (Baltimore) 2020; 99: e18619.

[13] Basta I, Bozovic I, Berisavac I, Stojiljkovic-Tamas O, Rajic SL, Dominovic-Kovacevic A, Stojanov A, Djordjevic G, Jovanovic D and Peric S. Recurrent Guillain-Barre syndrome - case series. Neurol India 2019; 67: 1536-1538.

[14] Osman C, Jennings R, El-Ghariani K and Pinto A. Plasma exchange in neurological disease. Pract Neurol 2020; 20: 92-99.

[15] Pham HP and Schwartz J. Therapeutic plasma exchange in Guillain-Barre syndrome and chronic inflammatory demyelinating polyradiculoneuropathy. Presse Med 2019; 48: 338-346.

[16] Doets AY, Jacobs BC and van Doorn PA. Advances in management of Guillain-Barré syndrome. Curr Opin Neurol 2018; 31: 541-550.

[17] Verboon C, van Doorn PA and Jacobs BC. Treatment dilemmas in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 2017; 88: 346-352.

[18] Wakerley BR, Uncini A and Yuki N; GBS Classification Group; GBS Classification Group. Guillain-Barré and miller fisher syndromes--new diagnostic classification. Nat Rev Neurol 2014; 10: 537-544.

[19] Doets AY, Hughes RA, Brassington R, Hadden RD and Pritchard J. Pharmacological treatment other than corticosteroids, intravenous immunoglobulin and plasma exchange for Guillain-Barré syndrome. Cochrane Database Syst Rev 2020; 1: CD008630.

[20] Kesici S, Tanyildiz M, Yetimakman F and Bayrakci B. A novel treatment strategy for severe Guillain-Barre syndrome: zipper method. J Child Neurol 2019; 34: 277-283.

[21] Huang P, Xu M and He XY. Correlations between microRNA-146a and immunoglobulin and inflammatory factors in Guillain-Barré syndrome. J Int Med Res 2020; 48: 30006052-0904842.

[22] Chang KH, Lyu RK, Ro YS, Chen YC, Ro LS, Chang HS, Huang CC, Liao MF, Wu YR, Kuo HC, Chu CC and Chen CM. Increased serum concentrations of transforming growth factor-β1 (TGF-β1) in patients with Guillain-Barré syndrome. Clin Chim Acta 2016; 461: 8-13.

[23] Zhao Y, Zhu RX, Tian DD and Liu X. Genetic polymorphisms in Guillain-Barre syndrome: a field synopsis and systematic meta-analysis. Autoimmun Rev 2020; 19: 102665.

[24] Morris G, Fernandes BS, Puri BK, Walker AJ, Carvalho AF and Berk M. Leaky brain in neurological and psychiatric disorders: drivers and consequences. Aust N Z J Psychiatry 2018; 52: 924-948.

[25] Drechsel DA, Estevez AG, Barbeito L and Beckman JS. Nitric oxide-mediated oxidative damage and the progressive demise of motor neurons in ALS. Neurotox Res 2012; 22: 251-264.

[26] Shang P, Zhu MQ, Baker M, Feng JC, Zhou CK and Zhang HL. Mechanical ventilation in Guillain-Barre syndrome. Expert Rev Clin Immunol 2020; 16: 1053-1064.

[27] Yuki N and Hartung HP. Guillain-Barré syndrome. N Engl J Med 2012; 366: 2294-2304.

[28] Van Doorn PA. Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). Presse Med 2013; 42: e193-201.