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Research Article

Clinical Study on the Treatment of Type 2 Diabetes with Bone Marrow Platelet-Rich Plasma (BMPRP)

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Abstract

Objective: To retrospectively analyze the effects of (bone marrow platelet-rich plasma BMPRP) precise pancreatic infusion therapy versus conventional treatment.

Methods: Bone marrow was collected from the iliac crest anterior superior spine, and platelet-rich plasma was separated by centrifugation. BMPRP was infused into the pancreas under ultrasound guidance. It was compared with conventional hypoglycemic drugs and insulin therapy.

Results: In the BMPRP treatment group of 32 cases, the fasting blood sugar and hemoglobin A1c were significantly lower than pre-treatment levels , while the C-peptide level did not change significantly. The insulin dose was reduced. In the conventional treatment group of 28 cases, the fasting blood sugar, hemoglobin A1c, and C-peptide levels did not change significantly after continuous treatment for one year, and the insulin dose was not reduced.

Conclusion: BMPRP precise pancreatic infusion therapy can improve pancreatic function, reduce insulin resistance, lower blood sugar, and reduce the required insulin dosage.

Research background

Type 2 diabetes is a metabolic disease caused by insulin resistance and β cell damage caused by over-nutrition and insufficient activity. Conventional treatments for diabetes include hypoglycemic agents and insulin, which still cannot prevent diabetic patients from developing microvascular and macrovascular complications. Stem cells are a kind of cells with multiple differentiation potential, which can differentiate into different cells in different organ microenvironment, or secrete some factors to repair damaged cells and improve organ function. Bone marrow contains multipotent stem cells. Bone marrow platelet-enriched plasma (BMPRP) containing bone marrow stem cells can be separated by density gradient centrifugation. Injecting BMPRP into pancreatic tissue of diabetic patients can improve islet function. This study retrospectively analyzed the clinical data of patients treated with pancreatic infusion of BMPRP and routine treatment, and compared the therapeutic effects to explore the therapeutic effect and principle of BMPRP in treating diabetes.

Clinical data and methods

From January 2022 to December 2023, the medical records of diabetic patients treated with BMPRP in Zigong Hospital affiliated to Southwest Medical University, Renji Hospital of Zhengzhou and Shandong Public Health Clinical Center were analyzed retrospectively. Inclusion criteria: male or female , aged 20-70. Fasting blood sugar is more than 7 mmol, and blood sugar is more than 12 mmol 2 hours after meals. It is necessary to use hypoglycemic agents or insulin to control blood sugar close to normal or still significantly higher than normal, and to exclude patients with evident coagulation disorders.

Treatment

32 cases in BMPRP treatment group, including 17 males

and 15 females, aged 31-64 years, with an average age of 54 years. Bone marrow was punctured in the anterior superior iliac crest, and 4 ml heparin saline was pre-filled with 20 mL syringes. Bone marrow was continuously aspirated and collected in five 20 mL syringes . The collected bone marrow was injected into eight 15 ml centrifuge tubes and placed in a centrifuge for density gradient centrifugation. After centrifugation, red blood cells settled at the bottom of the centrifuge tube, plasma and fat cells are located in the upper layer, and nucleated cells and platelets in bone marrow are located in the white membrane layer close to the upper part of the red blood cell layer. First, the plasma from the upper layer of the centrifuge tube was removed, and then 6 ml of bone marrow plasma including bone marrow nucleated cells and platelets was aspirated. Under B-ultrasound guidance, a fine-needle puncture was performed to infuse BMPRP into the pancreatic parenchyma. Then, the bone marrow plasma separated from BMPRP was mixed with red blood cells and reinfused from peripheral veins. Following the initial treatment, a one-month interval was maintained , and then the second and third treatments were done two months. Insulin and hypoglycemic agents were maintained post-treatment , and when the fasting blood sugar drops below 6 mmol, the amount of insulin and hypoglycemic agents should be gradually reduced. 28 patients in the conventional treatment group, including 15 males and 13 females, aged 32-69 years, with an average age of 55 years. Continuous treatment with hypoglycemic agents and insulin.

Statistical methods

SPSS 20.0 statistical software was used for analysis. The chi-square test was used for counting data, and mean ± standard deviation (SD) was used for measurement data. A p - value < 0.05 was considered statistically significant.

Results

60 cases of diabetes mellitus were followed up for more than one year, of which 32 cases were treated with BMPRP and 28 cases were treated with hypoglycemic agents and/or insulin. The comparison of fasting blood glucose, glycosylated hemoglobin, C-peptide, and insulin dosage between the two groups is shown in Tables 1-5, respectively.

