DOI: https://doi.org/10.54393/pbmj.v5i4.364

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

Volume 5, Issue 4 (April 2022)

Case Report

Management of Type II Diabetes Mellitus using Adult Autologous Adipose-derived stem Cells with Platelets Rich Plasma

Shahzad Anwar[1], Ayesha Nawaz[2] and Zaigham Abbas[2]*

[1]Iffat Anwar Medical Complex, Awaisia Housing Scheme, Lahore, Pakistan

[2]Institute of Microbiology and Molecular Genetics, University of the Punjab, Quaid-e-Azam Campus, Lahore, Pakistan

ARTICLE INFO

Key Words:

Diabetes Mellitus, Adults, Adipose, Platelets Rich Plasma

How to Cite:

Anwar, S. ., Nawaz, A. ., & Abbas, Z. . (2022). Management of Type II Diabetes Mellitus using Adult Autologous Adipose derived stem cells with Platelets Rich Plasma (PRP): Management of T2DM using stem cells with PRP. Pakistan BioMedical Journal, 5(4). https://doi.org/10.54393/pbmj.v5i4.364

***Corresponding Author:**

Zaigham Abbas,

Institute of Microbiology and Molecular Genetics, University of the Punjab, Quaid-e-Azam Campus, Lahore, Pakistan

zaigham.mmg@gmail.com

Received Date: 4th April, 2022

Acceptance Date: 22nd April, 2022

Published Date: 30th April, 2022

ABSTRACT

Type II diabetes mellitus (T2DM) is known as non-insulin-dependent diabetes mellitus. Insulin impairment and insulin resistance are the major causes of T2DM. People with T2DM are more prone to macro-vascular and microvascular impediments. Adult Autologous Adipose-derived stem cells (ADSC) hold the potential to develop into multi-lineage and they can secrete numerous growth factors that can regenerate the damaged neighboring cells. The chronic wound healing processes and diabetes-associated complications are reported to be treated by using stem cells by revascularization and by promoting microvascular remodeling. **Objective:** To evaluate the safety and efficacy of Adipose-derived autologous stem cells and PRP in patients suffering from Type 2 Diabetes Mellitus. **Methods:** We reported three cases aged 50, 69, and 72 years suffering from T2DM since 20, 10, and 20 years respectively. They were treated with Adult autologous ADSC and Platelets Rich Plasma (PRP). **Results:** Over a follow-up of twelve months, significant control in glycemia as well as stable glycosylated hemoglobin with a decrease in pain on the Visual Analogous scale (VAS) score has been observed. **Conclusions:** It is concluded that Adult Autologous ADSC with PRP is effective in the management of T2DM.

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders associated with a number of complications. Among non-communicable diseases NCDs, diabetes mellitus is on the fourth list identified by World Health Organization (WHO) which needs attention as the death rate over 10 years increased up to 31.1% in 2016 [1]. Prevalence of diabetes mellitus is increased to 8.5% globally with a standard mortality ratio of 4.5 in developed countries. An International Diabetes Federation (IDF) report in 2015 predicted that the number of diabetes-affected adults worldwide will rise from 422 million in 2017 to 642 million in 2040 [2]. There are three major types of diabetes which are classified as type I, type II, and Type III. Type II diabetes (T2DM) can be prevented and delayed by early diagnosis and screening tests of individuals having high risk [3]. The impaired insulin homeostasis involves the combined effect of both environmental and genetic factors. The pathophysiology commotions in this disease are the consequences of the abnormalities in multiple antidiabetic agents [4]. Different types of stem cells have been studied for the last few years. Adipose-derived stem cells (ADSC) are one of them [5]. Adult autologous ADSC emerged as an innovative therapy for repairing damaged tissues as well as being involved in reducing diabetes-associated complications [6]. Adipose tissues provide rich and accessible supplies of adult stem cells that are multipotent

