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Original article

# Therapeutic effect of autologous bone marrow stem cell mobilization combined with anti-infective therapy on moyamoya disease

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## ABSTRACT

**Objective:** The purpose of this study is to explore the therapeutic effect of autologous bone marrow stem cell (ABMSC) mobilization combined anti-infection therapy on patients with moyamoya disease (MMD), and to provide reference for the clinical treatment of MMD and cerebrovascular disease.

**Methods:** 54 adult patients with MMD diagnosed in Henan Provincial People's Hospital from March 2017 to March 2019 were chosen as research objects. All patients were randomly divided into study group (SG) and control group (CG), with 27 patients in each group. Patients in both groups received conventional drug treatment after diagnosis of MMD, and received dura turnover of brain - temporal muscle - superficial temporal artery application surgery during indirect vascular reconstruction. On the basis of surgical treatment, patients in the SG were given ABMSC mobilization combined with low-dose dexamethasone for anti-inflammatory and anti-infection treatment. ABMSCs were mobilized by recombinant human granulocyte colony stimulating factor (rhG-CSF) and recombinant human granulocyte - macrophage colony stimulating factor (rhoM-CSF). The therapeutic effects of the patients were evaluated BF, one month after treatment (AF), three months AF, and six months AF. The number of hematopoietic stem cells (HpCs) and inflammatory indicators were compared between the two groups before and 4 weeks AF.

**Results:** Firstly, the Barthel index of patients in the two groups showed a gradual increase trend at the 3rd and 6th months AF, and the ascensional range in the research group was higher than that in the CG ( $P < 0.05$ ). Secondly, at the 3rd and 6th month AF, national institute of health stroke scale (NIHSS) scores of patients in the CG were lower than those before treatment (BF), and there was an important change in NIHSS scores between the two groups at the same period ( $P < 0.05$ ). Thirdly, after 1 month of treatment and 3 months of treatment, Chinese stroke scale (CSS) scores of patients in both groups decreased obviously compared with those BF, and the SG was lower than the CG, with statistical changes ( $P < 0.05$ ). Fourthly, after 4 weeks of treatment, the hematopoietic stem cell counts in both groups were higher than those BF, and the hematopoietic stem cell counts in the SG were obviously higher than those in the CG ( $P < 0.05$ ). All three inflammatory indicators were improved compared with those BF, and the SG was better than the CG ( $P < 0.05$ ).

**Conclusion:** Autogenous bone marrow stem cell mobilization combined with dexamethasone anti-inflammation and anti-infection treatment after revascularization in patients with MMD can accelerate the recovery of nerve function and promote the formation of new blood vessels. At the same time, it can reduce inflammation and improve patients' quality of life, which is worthy of clinical reference.

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## 1. Introduction

At present, cerebrovascular diseases have become one of the three major diseases that endanger human health, with the annual death toll due to cerebrovascular diseases exceeding 5 million (Milam et al., 2019). MMD is a cerebrovascular disease. The main feature is that the bilateral internal carotid artery (ICA) terminal middle cerebral artery (MCA) and its branch vessels progressively appear stenosis or even complete obstruction, and may be accom-

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panied by the formation of abnormal vascular network of the skull base, which ultimately leads to stroke (Kort et al., 2016). In patients with MMD, a large number of dense small vascular shadow can be found during the whole cerebral angiography, and its general shape is similar to smoke, so it is called MMD. MMD occurs most frequently in east Asia, especially in Japan, with obvious regional characteristics (Nam et al., 2015). MMD mainly occurs in children aged 5–10 years and adults aged 45–50 years, and can be subdivided into infarction type, hemorrhagic type, transient ischemic attack (TIA) type, epilepsy type and so on. For adult patients with MMD, hemorrhagic type is the main one, which is mainly manifested as intraventricular hemorrhage and subarachnoid hemorrhage. Followed by ischemic MMD, cerebral infarction often occurs, patients with headache, dementia and other symptoms are more obvious, which has a great impact on their health and quality of life (Hyakuna et al., 2015; Morin et al., 2017; Abraham et al., 2017).

