

Clinical observation of 32 cases with transplantation of autologous bone marrow stem cells on diabetes and its complications

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Abstract: By observing the curative effect of autologous stem cells changes before and after the treatment, to explore the stem cell treatment of diabetes and its complications. 32 patients were type 2 diabetic patients with different complications. By intravenous injection of autologous stem cells, observe improving symptoms, signs and auxiliary examination of patients after three months. Evaluation index: glycated hemoglobin level; ankle brachial pressure index (ABI); limb electromyogram; 24h urine protein quantity. Diabetic complications of different systems and glycated hemoglobin can be effectively improved. Conclusion: This research and application of autologous bone marrow stem cell transplantation for treatment of type 2 diabetes chronic complications achieves certain results, non-toxic side effects occurring. Just only preliminary observes the clinical effect, a small sample size. We need to expand the sample and observation period further for the long-term efficacy and side effects.

Keywords: Autologous bone marrow stem, transplantation diabetes, complications.

INTRODUCTION

With the ever-increasing incidence of Type 2 diabetes, its chronic complications have done great harm to people's health while the regular treatment is not so efficient. The application of stem cell transplantation in clinical trials has begun in the 1990s (Asahara *et al.*, 1997; Isner *et al.*, 1999; Ji Bu-qiang *et al.*, 2004). At the very initial phase, the bone marrow transplantation was used for the treatment of intractable diseases such as cancer, leukemia. Then the application was gradually transformed into clinical trials from animal experiments (Tateishi-Yuyama *et al.*, 2002). The study from allogenic cord stem cell transplantation to autologous bone marrow stem cell transplantation has captured the widespread attention of the medical community, for which contributed to the improvement of the rejection reactions and the solution of medical ethics problems. The study on autologous bone marrow stem cell transplantation has expanded continuously since the entry of 21st century (Tes *et al.*, 2003; Tse *et al.*, 2003). Certain effects were achieved from the clinical trials on the upper extremity lesion and vascular lesion made by surgeons (Gu Yong Quan *et al.*, 2006). The number of samples per single study also expanded to 62pcs. The application also expanded into the treatment on diabetic foot and it showed fairly good curative effects (Yang Xiao Feng *et al.*, 2005, Du Wu ling *et al.*, 2005). The effects achieved on the autologous bone marrow stem cell transplantation in the treatment of type I diabetes were ever reported both at home and abroad (Jiang *et al.*, 2007). Influenced by the ethics problems, the basic researches on autologous bone marrow stem cell transplantation for the treatment of diabetes have grown except China in the recent 5 years, while the research on

its mechanism is immature yet and the researches on the treatment of type II diabetic chronic complications are little. The writers have launched the study of autologous bone marrow stem cell transplantation on the treatment of type 2 diabetic chronic complications, and achieved sound short-term effects. Now the clinical observations on the 32 cases of patients are reported as follows.

MATERIALS AND METHODS

General data

All the 32 cases were type II diabetic patients in our hospital, among which, there were 19 males and 13 females, aged from 52 to 85 years, averaged (66.5 ± 7.9) years, with the courses of disease from 10 to 25 years; 10 cases complicated with hypertension, 8 cases of lipid abnormality, 11 cases of coronary heart disease, 5 cases with old myocardial infarction, 7 cases of cerebral infarction. From the observations among the clinical record documents for the 32 cases, there were 26 cases with diabetic peripheral neuropathy, 16 cases with retinopathy, 28 cases with autonomic neuropathy, 16 cases with diabetic nephropathy (above period III), 14 cases with vascular lesions. Among those with autonomic neuropathy, there were 3 cases with male sexual dysfunction, 13 cases with cranial nerve lesion, 24 cases with gastroparesis, 13 cases with excretion disorder, 14 cases with cardiovascular disease and 13 cases with perspiration disorder.

Observation indexes

Patients with treatment of stem cell transplantation after 3 months. Glycated hemoglobin level; ankle brachial pressure index (ABI); limb electromyogram; 24h urine protein quantity.

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Extraction of autologous bone marrow stem cells

250 ml of bone marrow (heparin) was extracted from bilateral posterior superior iliac spines through the bone marrow puncture, after the local anesthesia with 2% lidocaine, under the strict aseptic conditions that were achieved after 4 weeks of conventional diffusion tube, hypoglycemic and anti infection treatments in the hospital. The bone marrow (heparin) extracted were further separated by way of lymphocyte separation medium according to gradient centrifugation on the ultra clean operation bench and constituted into mononuclear cell suspension with around 10ml for transplantation. The total amount of mononuclear cell suspension to be counted is (5 ~ 6) * 10⁸/ml/kg.

Transplantation of autologous bone marrow stem cells

Patients were slowly dripped with autologous bone marrow stem cell suspensions through intravenous infusion and attention were paid onto the monitoring of patients' vital signs. All the cases studied were based on the consent of patients' sides, after the sufficient communication, the signature on both medical informed consent and scheme options.

Main observation indexes: symptoms of patients after operation, signs improvement, auxiliary examination results, the occurrence of toxic and side-effects, therapeutic effect evaluated in three months after the operation.

