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Research Article

Analysis of Clinical Data on the Treatment of Type 2 Diabetes with BMPRP

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Abstract

Objective: This study aims to comprehensively analyze the factors influencing the efficacy of bone marrow platelet-rich plasma (BMPRP) therapy in patients with type 2 diabetes mellitus. *Methods:* In this clinical investigation, autologous bone marrow was harvested from participants, followed by the isolation of BMPRP. Patients then underwent ultrasound-guided infusion of BMPRP directly into the pancreas. The follow-up period for evaluating treatment outcomes spanned one year, during which various factors potentially affecting the therapeutic effects were systematically analyzed. *Results:* A total of 49 patients diagnosed with type 2 diabetes mellitus received BMPRP pancreatic infusion as a treatment modality. Among these patients, 32 demonstrated a positive response to the therapy, while 17 experienced no significant improvement. Notably, in the effective treatment group, fasting blood glucose levels exhibited a significant reduction after one month of intervention. Additionally, glycosylated hemoglobin (HbA1c) levels showed a substantial decrease at the three-month mark, and a gradual decline in insulin dosage requirements was observed over time. In contrast, changes in C-peptide levels were not pronounced. Analysis of the ineffective treatment group revealed that these patients often had obesity, demonstrated minimal physical activity, and did not adhere to dietary recommendations for carbohydrate control. *Conclusion:* The findings suggest that BMPRP pancreatic infusion can improve pancreatic function and glycemic control in type 2 diabetes patients. However, for optimal outcomes, it is crucial to combine this therapy with a regimen that includes regular exercise and strict management of carbohydrate intake. This multifaceted approach promises to enhance the effectiveness of BMPRP therapy and contribute to better overall management of type 2 diabetes.

Keywords

Bone Marrow Platelet-rich Plasma, Ultrasound-guided, Type 2 Diabetes

1. Introduction

Platelet-rich plasma (PRP) can be separated from peripheral venous blood, and if it is separated from bone marrow blood, it is called BMPRP. BMPRP, in addition to the components of PRP, mainly contains bone marrow stem cells.

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Bone marrow stem cells are a type of cell with multiple differentiation potential, which can differentiate into different cells in different organ microenvironments or secrete certain factors to repair damaged cells and improve organ function. Type 2 diabetes is a metabolic disease caused by nutritional overload and insufficient exercise, leading to insulin resistance and beta cell damage. High sustained blood sugar levels in diabetes patients can lead to microvascular and macrovascular complications. By infusing BMPRP containing bone marrow stem cells into the pancreatic tissue of diabetic patients, most patients can improve their pancreatic function. However, some patients show no obvious improvement. We retrospectively analyzed the clinical data of diabetic patients who received BMPRP pancreatic infusion treatment and continued to be observed for more than one year, to investigate the therapeutic effects and explore the possible factors that may affect the autologous bone marrow cell therapy for diabetes.

2. Clinical Data and Methods

Retrospectively analyze the case records of patients with diabetes treated with BMPRP at the Affiliated Hospital of Southwest Medical University in Zigong, Renji Hospital in Zhengzhou, and Shandong Provincial Public Health Clinical Center from January 2022 to December 2023. Inclusion criteria: male or female, aged 20-70. Fasting blood glucose of 7 mmol/L or more, postprandial blood glucose of 12 mmol/L or more, requiring hypoglycemic drugs or insulin to control blood glucose close to normal or still significantly higher than normal, excluding obvious thrombotic thrombocytopenic disease.

