

# Efficacy of Autologous Bone Marrow-Derived Mesenchymal Stem Cell Transplantation in patients with T2DM : A Randomized Placebo-Controlled Study

Shobhit Bhansali\*, V. Kumar#, V. Jha#, N. Marwaha‡, N. Khandelwal†, A. Bhansali\*, P. Dutta\*.

Department of Endocrinology\*, Nephrology/Translational and Regenerative Medicine #, Radiodiagnosis† and Transfusion Medicine‡, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

## INTRODUCTION

The prevalence of diabetes is rapidly increasing and the number is around 382 millions which is expected to reach 592 million by the year 2035. T2DM is characterized by two major defects : insulin resistance and insulin deficiency. Current therapies in T2DM targeting  $\beta$ -cells are insulin, glitazones and GLP-1 analogs. However these therapies have no role in  $\beta$ -cells regeneration. Therefore, this led to the emergence of novel  $\beta$ -cells regenerative therapies like HSC, MNCs and MSCs.

## AIM

To evaluate the efficacy of autologous bone marrow derived mesenchymal stem cell transplantation (AB-MSCT) in patients with T2DM.

### Objectives

- To analyze the efficacy and safety of ABMSCT in patients with T2DM.
- To assess the alteration in  $\beta$ -cell function and insulin sensitivity index by hyperglycemic clamp and glucagon stimulation test before and after six months of AB-MSCT in patients with T2DM.

### Primary outcome measure:

Reduction of insulin requirement by  $\geq 50\%$  compared with baseline while maintaining HbA1C < 7%

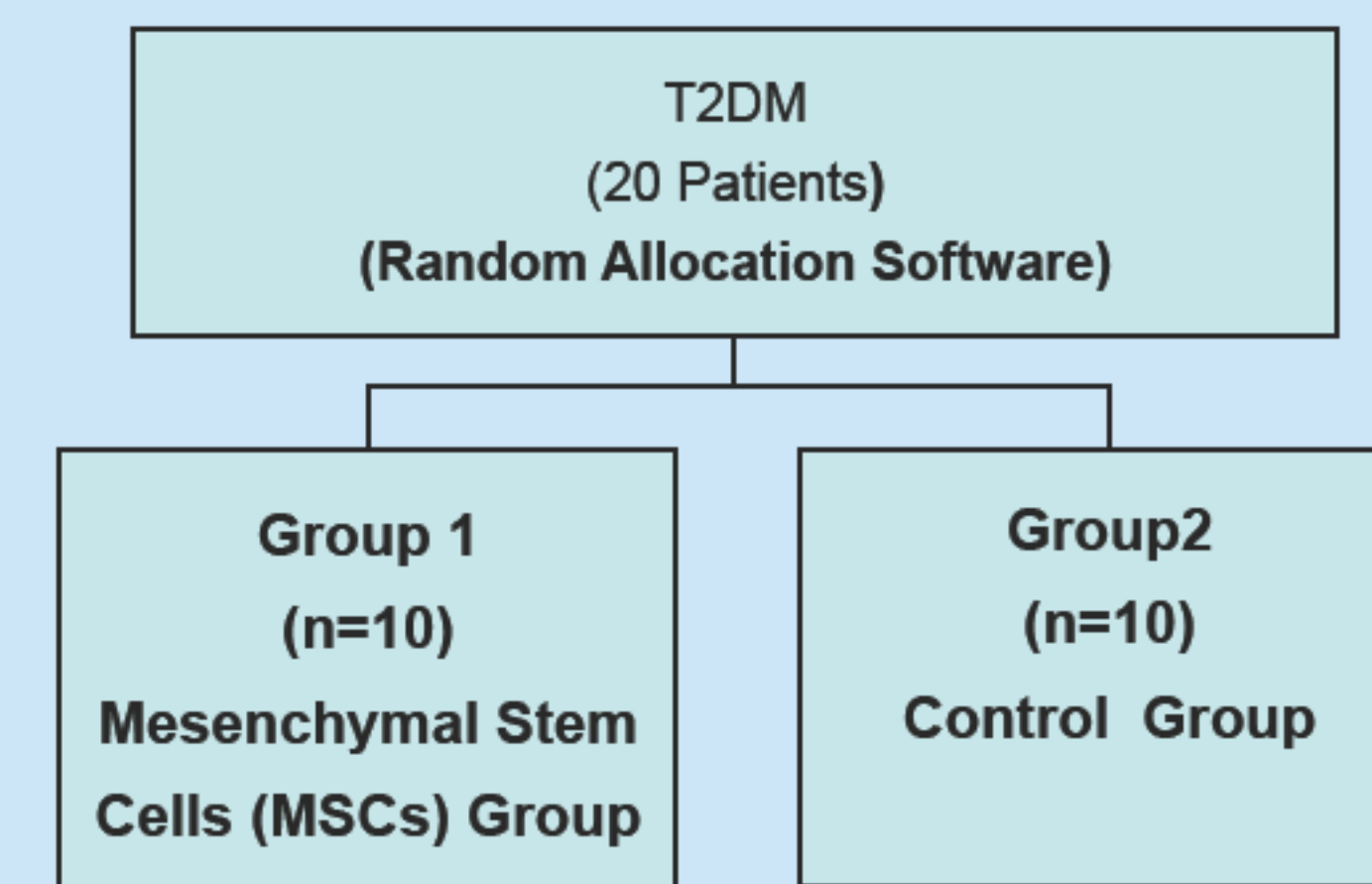
### Secondary outcome measure:

- Alterations in weight, HOMA – IR, HOMA - $\beta$
- Safety profile of ABMSCT at least for a period of six months.

## METHODS

Inclusion criteria	Exclusion criteria
Patients with T2DM aged 30-65 yrs	Patient with T1DM
Duration of diabetes >5 years	Serum creatinine >1.5 mg/dl
Failure of triple OHA	Active infections
Insulin requirement $\geq 0.4$ IU/kg/day for at least one year	Malignancy
GAD Ab negative	Acute coronary syndrome in the previous 3 months
On stable dose of insulin, metformin (2 g/day) and pioglitazone (15mg/day) for the past 3 months.	

### Study Design



MSCs Group	Control Group
Bone marrow aspiration (100 ml) were done from postero-superior iliac spine.	Bone marrow aspiration (20 ml) were done from postero-superior iliac spine
Marrow cell suspension- cultured in MSC specific media <sup>1</sup> After 10 days of culture- adherent cells formed homogenous fibroblast-like colonies.	
Characterization of MSC by Flow Cytometry (CD 73, CD 90, CD 105, CD 34 and CD 45).	
One million cells /kg body weight was injected through superior pancreatico-duodenal artery (SPD) <sup>2</sup> .	Vitamin B-12 was injected through SPD.

HbA1c, glucagon stimulation C-peptide, HOMA- $\beta$ , HOMA-IR and insulin sensitivity were done at baseline and at 6 month.

## RESULTS

### Comparison of baseline characteristics in different groups

Parameters	MSCs (n=10)	Controls (n=10)	P value
Age (years)	50.5 (36.0-58.0)	53.5 (43.3-58.8)	0.456
Sex (M:F)	8:2	6:4	
Duration of diabetes (years)	15.0 (8.0-22.8)	14.0 (9.0-15.0)	0.586
Duration of insulin therapy (years)	6.5 (2.5-11.0)	2.0 (0.9-5.3)	0.121
Weight (Kg)	81.5 (70.2-91.6)	69.3 (64.9-72.9)	0.265
BMI(kg/m <sup>2</sup> )	28.1 (26.5-31.6)	25.7 (24.5-28.9)	0.533
FPG(mg/dL)	104.0 (92.5-112.5)	103.5 (98.5-120.0)	0.600
Insulin requirement (U/day)	45.5 (34.0-52.25)	48.5 (29.5-76.0)	0.198
HbA1c(%)	6.9 (6.6-7.0)	6.5 (6.2-6.8)	0.563
Fasting C-pep (ng/ml)	1.1(1.0-1.3)	1.5 (1.3-2.1)	0.161
Stimulated C-pep (ng/ml)	2.1 (1.7-2.5)	2.7 (2.2-3.9)	0.226
HOMA-IR (%)	3.7(1.5-4.7)	1.2(0.9- 1.7)	0.046
HOMA- $\beta$ (%)	179.0(96.0-228.5)	79.7(59.7-97.3)	0.015
HOMA 2 (%S)	27.0 (21.6-82.8)	84.1(60.0-103.7)	0.045