DOI: https://doi.org/10.54393/pbmj.v5i4.364

and have the ability to differentiate along the chondrocyte, adipocyte, neuronal, myocyte, and osteoblast lineages. These cells have the ability to provide hematopoietic support and they can be used for gene transfer. Adult autologous ADSC holds potential repair applications for both acute and chronic tissue damage [7]. Platelet-rich plasma (PRP) contains various growth factors having a significant role in wound healing and tissues repair by inhibiting the release of inflammatory mediators as well as providing nutrients for cell proliferation and differentiation [8]. PRP has recently emerged as a promising therapeutic approach that accelerates the healing of damaged tissues by providing several essential growth factors such as platelet-derived growth factors, transforming growth factor-β, insulin-like growth factor, vascular endothelial growth factor, and epidermal growth factors which collectively play significant roles in repair mechanisms of soft and hard tissues Oxidative stress, known to be a root cause for dysfunctioning of β cells, impaired glucose tolerance and insulin resistance that can be overcome by using PRP which decreases oxidative stress and aid diabetic patients by reducing severe complications of diabetes [9]. In our study, Adult autologous ADSC with PRP has shown significant results. We report three patients with T2DM treated with stem cells therapy (SCT) in combination with PRP.

CASE REPORTS

Case 1

A 50-year-old man presented in March 2010 with classical characteristics of T2DM such as peripheral polyneuropathy, recurrent bleeding, and retinopathy. He was a known case of T2DM for last 20 years.

Case 2

A 69- year-old man was subjected in April 2017 with rheumatoid heart disease (RHD) and usual symptoms of T2DM such as polydipsia, polyphagia, paresthesia, and numbness in both feet accompanied by low ejection fraction, diabetic neuropathy defects with macrovascular changes. He has been subjected to T2DM for the past 10 years.

Case 3

A 72-year-old man was subjected in July 2017 with similar triads of T2DM such as hypertensive, hyperuricemia, renal insufficiency as creatinine level (1.6mg\dl) for the last 5 years, nephropathy with twisting of knee joints resulting in ligaments injury. He was a known case suffering from T2DM since 1999.

INVESTIGATIONS

Case 1

The fasting blood glucose level was 189mg/dL while the postprandial blood glucose level was recorded at 288mg/dL. On the onset of admittance, the glycosylated hemoglobin (HbA1c) was 12.3%. The pain score on Visual Analogous Scale (VAS) score was 7/10.

Case 2

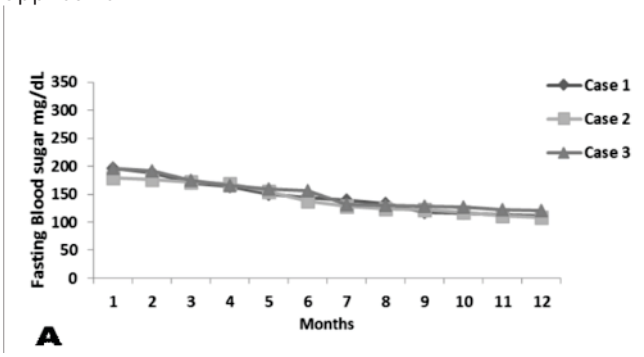
Fasting blood sugar and postprandial blood sugar were 180mg/dL and 307mg/dL respectively. At the start of treatment, the glycosylated hemoglobin (HbA1c) was 13.5% while the pain score on Visual Analogue Scale score was 7/10.

Case 3

Fasting blood sugar and postprandial blood sugar were 196mg/dL and 269mg/dL respectively. At the start of treatment, the glycosylated hemoglobin (HbA1c) was 12.6% while the pain score on Visual Analogue Scale score was 8/10.