Methods: Local anesthesia was used for ilioiliac crest bone marrow aspiration, and a 20 mL syringe was pre-filled with 4 mL heparin saline. The bone marrow was aspirated until five 20 mL syringes were full. The collected bone marrow was then injected into eight 15 mL centrifuge tubes and placed in a centrifuge for density gradient centrifugation. After centrifugation, red blood cells were located at the bottom of the tubes, plasma and fat cells were in the upper layer, and the nucleated cells, platelet and stem cells of the bone marrow were located in the white membrane layer immediately above the red blood cell layer. The nucleated cells of the bone marrow, including a small amount of bone marrow plasma (BMPRP), were then separated and collected into 6 mL. BMPRP was then injected into the pancreatic tissue under ultrasound guidance using a fine needle. The bone marrow plasma and red blood cells were then mixed and re-infused into the peripheral vein. After BMPRP therapy, patients were free to move about as usual. Treatments were performed one month for the first therapy, and then two months for the third treatments. After each treatment, the patient's insulin and diabetes medication were maintained at their previous levels. Once the fasting blood sugar had dropped below 6 mmol and was maintained for a week, the patient's insulin and diabetes medication were gradually reduced.

3. Statistical Methods

SPSS 19.0 statistical software was used for analysis. The measurement data were expressed by mean ± standard deviation (±s), and the counting data were measured by Chi-square test. $P < 0.05$ was considered statistically significant.

4. Result

49 cases of diabetes were followed up for more than 1 year, according to the fasting blood glucose decreased by more than 1 mmol than before treatment without increasing medication, or the dosage of insulin or hypoglycemic agents was reduced on the basis of the original blood glucose was not increased, the treatment was determined to be effective, otherwise it was ineffective. Results There were 32 cases in the effective group, including 17 males and 15 females, aged 31-64 years old, with an average age of 5 cases of obvious obesity, 27 cases of normal weight, 4 cases of insulin antibody positive, 28 cases of negative, drinking more than 320 cases a day, 26 cases of moderate exercise (walking more than 8000 steps), 6 cases of less exercise. There were 17 cases in the invalid group, including 9 males and 8 females, aged 32-69 years old with an average age of 12 cases of obvious obesity, 5 cases of normal body weight, 13 cases of insulin antibody positive and 4 cases of negative, 10 cases of drinking more than 3 or 2 a day, 7 cases of drinking a little or no alcohol. There were 6 cases of moderate exercise (more than 8000 steps) and 11 cases of less exercise. The comparison of fasting blood glucose changes between the two groups is shown in Table 1, glycosylated hemoglobin changes are shown in Table 2, C-peptide changes are shown in Table 3, insulin dosage changes are shown in Table 4, and general clinical data are shown in Table 5.

Table 1. *Changes of fasting blood glucose before and after BMPRP infusion (mmol/L).*

Group	N	Before	1 Month	3 Months	6 Months	12 Months
effective group	32	8.37 ±1.61	7.72 ±1.20	6.94 ±0.80	6.56 ±0.53	6.07 ±0.44
invalid group	17	7.92 ±1.54	7.83 ±1.36	7.78 ±1.56	7.24 ±0.82	6.71 ±0.74

Group	N	Before	1 Month	3 Months	6 Months	12 Months
T		0.8321	0.3012	2.506	3.511	3.781
P		0.4096	0.7646	0.0157	0.0010	0.0004

Comparison with before, *P<0.05

Table 2. *Changes of HBA1c before and after infusion of autologous bone marrow cells (%).*

Group	N	Before	1 Month	3 Months	6 Months	12 Months
effective group	32	8.27±1.58	7.91±1.45	7.15±1.06	6.57±0.73	6.12±0.70
invalid group	17	7.92±1.54	7.92±1.44	7.90±1.63	7.36±0.97	7.23±1.07
T		0.7263	0.03978	1.952	3.228	4.378
P		0.4713	0.9684	0.0569	0.0023	<0.0001

Comparison with before, *P<0.05

Table 3. *C-peptide changes before and after autologous bone marrow infusion (ng/ml).*

Group	N	Before	1 Month	3 Months	6 Months	12 Months
effective group	32	1.70±0.59	1.98±0.48	2.28±0.37	2.54±0.37	2.57±0.31
invalid group	17	1.66±0.54	1.78±0.46	2.23±0.49	2.45±0.48	2.55±0.42
T		0.2044	1.425	0.4165	0.7566	0.1189
P		0.8389	0.1608	0.6790	0.4531	0.9058