### Follow-up characteristics of patients treated with MSCs

Parameters	Baseline	6 months	P value
Weight (Kg)	81.5 (70.2-91.6)	79.8 (64.6-88.0)	0.004*
Insulin requirement (U/day)	45.5 (34.0-52.25)	25.0 (15.0-32.5)	0.008*
HbA1c(%)	6.9 (6.6-7.0)	6.8 (6.4-7.3)	0.441
BMI(kg/m <sup>2</sup> )	28.1 (26.5-31.6)	27.5 (24.0-30.4)	0.004*
FPG(mg/dL)	104.0 (92.5-112.5)	110.5 (106.7-115.5)	0.161
Fasting C-pep (ng/ml)	1.1 (1.0-1.3)	1.6 (1.4-1.7)	0.047*
Stimulated C-pep (ng/ml)	2.1 (1.7-2.5)	2.7 (1.9-3.7)	0.074
HOMA-IR (%)	3.7 (1.5-4.7)	1.2 (1.0-1.3)	0.028*
HOMA- $\beta$ (%)	179.0 (96.0-228.5)	65.6 (63.5-73.3)	0.028*
HOMA 2 (%S)	27.0 (21.6-82.8)	80.2 (76.6-91.3)	0.059

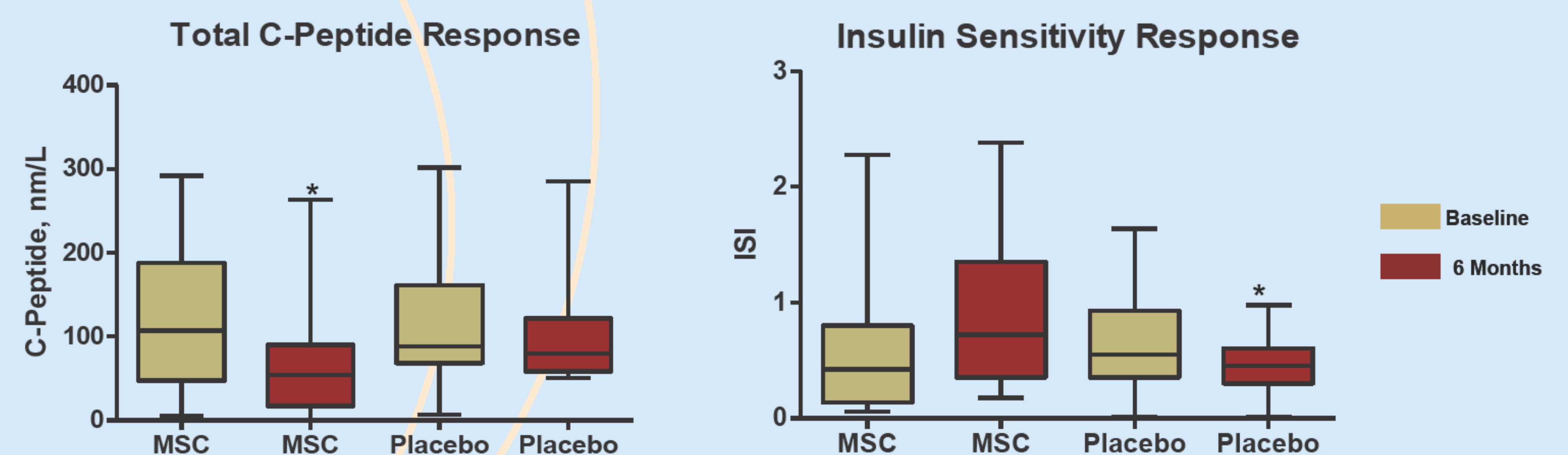
### Follow-up characteristics in control subjects

