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Clinical Efficacy of Autologous Bone Marrow Mesenchymal Stem Cell Transplantation for the Treatment of Patients with Refractory Cirrhotic Ascites

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Abstract: Objective: To analyze the efficacy of autologous bone marrow mesenchymal stem cell (BMSC) transplantation for the treatment of cirrhotic ascites (refractory). Methods: 64 patients with cirrhosis ascites (refractory) who were admitted to the hospital between May 2022 and April 2024 were selected and divided equally by random number table, the observation group was treated with BMSC autologous transplantation, and the reference group was treated with conventional medication, and the total effective rate, therapeutic indexes, liver and renal function indexes, and the change of urine volume were compared. Results: The total effective rate of the observation group was higher than that of the reference group ($P < 0.05$). Before treatment, there was no difference between the two groups in terms of therapeutic indexes such as depth of ascites, liver and kidney function indexes and 24-hour urine volume ($P > 0.05$). After treatment, the observation group's ascites depth and other indicators were better than that of the reference group, liver and kidney function indicators were better than that of the reference group, and 24h urine volume was more than that of the reference group ($P < 0.05$). Conclusion: BMSC autotransplantation can improve the clinical efficacy of patients with cirrhosis ascites (refractory), accelerate the absorption of ascites, reduce the values of body mass and abdominal circumference, and protect the liver and kidney functions and increase the amount of urination.

Keywords: Autologous bone marrow mesenchymal stem cell transplantation; Refractory cirrhotic ascites; Clinical efficacy

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1. Introduction

Cirrhosis is the end-stage manifestation of many liver diseases such as alcoholic liver disease, viral hepatitis, etc., and its loss-of-compensation stage leads to the symptoms of ascites [1]. Ascites, i.e. the pathological state, the fluid content inside the patient's abdominal cavity is > 200 mL, and its condition is critical and difficult to treat. For patients with cirrhotic ascites (refractory), conventional diuretic therapy is not effective in discharging ascites and surgical treatment is required. Conventional drug therapy is a common therapy for this

disease, which can reduce the symptoms of the disease and relieve the degree of pain of patients [2,3]. However, the long-term efficacy of this therapy is average, which may lead to more obvious adverse reactions and poor patient compliance. In comparison, BMSC autotransplantation is highly minimally invasive and can lead to the continuous differentiation of BMSC to bile ducts and hepatocytes, thereby protecting liver function and alleviating the manifestation of ascites [4]. Based on this, 64 patients with cirrhotic ascites (refractory) were selected in this study to evaluate the therapeutic advantages of BMSC autotransplantation.

2. Information and methods

2.1. General information

Sixty-four cases of cirrhotic ascites (refractory) patients admitted for treatment between May 2022 and April 2024 were selected and delineated by random number table, 32 cases in the observation group, 19 cases of male patients and 13 cases of female patients; their ages ranged from 41 to 81 years old, with a mean value of (55.27 ± 5.18) years old; and the duration of cirrhosis ranged from 0.5 to 3 years, with a mean value of (1.53 ± 0.49) years. In the reference group, there were 32 cases, 20 male patients and 12 female patients; their ages ranged from 40 to 82 years, with a mean value of (55.36 ± 5.15) years; the duration of cirrhosis ranged from 0.4 to 3 years, with a mean value of (1.56 ± 0.41) years. The general information between the two groups was compared $P > 0.05$.

Inclusion criteria: (1) meeting the criteria for cirrhosis listed in the Guidelines for the Diagnosis and Treatment of Ascites and Related Complications of Liver Cirrhosis; (2) accompanied by signs of ascites, whose ascites persisted for more than 3 months; (3) the patient's clinical data were relatively complete and (4) they were informed and consented to the study.

Exclusion criteria: (1) accompanied by hepatic encephalopathy, haemorrhagic ascites and other diseases; (2) combined with myocardial infarction and other cardiovascular and cerebral vascular diseases; (3) abnormal communication ability; (4) accompanied by depression; (5) accompanied by upper gastrointestinal bleeding in the past 3 months.

2.2. Methods

The treatment method of the reference group is as follows: conventional medication, anti-infective, hepatoprotective and hepatoprotective basic treatment, and take 20 mg dose of tachycardia and 10 g dose of albumin daily, to be administered intravenously, for 4 weeks consecutively. A 3-step diuretic regimen was also combined, and in the first week, mercaptopropionic acid was chosen at a daily oral dose of 75 mg, i.e., a single dose, and oral ambrisentan at a daily dose of 120 mg, i.e., a single dose. In the second week, ascites absorption was checked, and if it still did not meet the standard, tachyphylaxis was used, with a daily dose of 40–80 mg for intraperitoneal treatment, and dopamine was injected every other day, with a dose of 20–40 mg, both once daily. In the third week of poor efficacy, oral mannitol (20%) can be taken, the daily oral dose of 100–150 mL, once-a-day medication, treatment for 4 weeks.