Comparison with before, *P<0.05

Table 4. *Changes in insulin dosage before and after autologous bone marrow infusion (u).*

Group	N	Before	1 Month	3 Months	6 Months	12 Months
effective group	32	26.25±20.77	20.63±15.11	14.75±11.91	11.38±9.74	7.25±6.46
invalid group	17	30.59±18.62	31.06±18.26	29.41±17.63	30.35±18.00	31.76±17.89
T		0.7204	2.139	3.460	4.809	6.993
P		0.4749	0.0376	0.0012	<0.0001	<0.0001

Comparison with before, *P<0.05

Table 5. *Comparison of clinical data between the two groups based on treatment effect.*

Variable	effective group	invalid group	P value
Sex			>0.05
Number of Male (%)	17(54.13%)	9(52.94%)	

Variable	effective group	invalid group	P value
Number of Female (%)	15(46.88%)	8(47.06%)	
BMI n(%)			<0.05
Number of obese (%)	5(15.63%)	12(70.59%)	
Number of normal (%)	27(84.38%)	5(29.41%)	
Insulin Antibodies			<0.001
Number of positive (%)	4(12.50%)	13(76.47%)	
Number of negative (%)	28(87.50%)	4(23.53%)	
Drink			<0.001
Number of drinking more than 3 or 2 a day (%)	0(0.00%)	10(58.82%)	
Number of drinking a little or no alcohol (%)	32(100.00%)	7(41.18%)	
Exercise			<0.05
Number of moderate exercise (%)	26(81.25%)	6(35.29%)	
Number of less exercise (%)	6(18.75%)	11(64.71%)	

5. Discuss

Diabetes is a serious disease threatening human health [1-3]. The current commonly used treatment methods are difficult to achieve accurate control of blood sugar, leading to a variety of complications, seriously affecting the quality of life of patients, and even life-threatening [4-10]. Traditional medical treatment cannot solve the source of insulin resistance and islet beta cell dysfunction [11-15], in order to overcome this situation, the focus of research has shifted to the field of stem cell therapy for diabetes [16-20]. Islet allotransplantation is a commonly used method to treat diabetes. The purpose is to replace the function of damaged islet cells. This islet allograft requires immunosuppressive agents. However, with the extension of time, the body's rejection reaction will still make the transplanted islets lose function [21-24]. Animal experiments showed that umbilical cord mesenchymal stem cells can activate the expression of β-cell growth factor and secrete insulin-like growth factor 1 (IGF1) [25-27]. Improve islet activity and insulin secretion. But allogeneic umbilical cord mesenchymal stem cells can also be rejected and lose their function. The induced differentiation of induced pluripotent stem cells (IPSCs) [28-30] into islet cells can provide an unlimited source of pancreatic cells. However, this approach is complicated. At present, it is not clinically possible to obtain sufficient number of glucose-responsive β cells for transplantation therapy [31-36].

