

REVIEW ARTICLE

**Bone marrow- vs. umbilical cord-derived mesenchymal stem cells for type 2 diabetes mellitus treatment: A systematic review and meta-analysis**

**Supplementary Files**

**Table S1. Summary of included studies**

Study ID	Study design	Country	SCT type	Sample size (n)			Dose of intervention	Control	Follow-up period (months)
				SCT	Control	Total			
Bhansali <i>et al.</i> <sup>1</sup>	RCT	India	BM-MSCs	11	10	21	NA	Normal saline	12
Zang <i>et al.</i> <sup>2</sup>	RCT	China	UC-MSCs	45	46	91	1 × 10 <sup>6</sup> cells/kg	Saline with 3% albumin + multivitamins	12
Bhansali <i>et al.</i> <sup>3</sup>	RCT	India	BM-MSCs	10	10	20	1 × 10 <sup>6</sup> cells/kg	Vitamin B infusion	12
Hu <i>et al.</i> <sup>4</sup>	RCT	China	UC-MSCs	31	30	61	1 × 10 <sup>6</sup> cells/kg	Normal saline	12
Skyler <i>et al.</i> <sup>5</sup>	RCT	USA	BM-MSCs	45	16	61	1.1 × 10 <sup>6</sup> cells/kg	Normal saline	3
Liu <i>et al.</i> <sup>6</sup>	Self-controlled trial	China	UC-MSCs	23	NA	23	1 × 10 <sup>6</sup> cells/kg	Self-controlled	12
Lian <i>et al.</i> <sup>7</sup>	Self-controlled trial	China	UC-MSCs	16	NA	16	1 × 10 <sup>6</sup> cells/kg	Self-controlled	3

Abbreviations: BM-MSCs: Bone marrow-derived mesenchymal stem cells; NA: Not available; SCT: Stem cell therapy; UC-MSCs: Umbilical cord-derived mesenchymal stem cells.

Table S2. Baseline demographic characteristics of included studies

Study ID	Study arms	Age	Sex (no. of males, %)	HbA1c (%)	Fasting C-peptide (ng/mL)	Daily insulin requirements (U/ per day)	FBG (mg/dl)	HOMA-IR	Stimulated C-peptide (ng/mL)
Bhansali <i>et al.</i> <sup>1</sup>	Intervention	51.17 ± 7.04	9 (81.8%)	6.83 ± 0.68	NA	45.67 ± 27.99	95.20 ± 11.84	4.80 ± 5.70	1.60 ± 1.36 <sup>a</sup>
	Control	54.10 ± 2.44	7 (70.0%)	6.70 ± 0.69	NA	38.87 ± 10.75	103.43 ± 13.87	6.67 ± 3.93	2.07 ± 1.38 <sup>a</sup>
Zang <i>et al.</i> <sup>2</sup>	Intervention	50.00 ± 9.38	28 (62.2%)	9.02 ± 1.27	2.01 ± 0.70	57.36 ± 18.90	NA	NA	1.94 ± 0.61 <sup>a</sup>
	Control	50.45 ± 8.03	30 (65.2%)	8.89 ± 1.11	1.93 ± 0.65	56.41 ± 12.54	NA	NA	1.85 ± 0.28 <sup>a</sup>
Bhansali <i>et al.</i> <sup>3</sup>	Intervention	48.17 ± 16.30	8 (80.0%)	6.83 ± 0.30	1.11 ± 0.22	44.60 ± 13.60	103.90 ± 12.05	0.83 ± 0.07	2.11 ± 0.45 <sup>a</sup>
	Control	51.87 ± 11.48	6 (60.0%)	6.50 ± 0.45	1.61 ± 0.67	51.33 ± 34.06	108.11 ± 16.28	1.27 ± 0.59	2.92 ± 1.35 <sup>a</sup>
Hu <i>et al.</i> <sup>4</sup>	Intervention	52.43 ± 4.88	17 (54.8%)	7.67 ± 1.23	1.75 ± 0.64	45.92 ± 8.87	148.27 ± 27.81	2.79 ± 0.32	NA
	Control	53.21 ± 8.22	16 (53.3%)	7.54 ± 1.31	1.83 ± 0.59	43.09 ± 10.30	142.31 ± 25.88	2.64 ± 0.27	NA
Skyler <i>et al.</i> <sup>5</sup>	Intervention	56.73 ± 8.81	28 (62.2%)	8.27 ± 1.03	3.80 ± 1.42	NA	186.07 ± 49.25	NA	NA
	Control	58.70 ± 7.30	12 (75.0%)	8.14 ± 0.80	3.97 ± 1.59	NA	179.00 ± 55.00	NA	NA
Liu <i>et al.</i> <sup>6</sup>	Intervention	52.90 ± 10.50	15 (65.2%)	8.20 ± 1.69	1.29 ± 0.83	34.55 ± 16.73	135.50 ± 48.10	NA	4.06 ± 2.77 <sup>b</sup>
	Control	NA	NA	NA	NA	NA	NA	NA	NA
Lian <i>et al.</i> <sup>7</sup>	Intervention	52.50 ± 7.91	12 (75.0%)	8.01 ± 0.63	2.24 ± 1.40	NA	173.90 ± 47.70	4.22 ± 1.91	4.83 ± 2.99 <sup>b</sup>
	Control	NA	NA	NA	NA	NA	NA	NA	NA