The main pathological changes of MMD are vascular stenosis caused by irregular thickening of vascular intima, and the changes of affected vessels can be clearly observed by magnetic resonance imaging and high-resolution imaging technology (Sabapathy and Kumar, 2016). Studies have shown that the proliferation of vascular endothelial smooth muscle is related to the mutation of ACTA2 gene, which is the key cause of vascular occlusion in MMD. About 10% of patients with MMD have familial inheritance, and identified genetic inheritance sites include 3p24-26, 6q25, 8q23, 17q25, etc. In addition, among the MMD patients in east Asia, the gene in the 17q25-ter region has been identified as the most susceptible gene (Fitzhugh et al., 2017; Allen et al., 2017; Alonso et al., 2019). At present, the main treatment of MMD is surgical treatment, which aims to improve blood supply of brain tissue, restore normal hemodynamic state and reduce the occurrence of stroke. For patients with different types of MMD, it is of great significance to find the best surgical method (Nabetani et al., 2018; Ayoubi et al., 2017).

BMSCs have the potential of multi-layer differentiation, and can be differentiated into neuron cells, glia cells and vascular endothelial cells under certain circumstances, which play an important role in restoring damaged nerves and accelerating the reconstruction of damaged functions. It also finds that the application of ABMSCs mobilization in the treatment of ischemic cerebrovascular disease also has certain effects. Therefore, anti-inflammatory and anti-infective treatment in cerebrovascular diseases is also an important treatment direction. In conclusion, although there are many studies on the mobilization of ABMSCs for the treatment of moyamoya disease, relevant reports on the combination of ABMSCs mobilization and anti-infection treatment of moyamoya disease have not been found. Based on previous studies and the above theoretical basis, in this study, the therapeutic effect of ABMSC mobilization combined anti-infection therapy on patients with MMD was explored, providing reference basis for clinical treatment of MMD and cerebrovascular disease.

## 2. Materials and methods

### 2.1. Surgical treatment methods of MMD

The imaging manifestations of typical MMD are shown in Fig. 1. Fig. 1 shows anteroposterior angiography of the right internal carotid artery (Suffee et al., 2017). It can be observed from the figure that the end of the internal carotid artery is occluded and a large number of smoke-like blood vessels are formed. At present, the main treatment of MMD is surgical treatment, which aims to improve blood supply of brain tissue, restore normal hemodynamic state, and reduce the occurrence of stroke. For patients with

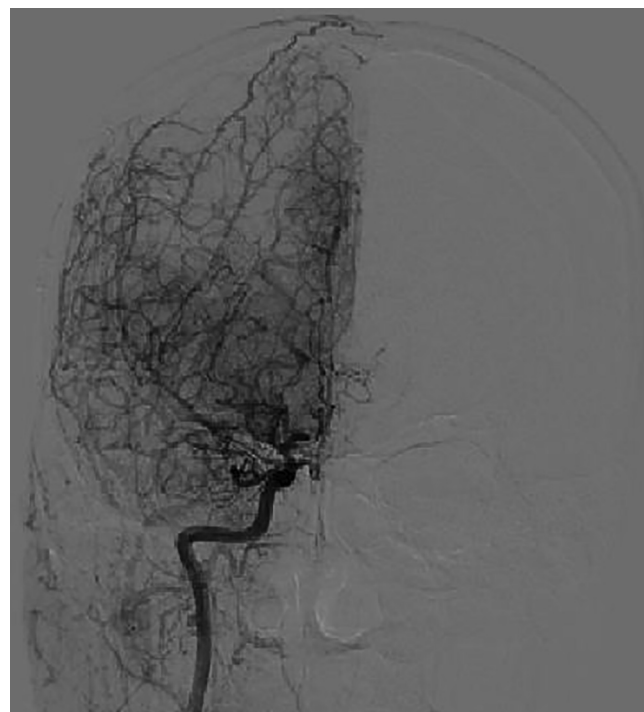


Fig. 1. Imaging manifestations of typical MMD.

