BOLETÍN
DE MALARIOLOGÍA
Y SALUD AMBIENTAL
2019, Vol. 59 (3): 50-55

Efecto de la preparación de espatolobus de la medicina china sobre la inmunoglobulina del líquido cefalorraquídeo en pacientes con esclerosis múltiple

Effect of Chinese Medicine Spatholobus Preparation on Cerebrospinal Fluid Immunoglobulin in Patients with Multiple Sclerosis

Rong Zhang[1,*], Na Xue[2]
[1]*Department of Neurology, Lanzhou Petrochemical Hospital, Lanzhou, 730050, China*
[2]*Preclinical Medical College, Gansu University of Chinese Medicine, Lanzhou, 730101, China*

**Correspondence author: Rong Zhang, Email: 89227203@qq.com*

Resumen
El diagnóstico de esclerosis múltiple es muy difícil. No se pueden diagnosticar las imágenes tempranas y el examen de rutina de la lesión, y se produce el aumento de la inmunoglobulina IgG en el líquido cefalorraquídeo del paciente. La electroforesis de proteínas del líquido cefalorraquídeo IgG forma una zona oligoclonal típica, que es importante para el diagnóstico precoz. Base. Este artículo analiza el efecto de la preparación de espatolobus de la medicina china sobre la inmunoglobulina del líquido cefalorraquídeo en pacientes con esclerosis múltiple. Observamos la eficacia clínica integral y los síntomas clínicos, signos neurológicos y puntajes de disfunción neurológica antes y después del tratamiento y potenciales evocados, resonancia magnética, inmunoglobulina G del líquido cefalorraquídeo y recurrencia y otros indicadores. Los resultados mostraron que en el grupo de tratamiento, la tasa efectiva fue del 85%, y la diferencia entre los dos grupos fue muy significativa (p <0,01). Después del tratamiento, disminuyeron los síntomas clínicos, los signos neurológicos, las puntuaciones de EDSS y las puntuaciones totales de los dos grupos. En comparación con antes del tratamiento, la diferencia fue significativa o muy significativa (p <0.01). Conclusión: La preparación de espatolobus de la medicina tradicional china para el tratamiento de la esclerosis múltiple no solo puede mejorar eficazmente los síntomas y signos clínicos, restaurar la función nerviosa, sino que también puede tener diferentes grados de mejora y recuperación de potenciales evocados, líquido cefalorraquídeo y bandas y exámenes oligoclonales, y puede También reducir el número de recurrencias reduce la tasa de recurrencia.

Palabras clave: esclerosis múltiple; preparación de spatholobus medicina tradicional china; inmunoglobulina; función immune

Abstract
The diagnosis of multiple sclerosis is very difficult. The early imaging and routine examination of the lesion cannot be diagnosed, and the increase of immunoglobulin IgG in the cerebrospinal fluid of the patient occurs. The cerebrospinal fluid protein electrophoresis IgG forms a typical oligoclonal zone, which is important for early diagnosis. Basis. This paper analyzes the effect of Chinese medicine spatholobus preparation on cerebrospinal fluid immunoglobulin in patients with multiple sclerosis. We observed the clinical comprehensive efficacy and clinical symptoms, neurological signs and neurological dysfunction scores before and after treatment and evoked potentials, magnetic resonance imaging, cerebrospinal fluid immunoglobulin G and recurrence and other indicators. The results showed that in the treatment group, the effective rate was 85%, and the difference between the two groups was very significant (p<0.01). After treatment, the clinical symptoms, neurological signs, EDSS scores and total scores of the two groups were decreased. Compared with before treatment, the difference was significant or very significant (p<0.01). Conclusion: Traditional Chinese medicine spatholobus preparation for the treatment of multiple sclerosis can not only effectively improve clinical symptoms and signs, restore nerve function, but also have different degrees of improvement and recovery of evoked potentials, cerebrospinal fluid and oligoclonal bands and examinations, and can also reduce the number of recurrences reduces the recurrence rate.