TREATMENT

All three patients were treated with PRP for 2 sessions; the treatment included taking 60 ml of blood from the patient and centrifuging it at 2800 rpm for 15 minutes with a soft spin centrifuge. After the centrifugation, the buffy coat was carefully extracted with a total volume of 6 ml. The buffy coat/ PRP was activated using monochromatic LED lights of different wavelengths for 15 min. After the photo-activation, the PRP was given intravenously in 100 ml of normal saline over a period of 2 hours with cardiac monitoring. Two sessions of PRP therapy was given at a 2-week interval. After another 2 weeks, patients were also administrated with one session of Adult Autologous ADSC treatment. The treatment included lipo aspiration under local anesthesia; a total of 200 ml of fat was aspirated in each patient. The fat was then transported to Cell processing lab into the Biosafety cabinet class II type A2. A. In the safety cabinet, the lipoaspirate is washed with an equal volume of normal saline or PBS three to four times to remove contaminants and red blood cells from the fat. 1% Novidat and Collagenase type 1 (1mg/ml) solution was added to the fat and mixed using a vortex followed by its incubation at 37°C for 30-45 minutes in a shaking incubator to digest the fat tissues. The digested fat is collected in a new falcon tube and centrifuge at 2800rpm for 15 minutes and SVF is collected in the form of a pellet. SVF pellet is washed two times with PBS and dissolved in PRP for clinical application.



DOI: https://doi.org/10.54393/pbmj.v5i4.364

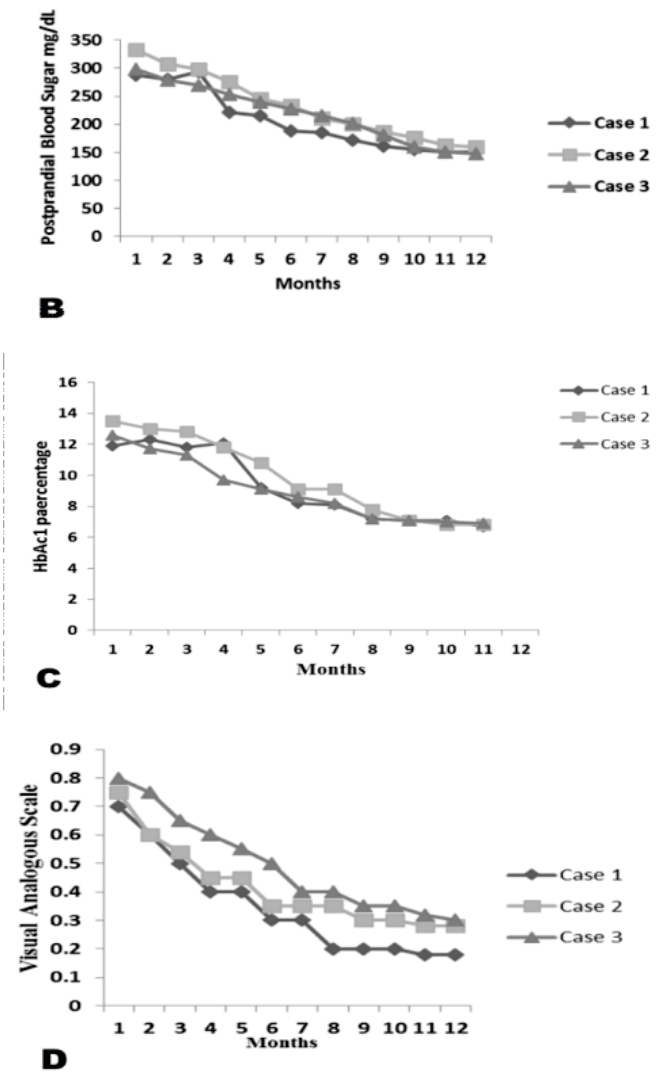


Figure 1: (A) Patients fasting blood sugar level before and after treatment; (B) Patients postprandial blood sugar level before and after treatment; (C) Patients HbAc1 control before and after treatment; (D) Patients visual analogous scale scores before and after treatment

OUTCOMES AND FOLLOW-UP

Over a follow-up of 12 months, significant results were obtained as the fasting blood sugar ranges 117-113mg/dL while the postprandial blood sugar was recorded as 167-162mg/dL. The HbA1c was 7.1% and VAS score was reduced to 2/10 for case 1. Whereas case 2 ,the fasting blood sugar ranges 162-108mg/dL while the postprandial blood sugar was recorded as 176-162mg/dL. The HbA1c was 7.0% and VAS score was reduced to 3.5/10. The fasting blood sugar of case 3 ranges from 126-122mg/dL while the postprandial blood sugar was recorded as 159-151mg/dL. The HbA1c was 7.2% and VAS score was reduced to 4/10.