different types of MMD, it is of great significance to find the best surgical method. The main surgical methods are vascular reconstruction, which can be divided into three types: direct vascular reconstruction, indirect vascular reconstruction and combined vascular reconstruction. Among them, superficial temporal artery (STA)-MCA anastomosis in direct vascular reconstruction is the most commonly used surgical method in clinic. Secondly, STA-anterior cerebral artery (ACA) anastomosis and STA cerebral artery (PCA) anastomosis are more common. Indirect vascular reconstruction for MMD can be divided into encephalo-muscle-synangiosis (EMS), encephalo-duro-arterio-myo-synangiosis (EDAS) and encephalo-dura-muscle-synangiosis (EDMS). In the treatment of MMD with combined revascularization, both direct and indirect revascularization procedures are used.

For MMD patients with ischemic disease, all the above three surgical methods can improve cerebral perfusion and relieve the symptoms of cerebral ischemia. Direct revascularization can quickly establish a collateral circulation, which is effective in the treatment of adult ischemic MMD. However, it is worth noting that this kind of direct vascular reconstruction is difficult to anastomosis, which is likely to cause anastomotic fistula, hyperperfusion syndrome and other complications, so the technical requirements for doctors are relatively high. Indirect revascularization is relatively easy, and the acreage of improving the blood supply area is relatively large. However, it usually takes more than three months to take effect, and some patients can't form effective collateral circulation AF. The method of combined revascularization has obvious advantages over the first two surgical methods. It can not only improve the ischemic condition of the brain in a short time, but also increase the blood supply artery of the brain tissue to the largest extent, and the risk of postoperative complications is also relatively low.

### 2.2. Relationship between serum inflammatory factor levels and cerebral artery stenosis

Numerous studies have confirmed that inflammation in the body increases the instability of cerebrovascular plaques, thereby

increasing the risk of acute ischemic stroke. Transient ischemic attack (TIA) is a transient focal brain or retinal dysfunction caused by intracranial vascular disease. The duration of clinical symptoms is generally about 15 min, no neurological defects will be left, and no lesions will be found through CT, MRI and other imaging examinations. In patients with ischemic cerebral artery stenosis, elevated levels of inflammatory cytokines, including IL-6 and hsCRP, can be observed in peripheral blood. Furthermore, levels of immune cell active molecules such as IFN- $\gamma$ , TNF- $\alpha$ , etc. are also elevated. Therefore, the occurrence of ischemic cerebral artery stenosis has a certain correlation with inflammatory factors in peripheral blood, and the occurrence and development of ischemic cerebral artery stenosis in patients with ischemic cerebrovascular disease can be directly affected by immune inflammatory reaction (Ballas, 2018).

A large number of studies have confirmed that immune activation and immune damage persist throughout the ischemic stroke. The occurrence of cerebral ischemia and hypoxia will cause a series of complex inflammatory immune responses, which are related to a variety of immune cells and immune factors. Dexamethasone, as a widely used glucocorticoid, mainly has the pharmacological effects of inhibiting immunity, anti-inflammation, anti-infection and anti-oxidative free radicals, and can reduce the damage caused by cerebral ischemia and hypoxia to nerve function.

### 2.3. Subjects and groups

54 adult patients with MMD diagnosed in Henan Provincial People's Hospital from March 2017 to March 2019 were chosen as research objects. Among them, there were 22 males and 27 females. The patients were 43–51 years old with an average age of 47.4 years old. All patients were randomly divided into a SG and a CG, with 27 patients in each group. There were no statistical changes in the general baseline data between the two groups, which was comparable. This study was approved by the ethics committee of the hospital, and patients and their families were informed of the study content and signed the informed consent.