Key words: Multiple sclerosis; traditional Chinese medicine spatholobus preparation; immunoglobulin; immune function

1. Introduction

Cerebrospinal fluid analysis is of great importance in the diagnosis and treatment of multiple sclerosis. Cerebrospinal fluid analysis (CSF) should be routinely performed in patients with multiple sclerosis (MS) who present the first clinical event suggestive of MS[1]. The diagnosis of relapsing-remitting multiple sclerosis no longer requires mandatory CSF analysis as long as the MRI diagnostic criteria are met. However, care should be taken when diagnosing patients with negative MRI or without CSF analysis, as CSF testing is helpful in eliminating other causes[2-4]. The detection of IgG oligoclonal bands in CSF has potential prognostic value and is useful for clinical decision making. In addition, CSF analysis is also very important for the study of the pathogenesis of MS. CSF analysis can be found in the pathophysiology and evidence of neurodegeneration of inflammation in MS patients[5]. New CSF biomarkers, although not yet validated, have been used for MS diagnosis, disease activity confirmation, prognosis, and treatment response analysis, and the number of biomarkers may continue to increase with the development of modern detection techniques[5-8]. Cerebrospinal fluid (CSF) analysis can be used to rule out other diseases during the differential diagnosis of multiple sclerosis (MS). Oligoclonal IgG band detection and elevated CXCL13 levels in CSF can be used to prognose and predict disease recurrence in patients with clinically isolated syndrome: CSF analysis helps to elucidate the inflammatory and neurodegenerative mechanisms in MS patients: already in CSF A variety of novel candidate markers for MS have been discovered; however, validation must be performed in large-scale patient populations. Standard methods for identifying and quantifying potential MS markers in CSF are needed to compare between different studies and patient populations[9].

Multiple sclerosis (MS) is the most common type of central nervous system demyelinating disease. The acute active phase of the disease has multiple inflammatory demyelinating plaques in the central nervous system. Older lesions form calcified plaques due to glial fibrosis[10-12]. They are characterized by multiple lesions, remission, and recurrence, and occur in the optic nerve, spinal cord, and brain. Dry, mostly in young and middle-aged, women are more common than men[13]. Multiple sclerosis lesions are more diffuse, so the symptoms and signs are more complicated, such as neuritis, retrobulbar optic neuritis, ophthalmoplegia, limb paralysis, pyramidal tract signs and mental symptoms. Ataxia, limb tremor, and nystagmus occur when the lesion is located in the cerebellum[14]. The lesion invades the medial longitudinal bundle and presents a variety of patterns of involuntary ocular myoclonus with persistent and irregular eyeballs. Such as vertigo and vertical nystagmus, which are difficult to explain, especially in young patients, acute vertigo and vertical nystagmus should continue to be thought of after vertigo.

2. Materials and Methods

2.1 General Information

A total of 90 cases were selected, all of which were hospitalized from June 2017 to December 2018. They were randomly divided into 2 groups according to the order of treatment. 60 patients in the treatment group, 19 males and 41 females: aged 1756 years, mean (32.1 ± 23.9) years; duration of 5~231 months, mean (61.5 ± 62.1) months: recurrence 1-6 times, average (1.53 ± 0.64)); classification: 42 cases of relapsing remission, 6 cases of secondary progression, 5 cases of primary progression, 2 cases of progressive recurrence, 3 cases of benign, and 2 cases of malignancy. 30 patients in the control group, 9 males and 21 females: aged 17-54 years, mean (31.6 ± 23.1) years; duration of disease 6-228 months, mean (60.5 ± 61.6) months; recurrence 1-6 times, average (1.53 ± 0.64) times; classification: 21 cases of relapsing remission, 3 cases of secondary progression, 2 cases of primary progression, 1 case of progressive recurrence, 2 cases of benign, and 1 case of malignancy. The general data of the two groups were statistically processed, and the differences were not significant (P>0.05), which was comparable.

2.2 Method

Oral Chinese medicine spatholobus sinensis preparation (composed of ginseng, velvet, turtle shell, dodder, sage, scorpion, scorpion, spatholobus, etc., containing 0.4g/grain), 8 capsules per day, 3 per day Times. Among them, 48 patients were still taking oral prednisone 5~20mg/d at the beginning of treatment. After taking the disease stable, prednisone was gradually reduced to 2.0. The control group received oral prednisone 1mg·kg/d, every 7 days after January. After the reduction of 5mg, after 15mg, the dosage is maintained. Both groups were treated with 1 month as a course of treatment, and the therapeutic effect was observed after 3 courses of treatment.