Parameters	Baseline	6 months	P value
Weight (Kg)	69.3 (64.9-72.9)	69.3 (63.1-75.6)	0.859
Insulin requirement (U/day)	48.5 (29.5-76.0)	45.0 (23.0-57.0)	0.022*
HbA1c(%)	6.5 (6.2-6.8)	6.2 (6.0-6.2)	0.262
BMI(kg/m <sup>2</sup> )	25.7 (24.5-28.9)	25.7 (24.0-28.8)	0.959
FPG(mg/dL)	103.5 (98.5-120.0)	107.0 (99.0-119.0)	0.917
Fasting C-pep (ng/ml)	1.5 (1.3-2.1)	1.8 (1.4-2.5)	0.048*
Stimulated C-pep (ng/ml)	2.7 (2.2-3.9)	3.1 (2.3-4.3)	0.192
HOMA-IR (%)	1.2 (0.9- 1.7)	1.3 (1.0-1.9)	0.093
HOMA- $\beta$ (%)	79.7 (59.7-97.3)	87.5 (74.6-100.9)	0.086
HOMA 2 (%S)	84.1 (60.0-103.7)	75.2 (51.1-92.6)	0.173

### Comparison of parameters among different groups

Parameter	MSCs (n=10)	Control (n=10)	P value
Primary End Point Achieved (%)	60%	10%	0.057
$\Delta$ Insulin requirement (U/day)	-19.0 (-25.0 to -12.3)	-4.5 (-17.3 to -2.0)	1.000
$\Delta$ HbA1c(%)	-0.1(-0.4 to 0.3)	-0.4 (-0.9 to 0.3)	0.481
$\Delta$ Fasting C-pep (ng/ml)	0.4 (0.3 to 0.6)	-0.2 (-0.3 to 0.0)	0.063
$\Delta$ Stimulated C-pep (ng/ml)	0.3 (0.0 to 0.6)	0.1 (-0.1 to 0.5)	0.529
$\Delta$ HOMA-IR (%)	-2.5 (-3.4 to -0.3)	0.1 (-0.0 to 0.3)	0.190
$\Delta$ HOMA- $\beta$ (%)	-117.1(-152.2 to -27.7)	11.2 (-2.9 to 16.9)	1.000
HOMA 2 (%S)	57.5 (-5.6 to 62.7)	-5.7 (-19.6 to 3.0)	0.105
Hypoglycemic episodes	8.5 (5.5-18.0)	4.0 (2.0-9.8)	0.218

### Total C-peptide response and insulin sensitivity response by hyperglycemic clamp (0-180 mins)



\* All values are expressed as median and interquartile range.  
\*p<0.05 for comparison between baseline and at 6 month.

## REFERENCES

- Safety and Efficacy of Autologous Mesenchymal Stromal Cells Transplantation in patients undergoing Living Donor Kidney Transplantation: A Pilot study, *Nephrology*.
- Efficacy and Safety of Autologous Bone Marrow-Derived Stem Cell Transplantation in Patients With Type 2 Diabetes Mellitus: A Randomized Placebo-Controlled Study, *Cell transplantation*

## CONCLUSION

- There is a decrease in insulin requirement in 60% of patients with use of AB-MSCT while maintaining HbA1c < 7%
- Patients receiving MSCs showed improvement in insulin sensitivity and consequently decrease in total C peptide response .
- AB-MSCT seems to be safe and effective

For any question, contact: [bhansali.o4@gmail.com](mailto:bhansali.o4@gmail.com)