Inclusion criteria: patients diagnosed with MMD according to the criteria in the guidelines for the diagnosis and treatment of MMD (Willis Ring Spontaneous Occlusion) in Japan in 2012; patients older than 18 years old; patients who were followed up for more than 3 months after surgery; and patients with complete imaging data.

Exclusion criteria: patients with MMD or moyamoya syndrome with other systemic diseases; patients with severe cognitive impairment, hemiplegia and other neurological deficits before surgical revascularization; patients with contraindications to adrenocortical hormones; patients who received bilateral hemispheric surgery successively; and patients with liver and kidney dysfunction.

### 2.4. Therapeutic method

Patients in both groups received conventional drug treatment after diagnosis of MMD, and received dura turnover of brain - temporal muscle - superficial temporal artery application surgery during indirect vascular reconstruction. All patients underwent routine cranial CT perfusion imaging examination before the operation, which was used to evaluate the hemodynamic status of brain tissue, microcirculation, the determination of preoperative surgical indications, and the postoperative efficacy of MMD. Contrast agent was injected into the external carotid artery to clarify the blood supply of the superficial temporal artery and its branches (Zhang et al., 2016).

The steps of surgical treatment were as follows: after general anesthesia, the patient was placed in the supine position, with

the head tilted to one side and with appropriate pad height, so that the anastomotic site in the operative field was in the highest position to avoid cerebrospinal fluid outflow. During the operation, the superficial temporal artery was fully exposed, the fascia and muscles were opened layer by layer, and holes were drilled in the skull at the starting and ending points of the artery. Craniotomy was performed along the blood vessels, the dura and arachnoid under the bone flap were opened layer by layer, and the muscle flap with superficial temporal artery was applied on the brain surface. The dura mater was turned into the subarachnoid space, and the outer layer of the dura mater was in direct contact with the cerebral cortex. Intraoperative superficial temporal artery markers are shown in Fig. 2.

In the CG, only indirect revascularization was performed. On the basis of surgical treatment, the patients in the SG were given ABMSC mobilization combined with low-dose dexamethasone for anti-inflammatory and anti-infection treatment.

First, ABMSC mobilization: one week after surgery, rhG-csF and rhoM-esF were injected subcutaneously at a dose of 2.5  $\mu\text{g}/\text{kg}$ , once every 3 days. The two drugs were used alternately for four weeks. Before the application of ABMSC mobilization agent, routine review of blood routine and coagulation function was required. When the number of white blood cells was less than  $20 \times 10^9/\text{L}$ , it could continue to be used. If the number of white blood cells was greater than or equal to  $20 \times 10^9/\text{L}$ , it needed to stop taking the drug. After reviewing the blood routine every other day, whether to continue applying the drug was judged according to the results, and the liver and kidney function was examined after a course of treatment.

Second, anti-inflammatory and anti-infection treatment: 5 mg of dexamethasone (manufacturer: Ma On Shan Fengyuan Pharmaceutical Co. Ltd; approval number: State Food and Drug Administration approval number H20051748) was given intravenously once a day for 4 weeks.

### 2.5. Evaluation index and test method

Firstly, the efficacy evaluation: in this study, the therapeutic effects of the patients were evaluated BF, one-month AF, three months AF and six months AF. Basic daily activity ability (Barthel index) was used to evaluate the recovery of patients' daily activity ability. The Chinese stroke inventory (CSS) and national institutes of health stroke scale (NIHSS) were used to evaluate the degree of neurologic impairment in patients. Among them, the lowest



Fig. 2. Intraoperative superficial temporal artery markers in patients with MMD.

score of CSS is 0 and the highest score is 45. The higher the score is, the more serious the disease is. The NIHSS scores were evaluated from the level of consciousness, gaze, vision, facial paralysis, body movement and ataxia, sensation, language, attention and other aspects.

Secondly, the number of hematopoietic stem cells (HpCs) BF and 4 weeks AF was determined by flow cytometry. By detecting the proportion of HpCs in peripheral blood mononuclear cells (MNCs), the number and differentiation of mobilized ABMSCs were judged.