Observed indicators: ①Clinical efficacy; ②Clinical symptoms, neurological signs and neurological dysfunction score before and after treatment. Clinical symptoms (including limb weakness, visual impairment, constipation, sensory disturbance, unstable walking, limb pain, numbness, convulsions, dizziness, deafness, tinnitus, chills, cold limbs, weak waist, dizziness, fatigue, laziness, etc.), neurological signs (including visual conditions, motor function, sensory function, intelligence, etc.) according to normal, mild abnormalities, moderate abnormalities, severe abnormalities, respectively, 0 to 3 points, 1 examination before and after treatment; neurological dysfunction score Kurtzke's EDSS scoring criteria score six neurological functions in

the patient's cone, cerebellum, brainstem, sensory, bladder and rectum, and brain: ③Evoked potentials: including visual evoked potential (VEP), brainstem evoked potential (BAEP), body Evoked potential (SEP), etc.; ④Before and after treatment by magnetic resonance imaging (MRI); 5 before and after treatment of cerebrospinal fluid immunoglobulin G (lgG) and oligoclonal band examination; 6 follow-up 2-2.5 years recurrence.

2.3 Statistical Method

Statistical analysis was performed using SAS statistical software. The paired t-test was used for the scores before and after treatment.

3. Result

Efficacy criteria were evaluated by nimodipine: (integration after treatment before treatment) / pre-treatment score × 100%. Complete remission ≥85%, markedly effective 50%~84%, effective 20%~49%, invalid <20%.

Treatment results: The clinical efficacy of the two groups is shown in Table 1. The total effective rate was 85.00% in the treatment group and 63.33% in the control group. In the 2 groups, the difference was very significant (P<0.01) (Note: there was no complete remission in the statistical efficacy time).

Table 1: Comparison of Clinical Efficacy of The Group

Group	n	Significant effect	Effective	Invalid	Total effective rate (%)
Treatment group	60	22 (36.67)	29 (48.33)	9 (15.00)	85
Control group	30	4 (13.33)	15 (50.00)	11 (36.67）	63

The clinical symptoms, neurological signs and EDSS scores of the two groups before and after treatment are shown in Table 2. After treatment, the clinical symptoms, neurological signs, EDSS scores and total scores of the two groups were decreased. Compared with before treatment, the difference was significant or very significant (P<0.05, P<0.01). After the two groups of treatment, the difference was very significant (P<0.01).

Table 2: Comparison of Clinical Symptoms, Neurological Signs and EDSS Scores before and after Treatment

Group	n		Clinical symptoms	Neurological signs	EDSS	Total Integral
Treatment group	60	Before treatment	18.98	9.08	6.37	34.4
		After treatment	10.27	6.75	4.38	21.4
Control group	30	Before treatment	17.90	9.21	6.29	33.4
		After treatment	14.06	7.98	5.24	27.28

The evoked potentials of the two groups before and after treatment were compared in the treatment group with 49 cases of abnormal VEP, BAEP and SEP before treatment. After treatment, they returned to normal in 2 cases, improved in 43 cases, and aggravated in 2 cases. No other changes were observed. In the control group, 25 patients with abnormal VEP, BAEP and SEP before treatment were treated, 15 cases were improved after treatment, 2 cases were aggravated, and other changes were not observed. The difference between the two groups was very significant (P<0.01). Before and after treatment, the MRI examination of the treatment group showed that there were brain and/or spinal cord abnormalities in the treatment group. Among them, 48 cases were multi-focal, and the lesions were spotted, patchy or oval, and the size was not, more common in the periventricular, cerebral cortical white matter and brain stem, cerebellum, cervical spinal cord, chest pulp, MRI examination after treatment showed a reduction in the number of lesions or a reduction in the extent of 37 cases. The MRI examination before treatment in the control group was similar to that in the treatment group. MRI examination showed that the number of lesions decreased or the extent of the lesion was reduced in 13 cases. The difference between the two groups was significant (P<0.05).