RESULT

Clinical effect

Among the 32 cases, there were 26 cases with diabetic peripheral neuropathy (A1 group), 21 cases of the 26 in effect thus the efficiency of 80%, and the onset time beginning from 2-6 weeks after transplantation; 16 cases with retinopathy (A2 group), all with invisible improvement after 4 weeks of observation thus the efficiency of 0%, 10 cases of the 16 with visible improvement after 3 months thus the efficiency of 62.5%; 28 cases with autonomic neuropathy thus the efficiency of 80% including one cases of male sexual dysfunction in effect (A3 group), 13 cases with brain lesion and all with symptom improvements thus the efficiency of 100% and onset time after 3-15 days (A4 group), 24 cases with gastroparesis (A5 group), all in effect after 1-3 weeks thus the efficiency of 100%; 13 cases with excretion disorder (A6 group), 10 cases of the 13 in effect, with the

Table 2: Comparison of curative effect before and after treatment

	Glycated-hemoglobin %		Ankle-brachial-pressure U/ml		Limb-electromyogram (cm/s)		24 urine-protein mg/l	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Patients	9.2 ± 3.8	7.5 ± 2.1	0.5 ± 0.2	0.8 ± 0.1	28 ± 8.4	55 ± 4.1	200 ± 38	56 ± 11

efficiency of 100% and the onset time after 7-15 days; 14 cases with cardiovascular disease (A7 group), 7 cases of the 14 in effect thus the efficiency of 50% and onset time after 4 weeks; 13 cases with perspiration disorder (A8 group), 6 cases of the 13 in effect thus the efficiency of 42.6%; 16 cases with diabetic nephropathy (above period III) with the efficacy of 100% and the onset time after 4-12 weeks (A9 group), 14 cases with vascular lesions (A10 group), all with rapid symptom improvements thus the efficiency of 100% and the onset time after 3-5 days, but with no visible improvement in the radiography after three months (table 1).

Table 1: Efficiency of diabetic complications

Groups	Efficiency (%)
A1	80
A2	62.5
A3	100
A4	100
A5	100
A6	100
A7	50%
A8	42.6%
A9	100
A10	100

Observation indexes

The glycated hemoglobin was effectively decreased to (7.5 ± 2.1)% in three months after the treatment from the (9.2 ± 3.8)% before the treatment; ankle brachial pressure index was increased to (0.8 ± 0.1) from the (0.5 ± 0.2); limb electromyogram was increased to (55 ± 4.1) cm/s from the (28 ± 8.4) cm/s; 24h urine protein quantity was effectively decreased to (56 ± 11) mg/l from the (200 ± 38) m g/l (table 2).

Toxicity and side effects

No toxic and side effect was found among all the medical records for study.

DISCUSSION

Due to materials extracted from autologous tissues of patients and no rejection nor ethical barriers, there is a high feasibility for the application of autologous bone marrow stem cell transplantation from the view of operation. And quite poor is the effect of the conventional

treatments on the chronic complications of diabetes mellitus. At the same time, the application of autologous bone marrow stem cell transplantation on the treatment of type 2 diabetes chronic complications has been proved to be effective and safe. Compared with the results from other researches in recent years, the study has the following features. First, the number of samples is much more. Second, the observation almost contains all the common chronic complications of type 2 diabetes. Third, preliminary observations have been made onto the most effective time of chronic complications, with a result of no side effects found in short-term.

CONCLUSION

The current clinical studies on stem cell transplantation as a new method for the treatment of diabetes mellitus have begun small-scale, and taken Preliminary results (Couri *et al.*, 2009) the Brazil researchers using large dose of immunosuppressant after autologous nonmyeloablative hematopoietic stem cell transplantation in the treatment of 15 patients with newly diagnosed type 1 diabetic patients, the results in 7~36 months of follow-up, 14 patients discontinued insulin (for up to 35 months, the shortest is also up to 1 months), including 13 cases of glycosylated hemoglobin maintain a level below 7%. Shen Shanmei *et al.* (2008) was the first domestic autologous nonmyeloablative hematopoietic stem cell transplantation for the treatment of type 1 diabetic patients, the twenty-seventh day after transplantation discontinued insulin began nearly 2 years, good blood sugar control, HbA1c stability in 7% the following, C-P level was increased before transplantation; Michael (Michael *et al.*, 2008) the 15 patients aged over 1 with type 1 diabetes itself through peripheral vein injection of umbilical cord blood. After 2 years of continuous observation, found that subjects with insulin and metabolic control of situation improved, without adverse reaction.

This study makes a preliminary observation on the clinical effect of autologous bone marrow stem cells transplantation in the treatment of type 2 diabetic chronic complications. Based on a bigger sample size and more cases about the chronic complications of type 2 diabetic, it deserves for further researches and applications. Due to the time limited, there is no observation on the curative effects in long term nor on the side effects. Though the sample size is big, the research method is quite simple, there is little discussion on the working mechanism. It needs further study based on the expansion of sample size and observation periods.

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