Thirdly, inflammation indicators: blood routine and erythrocyte sedimentation rate (ESR) values of the two groups were detected and compared before the treatment and 4 weeks AF.

## 2.6. Statistical method

SPSS 21.0 statistical software was used for statistical analysis of the obtained data. The measurement data were expressed as mean  $\pm$  standard deviation. The pairwise comparison between the data obtained was analyzed by one-way analysis of variance, and the comparison between the data was performed by chi-square test.  $P < 0.05$  was considered as statistical changes.

## 3. Results

### 3.1. Comparison of Barthel index between the two groups before and AF

BF, there was no important changes in Barthel index between the two groups ( $P > 0.05$ ). One-month AF, the Barthel indexes of the patients in the CG and the SG were  $41.12 \pm 11.86$  and  $42.03 \pm 12.93$ , respectively, which were obviously improved compared with those BF, but there were no statistical changes between the two groups ( $P > 0.05$ ). The Barthel index (Ali et al., 2019) of the two groups presented a gradually increasing trend at 3- and 6-months AF, and the ascensional range of the SG was higher than that of the CG, with statistical changes ( $P < 0.05$ ). The Barthel index results of the two groups of patients before and AF are shown in Table 1, and the Barthel index changes of the two groups of patients at different periods are shown in Fig. 3.

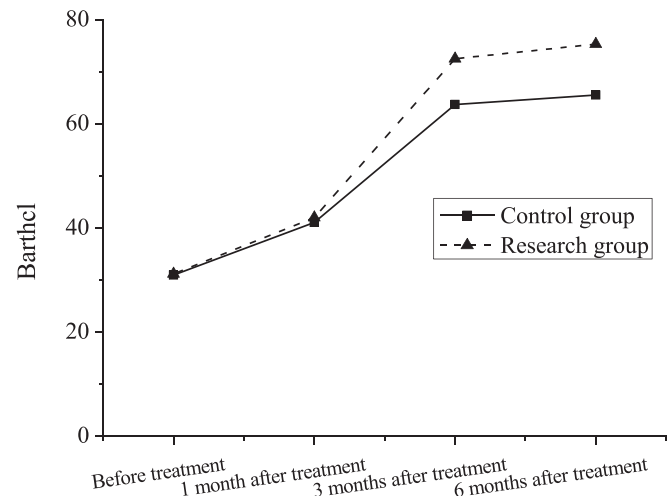
### 3.2. Comparison of NIHSS scores before and AF in both groups

BF, there was no important changes in NIHSS scores between the two groups ( $P > 0.05$ ). One-month AF, the NIHSS scores of the patients in the CG and the SG were  $14.12 \pm 2.85$  and  $13.23 \pm 2.33$ , respectively, which were obviously lower than those BF, but there were no statistical changes between the two groups ( $P > 0.05$ ). The NIHSS scores of the CG were  $13.37 \pm 2.40$  and  $12.05 \pm 1.98$  at 3 months and 6 months AF, respectively, and the NIHSS scores of patients in the SG were  $9.31 \pm 2.02$  and  $7.35 \pm 1.78$ , respectively. The changes in NIHSS scores between the two groups at the same period was statistical ( $P < 0.05$ ). NIHSS scores of patients in the two groups before and AF are shown in Table 2, and NIHSS scores of patients in the two groups at different periods are shown in Fig. 4.

**Table 1**

Barthel index results before and AF in the two groups.

| Group          | BF                | 1-month AF        | 3 months AF       | 6 months AF       |
|----------------|-------------------|-------------------|-------------------|-------------------|
| CG             | $30.98 \pm 12.96$ | $41.12 \pm 11.86$ | $63.76 \pm 12.40$ | $65.58 \pm 12.88$ |
| Research group | $31.22 \pm 13.25$ | $42.03 \pm 12.93$ | $72.58 \pm 13.22$ | $75.35 \pm 10.78$ |
| P              | $>0.05$           | $>0.05$           | $<0.05$           | $<0.05$           |