The treatment method of the observation group is as follows: BMSC autotransplantation treatment: keep the patient in the lying position, and the location of the bone marrow puncture point is at the bilateral posterior superior iliac spine. Disinfection and toweling, local infiltration anesthesia puncture point to the periosteal area. A bone marrow puncture needle (18 gauge) was taken so that it was vertically inserted into the puncture point, which was effectively fixed after entering the medullary cavity, and the bone marrow was withdrawn. The volume of bone marrow blood aspirated at the puncture point was 60 mL bilaterally and anticoagulation was done by adding sodium heparin at a dose of 7500 U. In vitro isolation operation and purification of bone

marrow stem cells was carried out by density centrifugation. Flow cytometry was performed to detect the markers of surface antigen-enriched monocytes: CD45-, CD34-, CD29+, CD90+ & CD44+. Mesenchymal hepatocytes, all with a body mass of 1.0 ´ 10^6/kg, were stored at 4 ℃ and sent to the intervention room. Local treatment was performed under the guidance of a digital subtraction angiography machine, and the right femoral artery was punctured by the Seldinger technique with an indwelling arterial sheath (5F), and an R-H hepatic artery catheter (5F) was placed with the innominate hepatic artery. The characteristics of vascular distribution were assessed using a contrast technique to observe the presence of abnormal vascular mass at the tumor site. The BMSC suspension after the separation operation was taken and injected into the interior of the liver. After treatment, the arterial sheath was slowly withdrawn, pressure was applied and the puncture point was bandaged, and the patient was instructed to lie in a flat position for 24h.

2.3. Observation indicators

(1) Overall effective rate: Significant efficacy: no ascites, only a small amount of diuretics used daily; Preliminary efficacy: the amount of ascites is significantly reduced, a large amount of diuretics is needed daily, intermittently combined with human blood albumin preparation; No efficacy: no change in ascites, a large number of diuretics and human blood albumin preparation are needed daily.

(2) Therapeutic indexes: Before and after 3 months of treatment, the depth of ascites was evaluated by a Doppler ultrasonic diagnostic instrument; the abdominal circumference was measured by a soft ruler; and the body mass was measured by weight measuring instrument (weight scale).

(3) Liver function indexes: At the same time, venous blood was collected from patients in fasting state, centrifuged and processed, and then total bilirubin (TBIL), aspartate aminotransferase (AST), and plasma albumin (ALB) levels were measured by automatic biochemistry analyzer.

(4) Renal function indexes and urine volume: At the same time, fasting venous blood was collected, and the levels of blood creatinine (Scr), urea nitrogen (BUN) and 24h urine volume were measured by the fully automatic biochemical analyzer.

2.4. Statistical analysis

The data processing software is SPSS 28.0, the expression of measurement data is mean ± standard deviation (SD), compare and test with t value, the expression of count data is (n/%), compare and test with χ^2 value, statistically significant i.e. $P < 0.05$.

3. Results

3.1. Comparison of the total effective rate of the two groups

The total effective rate of the observation group was higher than that of the reference group ($P < 0.05$). See Table 1.

Table 1. Comparison of the total effective rate of the two groups (n/%)

Subgroups	*n*	Remarkable results	Initial effect	No effect	Overall effective
Observation group	32	21 (65.63)	10 (31.25)	1 (3.13)	96.88 (31/32)
Reference group	32	17 (53.13)	8 (25.00)	7 (21.88)	78.13 (25/32)
χ^2	-	-	-	-	5.143
P	-	-	-	-	0.023

3.2. Comparison of treatment indicators between the two groups

Before treatment, there is no difference in the comparison of the clinical indicators of the two groups (P > 0.05). After 3 months of treatment, the clinical indicators of the observation group are lower than those of the reference group (P < 0.05). See Table 2.

Table 2. Comparison of the treatment indexes of the two groups (mean ± SD)

Subgroups	*n*	Depth of ascites (mm)		Abdominal circumference (cm)		Body mass (kg)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	32	72.28 ± 6.91	31.53 ± 4.12	94.36 ± 8.71	86.24 ± 4.15	62.53 ± 6.11	57.40 ± 3.62
Reference group	32	72.21 ± 6.83	52.19 ± 4.17	94.33 ± 8.66	89.02 ± 4.20	62.58 ± 6.13	59.44 ± 3.15
t	-	0.041	19.937	0.014	2.663	0.033	2.405
P	-	0.968	0.000	0.989	0.010	0.974	0.019

3.3. Comparison of liver function indexes between the two groups

Before treatment, there is no difference in the comparison of liver function indexes between the two groups (P > 0.05). After 3 months of treatment, the liver function indexes of the observation group were better than those of the reference group (P < 0.05). See Table 3.