Notes: <sup>a</sup>Glucagon-stimulated C-peptide; <sup>b</sup>Postprandial-stimulated C-peptide. Abbreviations: C-peptide: Connecting peptide; FBG: Fasting blood glucose; HbA1c: Glycated hemoglobin; HOMA-IR: Homeostatic model assessment for insulin resistance; NA: Not available.

Table S3. Outcomes availability

Study	Design	Follow-up points	HbA1c	Fasting C-peptide	Stimulated C-peptide	FBG	Insulin Requirement	HOMA-IR
Bhansali <i>et al.</i> <sup>1</sup>	RCT	B, 6M, 12M	Available	NA	Available <sup>a</sup>	NA	Available	NA
Zang <i>et al.</i> <sup>2</sup>	RCT	B, 3M, 6M, 12M	Available	Available	Available <sup>a</sup>	NA	Available	NA
Bhansali <i>et al.</i> <sup>3</sup>	RCT	B, 3M, 6M, 12M	Available	Available	Available <sup>a</sup>	Available	Available	Available
Hu <i>et al.</i> <sup>4</sup>	RCT	B, 3M, 6M, 12M	Available	Available	NA	Available	Available	Available
Skyler <i>et al.</i> <sup>5</sup>	RCT	B, 3M	Available	Available	NA	Available	NA	NA
Liu <i>et al.</i> <sup>6</sup>	Non-RCT (self-controlled)	B, 3M, 6M, 12M	Available	Available	Available <sup>b</sup>	Available <sup>c</sup>	Available	NA
Lian <i>et al.</i> <sup>7</sup>	Non-RCT (self-controlled)	B, 3M	Available	Available	Available <sup>b</sup>	Available	NA	Available

Notes: <sup>a</sup>Glucagon-stimulated C-peptide; <sup>b</sup>Postprandial C-peptide; <sup>c</sup>FBG available at 6 and 12 months only for Liu *et al.*  
 Abbreviations: B: Baseline; C-peptide: Connecting peptide; FBG: Fasting blood glucose; HbA1c: Glycated hemoglobin; HOMA-IR: Homeostatic model assessment for insulin resistance; M: Months; NA: Not Available; RCT: Randomized controlled trial.

## References

1. Bhansali A, Asokumar P, Walia R, *et al.* Efficacy and safety of autologous bone marrow-derived stem cell transplantation in patients with type 2 diabetes mellitus: a randomized placebo-controlled study. *Cell Transplant.* 2014;23(9):1075–1085.  
doi: 10.3727/096368913X665576
2. Zang L, Li Y, Hao H, *et al.* Efficacy and safety of umbilical cord-derived mesenchymal stem cells in Chinese adults with type 2 diabetes: a single-center, double-blinded, randomized, placebo-controlled phase II trial. *Stem Cell Res Ther.* 2022;13(1).  
doi: 10.1186/s13287-022-02848-6
3. Bhansali S, Dutta P, Kumar V, *et al.* Efficacy of Autologous Bone Marrow-Derived Mesenchymal Stem Cell and Mononuclear Cell Transplantation in Type 2 Diabetes Mellitus: A Randomized, Placebo-Controlled Comparative Study. *Stem Cells Dev.* 2017;26(7):471–481.  
doi: 10.1089/scd.2016.0275
4. Hu J, Wang Y, Gong H, *et al.* Long term effect and safety of Wharton's jelly-derived mesenchymal stem cells on type 2 diabetes. *Exp Ther Med.* 2016;12(3):1857–1866.  
doi: 10.3892/etm.2016.3544
5. Skyler JS, Fonseca VA, Segal KR, Rosenstock J. Allogeneic Mesenchymal Precursor Cells in Type 2 Diabetes: A Randomized, Placebo-Controlled, Dose-Escalation Safety and Tolerability Pilot Study. *Diabetes Care.* 2015;38(9):1742–1749.  
doi: 10.2337/dc14-2830
6. Liu X, Zheng P, Wang X, *et al.* A preliminary evaluation of efficacy and safety of Wharton's jelly mesenchymal stem cell transplantation in patients with type 2 diabetes mellitus. *Stem Cell Res Ther.* 2014;5(2).  
doi: 10.1186/scrt446
7. Lian XF, Lu DH, Liu HL, *et al.* Effectiveness and safety of human umbilical cord-mesenchymal stem cells for treating type 2 diabetes mellitus. *World J Diabetes.* 2022;13(10):877–887.  
doi: 10.4239/wjd.v13.i10.877