**Fig. 3.** Changes in Barthel index at different periods in the two groups.

### 3.3. Comparison of CSS scores before and AF between the two groups

BF, the CSS scores of the CG and the SG were  $27.46 \pm 0.96$  and  $27.05 \pm 0.87$ , respectively, and there were no important changes between the two groups ( $P > 0.05$ ). One-month AF, the CSS scores of patients in the CG and the SG were  $21.24 \pm 0.76$  and  $18.73 \pm 0.62$ , respectively, which were obviously lower than those BF, and the changes between the two groups were statistical ( $P < 0.05$ ). After 3 months of treatment, CSS scores of patients in both groups were obviously decreased compared with those before the treatment and 1-month AF, and the SG was lower than the CG, with statistical changes ( $P < 0.05$ ). The results of CSS scores before and AF in the two groups of patients are shown in Table 3, and the changes of CSS scores in the two groups at different periods are shown in Fig. 5.

### 3.4. Counting results of hematopoietic stem cells BF and after 4 weeks of treatment in both groups

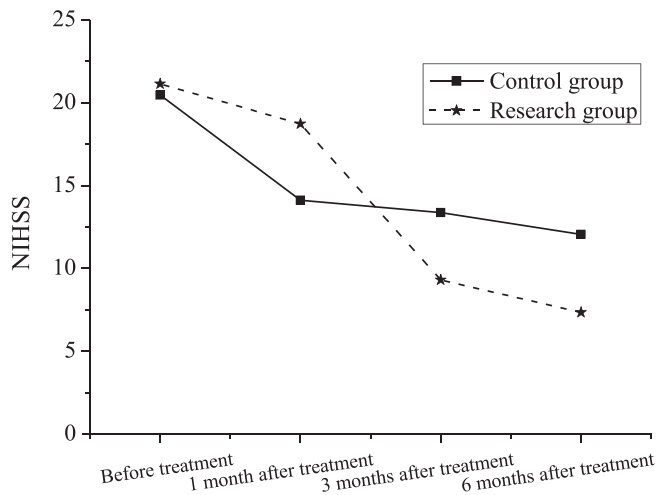
BF, the hematopoietic stem cell counts of the CG and the SG were  $0.12 \pm 0.06$  and  $0.13 \pm 0.08$ , respectively. There were no important changes between the two groups ( $P > 0.05$ ). After 4 weeks of treatment, the hematopoietic stem cell counts of the two groups were  $1.74 \pm 0.16$  and  $3.25 \pm 0.22$ , respectively, which were higher than BF, the SG was obviously higher than the CG, and the changes was statistical ( $P < 0.05$ ). The counts results of hematopoietic stem cell in the two groups BF and after 4 weeks of treatment are shown in Table 4. And the comparison result of hematopoietic stem cell counts between the two groups BF and 4 weeks AF is shown in Fig. 6.

### 3.5. Comparison of inflammatory indicators between the two groups BF and 4 weeks AF

BF, the white blood cell count, neutrophil count and sedimentation rate of the two groups were compared, and there were no

**Table 2**  
NIHSS scores before and AF in the two groups.

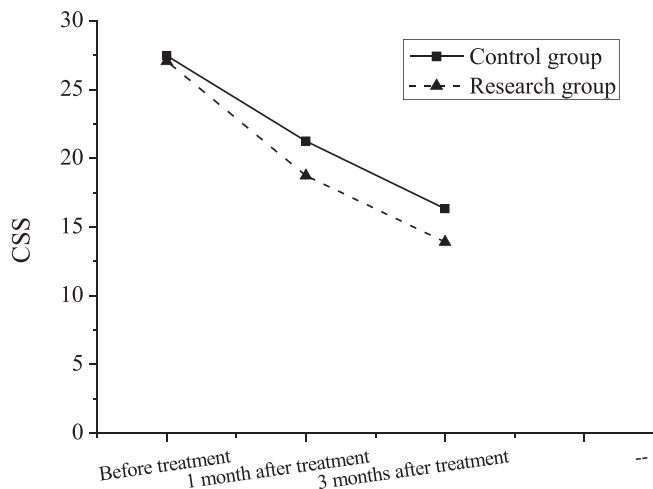
| Group          | BF           | 1-month AF   | 3 months AF  | 6 months AF  |
|----------------|--------------|--------------|--------------|--------------|
| CG             | 20.46 ± 2.96 | 14.12 ± 2.85 | 13.37 ± 2.40 | 12.05 ± 1.98 |
| Research group | 21.14 ± 2.25 | 13.23 ± 2.33 | 9.31 ± 2.02  | 7.35 ± 1.78  |
| P              | >0.05        | >0.05        | <0.05        | <0.05        |