Table 3. Comparison of liver function indexes between the two groups (mean ± SD)

Subgroups	*n*	TBIL (μmol/L)		AST (U/L)		ALB (g/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	32	88.25 ± 6.12	60.73 ± 5.11	67.63 ± 5.93	28.75 ± 2.42	27.51 ± 4.11	33.62 ± 3.18
Reference group	32	88.29 ± 6.20	70.29 ± 5.27	67.66 ± 5.91	38.91 ± 2.58	27.58 ± 4.16	30.15 ± 3.14
t	-	0.026	7.367	0.020	16.248	0.068	4.392
P	-	0.979	0.000	0.984	0.000	0.946	0.000

3.4. Comparison of renal function indexes and urine volume of the two groups

Before treatment, there was no difference in the comparison of renal function indexes and 24-hour urine volume between the two groups (P > 0.05). After 3 months of treatment, the renal function indexes of the observation group were lower than those of the reference group, and the 24h urine volume was more than that of the reference group (P < 0.05). See Table 4.

Table 4. Comparison of renal function indexes and urine volume between two groups (mean ± SD)

Subgroups	*n*	Renal function indicators (μmol/L)				24h urine volume (mL)	
		Scr		BUN		Before treatment	After treatment
		Before treatment	After treatment	Before treatment	After treatment		
Observation group	32	177.53 ± 15.35	105.39 ± 8.31	12.35 ± 2.08	6.81 ± 1.57	845.95 ± 17.36	1386.92 ± 29.37
Reference group	32	177.01 ± 16.23	131.65 ± 8.44	12.39 ± 2.11	9.23 ± 1.61	844.53 ± 17.23	1089.53 ± 25.41
t	-	0.132	12.542	0.076	6.088	0.328	43.317
P	-	0.896	0.000	0.939	0.000	0.744	0.000

4. Discussion

The pathogenesis of liver cirrhosis is complex, as follows: (1) plasma colloid osmotic pressure decreases, and the ALB content in the body decreases, which produces a persistent extravasation reaction of the blood components; (2) the generation of lymphatic fluid increases and the reabsorption capacity decreases, which causes lymphatic fluid to penetrate into the interior of the patient's abdominal cavity [5]; and (3) the dysfunction of inactivation of hepatic tissues increases the secretion of a variety of substances, such as aldosterone or antidiuretic hormone that induces water and sodium retention. Based on the above pathogenesis, cirrhotic ascites (refractory) are treated with water and salt restriction, and ALB supplementation with drainage of ascites [6,7].

Pharmacological treatment is a common treatment for this disease, in which tachycardia has a strong effect on the renal tubules, amphotericin can act efficiently on the aldosterone receptor in the body, and mannitol can significantly increase blood volume so that the osmolality of the intra-tubular fluid in the renal tubules can be significantly increased. The combination of the three drugs can have a diuretic effect. At the same time, the combination of dopamine and mercaptopropionic acid can enhance renal blood flow, which in turn enhances the therapeutic effect. However, it is difficult to improve liver and kidney functions with drug treatment, so the long-term efficacy is general [8,9]. BMSC autotransplantation selects the patient's autologous cells, and there is no immune rejection after transplantation, which is safe and can reduce treatment complications. BMSC has strong differentiation ability and proliferation function, and can effectively differentiate hepatocytes and hematopoietic cells, etc. Therefore, it has more therapeutic targets. BMSC can secrete cytokines and growth factors in vivo to repair the damaged tissues and can improve the immune function of the patients [10].

The results showed that the indicators of ascites depth and other indicators of the observation group after treatment were better than those of the reference group, the indicators of liver and kidney function were better than those of the reference group, and the 24h urine volume was more than that of the reference group ($P < 0.05$). The reason is that the collection method of BMSC is relatively simple, and bone marrow blood can be extracted by the bone marrow aspiration method, and the treatment is less painful. BMSC can regulate vascular permeability, promote the flow of ascites into the blood circulation through the wall of the blood vessels, and accelerate its absorption [11]. BMSC has a strong and continuous stimulating effect on the primitive progenitor cells of the liver, which can increase the number of newborn hepatocytes, cause them to produce a large number of ALBs, and improve the level of plasma osmolality, and promote the discharge of ascites from the body [12], prompting the drainage of ascites out of the body. In addition, BMSC autotransplantation can have a direct effect on the patient's liver tissue, improve the systemic microenvironment, regulate the function of water and sodium metabolism, and improve the ability of liver and kidney tissues to excrete electrolytes and excess water, so that the 24h urine output increased significantly [12].

5. Conclusion

In conclusion, BMSC autotransplantation can enhance the therapeutic efficiency of patients with cirrhotic ascites (refractory), improve the level of abdominal circumference and body mass of patients, reduce the number of ascites, and protect the liver and kidney functions of patients, which has a high therapeutic feasibility.

Disclosure statement

The authors declare no conflict of interest.

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