The results of biochemical indexes in cerebrospinal fluid of the two groups were compared with those of the control group. The levels of immunoglobulin and CRP in cerebrospinal fluid of the patients in the observation group were significantly higher than those in the control group (P < 0.05), and the difference was statistically significant (P < 0.05), as shown in Table 3.

Comparison of biochemical indexes of brain barren fluid between patients with different diseases and bacterial suppuration

Table 3: Biochemical Indices of Cerebrospinal Fluid in Two Groups of Subjects

Index	Observation group	Control group	T	P
IgA	75.1±9.1	8.3±5.7	41.246	<0.05
IgM	59.5±11.2	3.1±1.4	28.954	<0.05
IgG	224.6±24.6	36.7±9.3	51.352	<0.05
CRP	4.9±1.3	0.6±0.2	21.375	<0.05

Compared with patients with meningitis and viral meningitis, the levels of IgA and IgM in cerebrospinal fluid of patients with tuberculous meningitis were significantly lower ($P < 0.05$). Compared with patients with bacterial suppurative meningitis and tuberculous meningitis, the level of 1gG in cerebrospinal fluid of patients with viral meningitis was significantly higher ($P < 0.05$). In the level of CRP in cerebrospinal fluid, the ratio of three infective meningitis patients was higher ($P < 0.05$). The difference was statistically significant. See Table 4.

Table 4: Results of Biochemical Indicators of Different Diseases in The Present Observation Group

Index	Bacterial suppurative meningitis	Viral meningitis	Tuberculous meningitis	F	p
IgA	53.5±9.6	86.7±23.7	9.6±4.2	113.42	<0.05
lgM	69.1±11.5	26.1±5.4	6.7±3.2	29.86	<0.05
lgG	124.6±34.6	236.7±139.3	25.6±12.l	72.41	<0.05
CRP	7.2±2.3	1.6±0.3	0.5±0.2	16.79	<0.05

4. Discussion

The author believes that the pathogenesis of this disease is deficiency of kidney essence, insufficiency of medullary sea, emptiness of governor veins and disgrace of collaterals. Modern medicine considers this disease as an autoimmune disease. Pharmacological studies on the medicines used in Chinese herbal medicine Jixuetong have an effect on immune function. For example, ginseng can enhance immune function and increase white blood cells. Among them, ginsenoside can promote serum production and lymphocyte transformation in mice. The extract can obviously enhance the phagocytic function of peritoneal macrophages, increase the content of serum hemolysin antibody and agglutinin titer in mice.

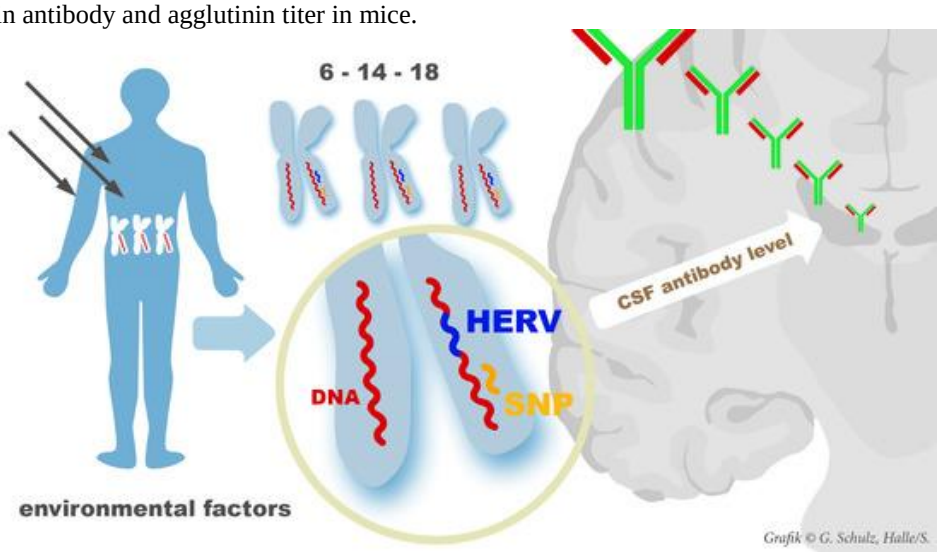

Figure 1. Cerebrospinal Fluid Immunoglobulin G

The main source of cerebrospinal fluid immunoglobulin: (1) Local synthesis, activation of immune cells produced by central nervous system infection. (2) Changes in the blood-brain barrier, through the increase in capillary permeability of the brain, so that the blood's immunoglobulin into the cerebrospinal fluid. Due to