**Fig. 4.** Changes in NIHSS score at different periods in the two groups.

**Table 3**  
CSS scores before and AF in the two groups.

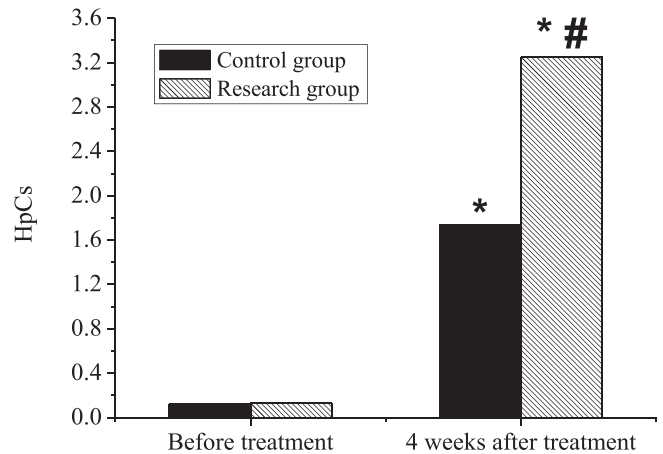
| Group          | BF           | 1-month AF   | 3 months AF  |
|----------------|--------------|--------------|--------------|
| CG             | 27.46 ± 0.96 | 21.24 ± 0.76 | 16.33 ± 0.66 |
| Research group | 27.05 ± 0.87 | 18.73 ± 0.62 | 13.90 ± 0.65 |
| P              | >0.05        | <0.05        | <0.05        |



**Fig. 5.** Changes in CSS scores at different periods in the two groups.

**Table 4**  
Hematopoietic stem cell count results BF and 4 weeks AF in the two groups (%MNCs).

| Group          | BF          | 4 weeks AF  |
|----------------|-------------|-------------|
| CG             | 0.12 ± 0.06 | 1.74 ± 0.16 |
| Research group | 0.13 ± 0.08 | 3.25 ± 0.22 |
| P              | >0.05       | <0.05       |



**Fig. 6.** Comparison of hematopoietic stem cell counts before and after 4 weeks of treatment in both groups Note: \* was compared with the same group BF,  $P < 0.05$ ; # was compared with the CG in the same period,  $P < 0.05$ .

important changes ( $P > 0.05$ ). After 4 weeks of treatment, the white blood cell counts of the CG and the SG were  $(9.4 \pm 2.9) \times 10^9$  and  $(5.7 \pm 2.7) \times 10^9$ , respectively, the neutrophil counts were  $(6.2 \pm 1.0) \times 10^9$  and  $(3.8 \pm 0.8) \times 10^9$ , respectively, and the sedimentation rate was  $(15.6 \pm 2.4)$  mm/h and  $(11.2 \pm 1.6)$  mm/h, respectively. There were statistical changes among the three inflammatory indicators between two groups ( $P < 0.05$ ). The results of inflammatory indicators BF and 4 weeks AF in the two groups are shown in Table 5.