DISCUSSION

Diabetes is a serious, chronic disorder associated with many complications. It is a metabolic disorder in which defects in insulin secretion or destruction of insulin action or the occurrence of both take place [10]. The long-term hyperglycemic state can result in serious and chronic complications including peripheral neuropathy, which is responsible for damaging the autonomic, sensory, and motor nerve fibers in diabetic patients [11]. PRP is a revolutionary treatment, which can be used as an alternative, and a more secure mean for the reduction of diabetic-associated complications [12]. As, PRP is known to be a suitable cost-effective as well as an easy method that is capable of providing all the necessary growth factors for proper angiogenesis, wound healing, and axon healing and proving itself an effective therapy for the cure of diabetic associated nephropathy [13]. The current treatment modalities for curing diabetic-associated complications include the use of bone marrow-derived stem cells, negative pressure dressings, bioengineered skin transplant, growth factors therapies, hyperbaric oxygen treatment, and chemical debridement techniques [14]. In this context, the adult Autologous ADSC has the capability to differentiate and give rise to multiple lineages. These stem cells possess angiogenic properties due to the secretion of their cytokines thus capable of healing acute as well as chronic wounds [15]. Tissue damage in chronic diseases as well as in acute ADSC has the potential to treat them. These stem cells can be copiously and safely isolated this feature makes them an ideal candidate for the treatment of diabetic-associated complications [16]. Treatment with stem cells affected by cell singling pathways like Wnt, Notch, hedgehog as well as different transcription factors Ngn-3, MafA, PDX-1 and Nkx6-1. Gene regulation is a controlling factor to differentiate the stem cells into specialized cells [17]. In streptozotocin-induced diabetic rats, transplantation of Adult Autologous ADSC with transduction in pancreatic duodenal homeobox 1(PDX-1) gene results in lowering blood glucose level, increased glucose tolerance, fewer cataracts with smoothing of fur [18]. The report shows that patients are prevented from the deterioration and end-organ damage occurring during diabetes with time-scale progression. As the steady decrease in blood glucose sugar has been evident which on other hand is possibly responsible for lowering glycosylated HbA1C and reducing pain on the visual analogue scale (VAS) score. PRP is a new treatment known as 'orthobiologics' in the current health sector. The purpose of this practice is to improve the body's natural ability to heal and renew. PRP therapy has recently attracted a lot of attention as a non-surgical, biological treatment for diabetes and its consequences [19,20]. According to our knowledge, this case report showed significant approach for the treatment of T2DM and

DOI: https://doi.org/10.54393/pbmj.v5i4.364

associated complications and these strategies will open up new avenues for the treatment of T2DM and its associated complications.

CONCLUSIONS

It is concluded that Adult Autologous ADSC with Platelets Rich Plasma (PRP) is effective in the management of type II Diabetes Mellitus.

REFERENCES

[1] Liu M, Liu SW, Wang LJ, Bai YM, Zeng XY and Guo HB et al. Burden of diabetes, hyperglycaemia in China from to 2016: Findings from the 1990 to 2016, global burden of disease study. Diabetes Metab. 2019;45(3):286-293. doi: 10.1016/j.diabet.2018.08.008.

[2] Chatterjee S, Khunti K and Davies MJ. Type 2 diabetes. Lancet. 2017;389(10085):2239-2251. doi: 10.1016/S0140-6736(17)30058-2.

[3] Songthung P and Sripanidkulchai K. Improving type 2 diabetes mellitus risk prediction using classification. In2016 13th International Joint Conference on Computer Science and Software Engineering (JCSSE). 2016:1-6. doi: 10.1109/JCSSE.2016.7748866.

[4] DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH and Holst JJ et al. Type 2 diabetes mellitus. Nat Rev Dis Primers. 2015;1:15019. doi: 10.1038/nrdp.2015.19.