differences in assay methods, immunoglobulins in normal cerebrospinal fluid are slightly different. Generally, IgG, IgA, and IgM can be measured, and the other two are very small[15-16]. There are many studies on the IgG subclass of cerebrospinal fluid. Pediatric haemophilic influenza bacillus meningitis, pediatric pneumococcal meningitis, otogenic meningitis, acute disseminated encephalomyelitis, purulent meningitis, traumatic meningitis, recurrent aseptic meningitis, virus Meningitis, alcoholic brain atrophy, meningococcalemia, etc[17].

Inspection process (1) The patient is lying on the hard bed, the back is perpendicular to the tabletop, the head is bent as far as possible to the chest, the knees are tightly attached to the abdomen, so that the trunk is as arched as possible; or the assistant is holding the hand opposite the surgeon. The patient's head, the other hand to pull the lower limbs of the armpits and hold tightly, so that the spine as much as possible to kyphosis to widen the intervertebral space, easy to enter the needle. (2) Determine the puncture point, usually the junction point of the highest point of the bilateral iliac spine and the posterior midline is the puncture point, which is equivalent to the 3-4 lumbar spinous process gap, sometimes in the previous or next the lumbar intervertebral space is performed. (3) After routine disinfection of the skin, wear sterile gloves, cover the hole towel, and use 2% lidocaine to do local anesthesia from the skin to the interspinous ligament. (4) The surgeon fixes the puncture point skin with his left hand, and the right-hand puncture needle is inserted slowly in the direction of the vertical back and the needle tip slightly obliquely to the head. The depth of the adult needle is about 4-6 cm, and the child is about 2-4 cm. When the needle passes through the ligament and the dura mater, there is a sudden loss of resistance. At this point, the needle core can be slowly withdrawn (to prevent the cerebrospinal fluid from flowing out quickly, causing cerebral palsy), and the cerebrospinal fluid can be seen to flow out. (5) Connect the pressure measuring tube to measure the pressure before draining. The cerebrospinal fluid pressure in the normal lateral position is 70-180 mmH2O (0.098 Kpa = 10 mm H2O) or 40-50 d/min. If you continue to do the queckstedt test, you can see if there is any obstruction in the subarachnoid space. That is, after the initial pressure is measured, the assistant first compresses one side of the carotid artery for about 10 s, then presses the other side, and finally presses both sides of the carotid artery. When the carotid artery is compressed at normal time, the pressure of the cerebrospinal fluid immediately increases by about one time, and after 10-20 s of compression, it rapidly drops to the original level, which is called negative in the obstruction test, indicating that the subarachnoid space is unobstructed; if the carotid artery is compressed, it cannot When the pressure of the cerebrospinal fluid is raised, the obstruction test is positive, indicating that the subarachnoid space is completely blocked. If it rises slowly after applying pressure, it will slowly fall after relaxation, indicating incomplete obstruction. However, those with increased intracranial pressure are forbidden to do this test. (6) Remove the pressure measuring tube and collect 2-5ml of cerebrospinal fluid for examination; if it is needed for cultivation, use sterile tube to keep the specimen. (7) After the operation, insert the needle core and pull out the puncture needle together, cover the sterile gauze, and fix it with tape. (8) Go to the pillow for 4-6 hours, so as not to cause postoperative low intracranial pressure headache.

5. Conclusion

There are four cases of protein immunofixation electrophoresis and color development: no clonal bands appear in the patient's cerebrospinal fluid and serum samples, indicating that there is no relevant immune disease in the central nervous system: oligoclonal bands appear in the patient's serum. The absence of cerebrospinal fluid indicates that the blood-brain barrier has not been damaged; the same band appears in the cerebrospinal fluid and serum specimens of the patient, indicating that the blood-brain barrier is damaged; a strong band and a monoclonal region that are present in the cerebrospinal fluid but not present in the serum A band of additional, or weak, monoclonal bands that indicate endogenously synthesized immunoglobulin lgG, showing a related immune disorder in the central nervous system; the latter two are important for reflecting central nervous system disorders The mark can be judged as a positive result.