#### 4. Discussion

Moya disease is a kind of chronic cerebrovascular disease, which is mainly characterized by progressive narrowing or complete obstruction of the MCA and its branch vessels at the end of bilateral ICA, accompanied by the formation of abnormal vascular network at the skull base, resulting in stroke. With the popularization of magnetic resonance angiography (MRA) technology in recent years, the detection rate of MMD in the world has been obviously increased. Japan is the area with the highest incidence of the disease, and its incidence rate is about 10 times that of Europe and America, and the ratio of male to female is about 1:1.8. MMD in children is more common with infarction type, and the main symptoms are cerebral ischemia, intellectual development disorder and dementia. 80% of children with cerebral ischemia will be accompanied by paralysis or weakness of lower limbs. MMD in adults usually presents as short-term memory disorder and irritability, and a few patients are accompanied by cognitive dysfunction. Therefore, differential diagnosis with mental diseases is needed to avoid missed diagnosis and misdiagnosis.

The treatment of MMD is divided into internal conservative treatment and surgical conservative treatment. Among them, the medical treatment is mainly symptomatic treatment. For the ischemic MMD, anti-platelet drugs and vasoactive drugs can be

**Table 5**

Inflammatory indicators BF and 4 weeks AF in the two groups.

| Group          | BF                                 |                               |                | 4 weeks AF                         |                               |                |
|----------------|------------------------------------|-------------------------------|----------------|------------------------------------|-------------------------------|----------------|
|                | White blood cell ( $\times 10^9$ ) | Neutrophils ( $\times 10^9$ ) | ESR (mm/h)     | White blood cell ( $\times 10^9$ ) | Neutrophils ( $\times 10^9$ ) | ESR (mm/h)     |
| CG             | 16.8 $\pm$ 3.9                     | 8.4 $\pm$ 2.0                 | 19.5 $\pm$ 3.1 | 9.4 $\pm$ 2.9                      | 6.2 $\pm$ 1.0                 | 15.6 $\pm$ 2.4 |
| Research group | 16.9 $\pm$ 3.8                     | 8.2 $\pm$ 1.8                 | 20.3 $\pm$ 3.4 | 5.7 $\pm$ 2.7                      | 3.8 $\pm$ 0.8                 | 11.2 $\pm$ 1.6 |
| P              | >0.05                              | >0.05                         | >0.05          | <0.05                              | <0.05                         | <0.05          |

applied; for hemorrhagic MMD, patients can be given hemostatic agents, dehydrating agents and other drugs. For TIA MMD and headache MMD, the application of calcium antagonist has obvious curative effect. For different types of patients, there is no same standard for the optimal surgical scheme, which needs to be chosen according to the specific situation of cerebrovascular vessels. Studies have shown that BMSCs, as a complex group of cells, can protect nerve and promote nerve regeneration. BMSCs differentiate into nerve cells in the specific pathological environment of cerebral ischemia, and there are many mechanisms to repair damaged brain tissues such as anti-apoptosis and promoting angiogenesis. After acute cerebral ischemia, ischemia and hypoxia of cerebral tissue will activate neutrophils in the body, which will lead to infiltration of white blood cells and irreversible necrosis of neurons.

In the treatment of MMD, anti-inflammatory and anti-infection treatment have positive effects on preventing the further progress of the disease and protecting brain tissue. In this study, autogenous bone marrow stem cell mobilization and anti-infection therapy were given to patients with MMD who had been treated with indirect revascularization, and the clinical efficacy was analyzed. The results showed that ABMSC mobilization combined with dexamethasone anti-inflammatory and anti-infective treatment for patients with MMD after revascularization can accelerate the recovery of nerve function and promote neovascularization. At the same time, it can reduce inflammation and improve patients' quality of life, which is worthy of clinical reference. At present, there are still some controversies at home and abroad about whether dexamethasone plays an active role in the treatment of moyamoya disease. Considering that the side effects of glucocorticoids are positively correlated with the dose and duration of glucocorticoid administration, this issue has not been discussed in this research. Therefore, the dose of dexamethasone for moyamoya disease will be further discussed in future studies.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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