Table 1: Comparison of clinical data between the two groups based.

Variable	BMPRP group	Conventional group	p value
Sex			0.9724
Male	17	15	
Female	15	13	
BMI n(%)			0.9819
Number of obese	6	6	
Number of normal	26	22	
Insulin Antibodies			0.8848
Number of positive	5	4	
Number of negative	27	24	
Drink			0.9819
yes	6	5	
no	26	23	
Exercise			0.7442
yes	24	22	
no	8	6	

Table 2: Changes of fasting blood glucose before and after BMPRP infusion (mmol/L).

Group	N	Before	1 Month	3 Months	6 Months	12 Months
BMPRP group	32	8.07 ± 1.59	7.54 ± 1.31	6.86 ± 0.98	6.59 ± 0.7	6.13 ± 0.66
Conventional group	28	7.91 ± 1.88	7.9 ± 1.8	7.9 ± 1.8	7.35 ± 1.15	7.26 ± 1.42
t		0.3598	0.8728	2.623	3.134	3.867
P		0.7203	0.387	0.0121	0.0027	0.0004

*Compared to baseline, $p < 0.05$

Table 3: Changes of HbA1c before and after infusion of autologous bone marrow cells (%).

Group	N	Before	1 Month	3 Months	6 Months	12 Months
BMPRP group	32	8.27 ± 1.58	7.91 ± 1.45	7.15 ± 1.06	6.58 ± 0.74	6.18 ± 0.78
Conventional group	28	7.67 ± 1.52	7.67 ± 1.38	7.69 ± 1.45	7.35 ± 1.05	7.16 ± 1.09
t		1.489	0.6416	1.633	3.201	4.019
P		0.1421	0.5237	0.1089	0.0024	0.0002

*Compared to baseline, $p < 0.05$

Table 4: C-peptide changes before and after autologous bone marrow infusion (ng/ml).

Group	N	Before	1 Month	3 Months	6 Months	12 Months
BMPRP group	32	1.7 ± 0.59	1.95 ± 0.44	2.21 ± 0.31	2.35 ± 0.38	2.33 ± 0.41
Conventional group	28	1.69 ± 0.65	1.82 ± 0.55	2.02 ± 0.57	2.09 ± 0.63	2.2 ± 0.64
t		0.04454	1.024	1.587	1.947	0.9379
P		0.9646	0.3101	0.1179	0.0564	0.3522

*Compared to baseline, $p < 0.05$

Table 5: Changes in insulin dosage before and after autologous bone marrow infusion (u).

Group	N	Before	1 Month	3 Months	6 Months	12 Months
BMPRP group	32	26.56 ± 21	20.63 ± 15.11	14.75 ± 11.91	11.38 ± 9.74	7.25 ± 6.46
Conventional group	28	28.21 ± 18.72	28.5 ± 17.84	28 ± 17.38	29.25 ± 17.92	31.36 ± 18.4
t		0.3222	1.831	3.481	4.883	6.586
P		0.7485	0.0727	0.001	< 0.0001	< 0.0001

*Compared to baseline, $p < 0.05$

Discussion

Diabetes is a major disease that threatens human health. At present, the commonly used treatment methods are difficult to achieve accurate regulation of blood sugar, which leads to a variety of complications, seriously affecting the quality of life of patients and even endangering their lives. Traditional medical treatment can't solve the problem of insulin resistance and islet β cell dysfunction from the source. In order to overcome this situation, the current research focus has shifted to the field of stem cell therapy for diabetes [1-5].

There are stem cells in bone marrow [6-9]. Transplantation of bone marrow stem cells into pancreatic microenvironment with islet cell injury may transform bone marrow stem cells into islet β cells, or secrete some cytokines to promote the repair and reconstruction of islet damaged cells, and the regulation function of blood sugar will improve. If autologous bone marrow cells are infused through peripheral veins, most stem cells may stay in the lungs after pulmonary circulation, and a small amount of stem cells may enter the pancreas through systemic circulation. Due to the limited number of stem cells, the improvement of islet function may be minimal .

Studies have reported that agents such as granulocyte colony-stimulating factor are used to mobilize bone marrow stem cells into peripheral blood, and then bone marrow stem cells are collected from peripheral blood. Through interventional radiology, bone marrow stem cells can be infused from femoral artery cannula into pancreaticoduodenal artery, which can improve islet function and have a good effect on the treatment of type 2 diabetes. This method further supports the hypothesis that bone marrow stem cells transplanted into pancreatic microenvironment can be transformed into islet β cells to improve islet function [10-13].