References

[1] Orlandi RR, Kingdom TT, Hwang PH, Smith TL, Alt JA, Baroody FM, Batra PS, Bernal-Sprekelsen M, Bhattacharyya N, Chandra RK, et al. International Consensus Statement on Allergy and Rhinology: Rhinosinusitis. Int Forum Allergy Rhinol. 2016;6(Suppl 1):S22–209.

[2] Hopkins C, Slack R, Lund V, Brown P, Copley L, Browne J. Long-term outcomes from the English national comparative audit of surgery for nasal polyposis and chronic rhinosinusitis. Laryngoscope. 2009;119(12):2459–65.

[3] Varvyanskaya A, Lopatin A (2014). Efficacy of long-term low-dose macrolide therapy in preventing early recurrence of nasal polyps after endoscopic sinus surgery. Int Forum Allergy Rhinol 4(7):533–541.

[4] Videler WJ, Badia L, Harvey RJ, Gane S, Georgalas C, van der Meulen FW et al (2011). Lack of efficacy of long term, low-dose azithromycin in chronic rhinosinusitis: randomized controlled trial. Allergy 66:1457–1468.

[5] Jackson DJ, Johnston SL (2010) The role of viruses in acute exacerbations of asthma. J Allergy Clin Immunol 126:1178–1187

[6] Minor TE, Baker JW, Dick EC, DeMeo A. (1974) Greater frequency of viral respiratory infections in asthmatic children as compared with their non-asthmatic siblings. J Pediatr 85:472–477.
[7] Seemann T. Prokka: rapid prokaryotic genome annotation. Bioinformatics. 2014;30(14):2068–9.
[8] Ji Y., Ying H., Tran J., Dews P. (2013). A method for mining infrequent causal associations and its application in finding adverse drug reaction signal pairs. IEEE Transactions on Knowledge and Data Engineering, 25 (4), pp. 721-733.
[9] Koh H., Tan G. (2011). Data mining applications in healthcare. Journal of Healthcare Information Management, 19 (2), pp. 65-69.
[10] Nahar J., Imam T., Tickle K. (2013). Association rule mining to detect factors which contribute to heart disease in males and females. Expert Systems with Applications, 40 (4), pp. 1086-1093.
[11] Thelwall M., Buckley K., Paltoglou G. (2012). Sentiment strength detection for the social web. Journal of the Association for Information Science and Technology, 63, pp. 163-173.
[12] Aziz H, Moustafa G, Abbas S, Derayea S, Abuorahma G (2017). New norfloxacin/nitric oxide donor hybrids: Synthesis and nitric oxide release measurement using a modified Griess colorimetric method. Eur J Chem 8:119–124.
[13] Mukai A, Fukai T, Hoshino Y, Yazawa K, Harada K, Mikami Y (2009). Nocardithiocin, a novel thiopeptide antibiotic, produced by pathogenic Nocardia pseudobrasiliensis IFM 0757. J Antibiot 62:613–619
[14] Faidallah HM, Rostom S (2013). Synthesis, in vitro antitumor evaluation and DNA-binding study of novel tetrahydroquinolines and some derived tricyclic and tetracyclic ring systems. Eur J Med Chem 63:133–143.
[15] Bhat UG, Zipfel PA, Tyler DS, Gartel AL (2008). Novel anticancer compounds induce apoptosis in melanoma cells. Cell Cycle 7:1851–1855.
[16] Vilian AE, Rajkumar M, Chen S-M (2014). In situ electrochemical synthesis of highly loaded zirconium nanoparticles decorated reduced graphene oxide for the selective determination of dopamine and paracetamol in presence of ascorbic acid. Coll Surf B Biointerfaces ,115:295–301.
[17] Orain D, Ofner S, Koller M, Carcache DA, Froestl W, Allgeier H, Rasetti V, Nozulak J, Mattes H, Soldermann N, Floersheim P, Desrayaud S, Kallen J, Lingenhoehl K, Urwyler S (2012) .6-Amino quinazolinedione sulfonamides as orally active competitive AMPA receptor antagonists. Bioorg Med Chem Lett 22:996–999.