[5] Hassan WU, Greiser U and Wang W. Role of adipose-derived stem cells in wound healing. Wound Repair Regen. 2014;22(3):313-25. doi: 10.1111/wrr.12173.

[6] Moshtagh PR, Emami SH and Sharifi AM. Differentiation of human adipose-derived mesenchymal stem cell into insulin-producing cells: an in vitro study. Journal of physiology and biochemistry. 2013;69(3):451-458. doi.org/10.1007/s13105-012-0228-1.

[7] Gimble J and Guilak F. Adipose-derived adult stem cells: isolation, characterization, and differentiation potential. Cytotherapy. 2003;5(5):362-9. doi: 10.1080/14653240310003026.

[8] Wei S, Xu P, Yao Z, Cui X, Lei X and Li L et al. A composite hydrogel with co-delivery of antimicrobial peptides and platelet-rich plasma to enhance healing of infected wounds in diabetes. Acta Biomater. 2021;124:205-218. doi: 10.1016/j.actbio.2021.01.046.

[9] Wright E Jr, Scism-Bacon JL and Glass LC. Oxidative stress in type 2 diabetes: the role of fasting and postprandial glycaemia. Int J Clin Pract. 2006;60(3):308-14. doi: 10.1111/j.1368-5031.2006.00825.x.

[10] Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H and Uribe KB et al. Pathophysiology of Type 2 Diabetes Mellitus. Int J Mol Sci. 2020;21(17):6275. doi: 10.3390/ijms21176275.

[11] Wu B, Niu Z and Hu F. Study on Risk Factors of Peripheral Neuropathy in Type 2 Diabetes Mellitus and Establishment of Prediction Model. Diabetes Metab J. 2021;45(4):526-538. doi: 10.4093/dmj.2020.0100.

[12] Del Pino-Sedeño T, Trujillo-Martín MM, Andia I, Aragón-Sánchez J, Herrera-Ramos E and Iruzubieta Barragán FJ et al. Platelet-rich plasma for the treatment of diabetic foot ulcers: A meta-analysis. Wound Repair Regen. 2019;27(2):170-182. doi: 10.1111/wrr.12690.

[13] El-Tahawy NF, Rifaai RA, Saber EA, Saied SR and Ibrahim RA. Effect of platelet rich plasma (PRP) injection on the endocrine pancreas of the experimentally induced diabetes in male albino rats: a histological and immunohistochemical study. J Diabetes Metab. 2017;8(730):2. DOI: 10.4172/2155-6156.1000730.

[14] Mulder G, Tenenhaus M and D'Souza GF. Reduction of diabetic foot ulcer healing times through use of advanced treatment modalities. Int J Low Extrem Wounds. 2014;13(4):335-46. doi: 10.1177/15347 34614 557925.

[15] Bajada S, Mazakova I, Richardson JB and Ashammakhi N. Updates on stem cells and their applications in regenerative medicine. J Tissue Eng Regen Med. 2008;2(4):169-83. doi: 10.1002/term.83.

[16] Utsunomiya T, Shimada M, Imura S, Morine Y, Ikemoto T and Mori H et al. Human adipose-derived stem cells: potential clinical applications in surgery. Surgery today. 2011;41(1):18-23.

[17] Biswas S. A review on the progress of stem cell therapy as a treatment for Diabetes mellitus (Doctoral dissertation, Brac University). 2022.

[18] Lin G, Wang G, Liu G, Yang LJ, Chang LJ and Lue TF et al. Treatment of type 1 diabetes with adipose tissue-derived stem cells expressing pancreatic duodenal homeobox 1. Stem Cells Dev. 2009;18(10):1399-406. doi: 10.1089/scd.2009.0010.

[19] Dhillon RS, Schwarz EM and Maloney MD. Platelet-rich plasma therapy-future or trend?. Arthritis research & therapy. 2012;14(4):1-0. doi.org/10.1186/ar3914.

[20] Monnier L, Mas E, Ginet C, Michel F, Villon L and Cristol JP et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA. 2006;295(14):1681-7. doi: 10.1001/jama.295.14.1681.