We can collect bone marrow from the anterior superior iliac spine under local anesthesia, and we can collect more primitive bone marrow stem cells than those from peripheral blood after applying granulocyte stimulating factor. After collecting bone marrow, density gradient centrifugation is used to stratify bone marrow components. Red blood cells in bone marrow are thrown to the lowest part of the centrifuge tube because they contain the highest specific gravity of hemoglobin. White blood cells in bone marrow include stem cells, and platelets are lighter than red blood cells and heavier than plasma. After centrifugation, it clings to the red blood cell layer. The plasma is in the upper part of the centrifuge tube. First, remove the plasma from the upper part of the centrifuge tube, and then suck out nucleated cells such as stem cells and platelets, including some plasma, which is bone marrow-derived platelet-rich plasma (BMPRP). Some researchers refer to this as bone marrow aspirate concentrate (BMAC) [14] , but it should be bone marrow aspirate concentrate after removing red blood cells. BMPRP may be a more precise term in this context .

Under the guidance of B-ultrasound, the No.7 puncture needle is punctured through the upper abdomen, and the fine needle enters the pancreas through the stomach and injects BMPRP into pancreatic islet tissue. Because the density of BMPRP is different from that of pancreatic tissue, ultrasonic waves will echo at different density interfaces, and the ultrasonic probe emits ultrasonic waves and receives the reflected ultrasonic waves. After computer processing, these reflected ultrasonic waves are displayed on the screen in the form of bright spots, so B-ultrasound can show that BMPRP is infused into pancreatic tissue and the brightness of the pancreas is increased. Because the puncture needle is very thin, after infusion of bone marrow cells, Patients could resume movement shortly after needle removal , which is more convenient and less harmful than radiotherapy [15-19].

Comparing the general conditions, gender, age, body type, exercise, diet, alcohol consumption, insulin antibodies, etc. between the BMPRP treatment group and the conventional treatment group showed no significant differences (Table 1). Bone marrow stem cells may differentiate into pancreatic beta cells or secrete certain factors to promote the repair of damaged pancreatic beta cells in the pancreatic microenvironment. Clinical observations indicated a progressive decline in blood glucose levels and glycated hemoglobin levels of patients treated with BMPRP . There was a statistically significant difference in fasting blood glucose and glycated hemoglobin between the two groups (Tables 2,3), but there was no significant difference in C-peptide levels between the two groups (Table 4). This may be attributed to the average C-peptide levels in both groups of type 2 diabetes patients was not significantly low, and some patients had lower C-peptide levels, while others had higher C-peptide levels than normal. After self-bone marrow cell pancreatic infusion treatment, combined with appropriate exercise and control of carbohydrate diet, pancreatic function improved, fasting blood glucose and glycated hemoglobin levels decreased, and some patients' C-peptide levels also decreased, which may indicate a reduction in insulin resistance, allowing blood sugar to be controlled within a normal range without the need for more insulin [20,21]. Some diabetic patients had lower C-peptide levels prior to BMPRP treatment, and their pancreatic function improved and C-peptide levels increased after treatment, suggesting an increase in insulin secretion. After BMPRP treatment, fasting blood glucose and glycated hemoglobin levels decreased, and insulin use was gradually reduced, with some patients being able to maintain normal blood sugar without insulin after stopping insulin use (Table 5). The conventional treatment group did not see a decrease in blood sugar, and insulin use could not be reduced.

This study conducted a retrospective statistical analysis of clinical data. Randomization was not applicable. The sample size was determined based on the availability of complete medical records. A formal power analysis was not feasible, but the sample was deemed sufficient to detect statistically significant differences in key outcome measures. Due to the absence of some clinical data, statistical analysis was carried out after deleting these incomplete clinical cases. Therefore, the statistical results may have some limitations. In the future, with an increase in the number of enrolled clinical cases, more comprehensive conclusions may be drawn.

Conclusion

After BMPRP pancreatic infusion therapy, blood sugar levels decreased. Insulin sensitivity improved, and insulin resistance decreased . It is an effective treatment for type 2 diabetes.

Authors' contributions

Baochi Liu conceptualized and designed the study . All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study received ethical approval from the Ethics Committee of the Zigong Hospital, Affiliated with

Southwest Medical University. The ethical approval number ZGLCZXEC2022-0314. Written informed consent was obtained from all participants for the use of their samples for the detection and publication of their relevant data.

Patient consent for publication

All participants in this study provided written informed consent for the use of their samples and publication of their data.

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