In the pancreatic microenvironment with islet cell injury, bone marrow stem cells may transform into islet beta cells, or secrete some cytokines to promote the repair and reconstruction of islet cells and improve the regulation of blood sugar. If the autologous bone marrow cells are transfused through peripheral veins, most of the stem cells may remain in the lungs after pulmonary circulation, and a small number of stem cells may enter the pancreas through systemic circulation. Because the number of stem cells is too small, the improvement of islet function is not obvious. It has been reported that bone marrow stem cells were mobilized into peripheral blood with drugs such as granulocyte-stimulating factor, and then bone marrow stem cells were collected from peripheral blood. Then through radiology interventional therapy from the femoral artery cannula into the pancreaticoduodenal artery infusion of bone marrow stem cells, can improve the islet function, the treatment of type 2 diabetes has a good effect. This method also verified that bone marrow stem cells transplanted into the pancreatic microenvironment could transform into islet beta cells to improve islet function. We obtained bone marrow from the anterior upper iliac spine under local anaesthesia, and were able to obtain more primitive bone marrow stem cells than from peripheral blood after the application of granulocyte stimulating factor. Autologous bone marrow cells were isolated after collecting autologous bone marrow. Under the guidance of B-ultrasound, puncture needle No. 7 was used through the upper abdomen, and the fine needle was inserted into the pancreas through the stomach. Autologous bone marrow nucleated cells were injected into the islet tissue. After processing by computer, these reflected ultrasound waves are displayed on the screen in the form of bright spots, so the B-ultrasound can show the increased brightness of the pancreas as the bone marrow cells are injected into the pancreatic tissue. Because the puncture needle is very thin, after the infusion of BMPRP, you can move freely after pulling out the puncture needle, which is more convenient than radiation

interventional therapy.

Bone marrow stem cells may differentiate into islet cells in the pancreatic microenvironment, or secrete some factors to promote the repair of damaged islet cells. The clinical observation showed that the blood glucose and hemoglobin A1C decreased gradually. But in some patients the change is not significant. Among 49 patients with type 2 diabetes who underwent BMPRP pancreas transplantation, there were 32 effective cases and 17 cases with no obvious effect. There was no difference in general, gender or age between the effective and ineffective groups. However, the body size of the ineffective group was obese, did not exercise, did not pay attention to the control of carbohydrate diet, could not control alcohol consumption, and tested positive insulin antibodies, which were significantly different from the effective group. Comparing the changes of fasting blood glucose between the two groups, the effective group was significantly lower than the ineffective group after 3 months, and the HBA1c in the effective group had a decreasing trend at 3 months, which was not statistically significant, and the decrease was very significant after 6 months. There was no significant change in C-peptide level between the two groups. It may be because C-peptide level of type 2 diabetes is not significantly lower, and some patients are higher than normal level. After pancreatic infusion therapy with autologous bone marrow cells, combined with appropriate exercise and controlled carbohydrate diet, islet function is improved, fasting blood glucose and glycated hemoglobin levels are reduced, and C-peptide level is not changed much. Some diabetic patients with insulin and hypoglycemic drugs combined with proper exercise and carbohydrate-controlled diet for a long time still have high and unstable blood sugar, and their blood sugar decreased after pancreas infusion of autologous bone marrow cells. It could be that the islet function has improved.

The mechanism of BMPRP treating diabetes may be as follows: 1. Protection of islet beta cells: the low immunogenicity and immunomodulatory ability of stem cells can protect islet beta cells and reduce the damage caused by autoimmunity; 2. Promote β cell regeneration: the repair and regeneration function supports the differentiation of stem cells into islet cells, promotes the repair of islets and the improvement of islet structure; 3. Improving insulin resistance: Acting on target organs such as liver, skeletal muscle and fat, improving insulin sensitivity and alleviating insulin resistance in diabetic patients; 4. Immune regulation and improvement of tissue microenvironment: stem cell paracrine effect can improve tissue microenvironment and promote islet damage repair.

6. Conclusion

The findings suggest that BMPRP pancreatic infusion can improve pancreatic function and glycemic control in type 2 diabetes patients. However, for optimal outcomes, it is crucial to combine this therapy with a regimen that includes regular exercise and strict management of carbohydrate intake. This multifaceted approach promises to enhance the effectiveness of BMPRP therapy and contribute to better overall management of type 2 diabetes.

Abbreviations

BMPRP	Bone Marrow Platelet-Rich Plasma
IGF1	Insulin-like Growth Factor 1
IPSCs	Induced Pluripotent Stem Cells
BMI	Body Mass Index
HbA1c	Hemoglobin A1c

Conflicts of Interest

The authors declare no conflicts of interest.

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