

# Dose Response Analysis of Bone Marrow Derived Stem Cell Intra-articular Injection for The Treatment of Knee Osteoarthritis: A Systematic Review

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## INTRODUCTION:

Bone marrow-derived mesenchymal stem cells (MSCs) are a promising option to treat knee osteoarthritis (OA). Their safety and usefulness have been reported in several clinical trials. This was a systematic review aimed to determine the optimal dosage of Intraarticular Bone Marrow Derived Mesenchymal Stem Cell Injection for patients with Knee Osteoarthritis.

## METHODS:

Two independent authors performed the literature search. This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA). The main databases were accessed: Pubmed via Ovid, Cochrane Library and Scopus. For this systematic review, all articles treating percutaneous injections of bone marrow-derived mesenchymal stem cells for knee OA were considered. We included relevant studies published up till 31 May 2022 which assesses safety and efficacy of bone marrow derived stem cell injection in knee osteoarthritis and the dosage given. The statistical analysis was performed with Review Manager Software 5.4.

## RESULTS:

Ten studies met the inclusion criteria. There were no significant adverse events from the injection of MSCs compared to their controls. Our review revealed that all functional outcome indicators, including VAS for Pain, WOMAC, Lysholm, and Tegner, as well as radiological outcome metrics, such WORMS, revealed a significant improvement after MSC transplantation when compared to their corresponding controls over time. Table 1 showing the characteristics of the included studies.

Table 1. Characteristics of Included Studies.

Authors	Year	Country	Nature of Study	Reference Level/Grade	Sample Size	Treatment Group	Control Group	Mean Age (SD)		MSC Source	MSC Concentration (cells)	Follow-up (Months)			
								Treatment Group	Control Group						
Vega et al. (20)	2014	Spain	RCT	II/III	30	1515	1515	36.6 ± 9.24	37.2 ± 9.80	0609	0510	BM	Auto	4	12
Symonides et al. (21)	2014	USA	RCT	NR	55	3619	3619	44.6 ± 9.82	47.8 ± 8.4	2511	1106	BM	Auto	5.15	24
Cheng et al. (22)	2017	Malaysia	RCT	NR	45	3031	3031	35.07 ± 10.22	35.22 ± 10.28	0923	0922	BM	Auto	4	6
Labana et al. (23)	2016	Spain	RCT	II/III	30	2010	2010	45.9 ± 10.3	45.3 ± 12.08	0903	0903	BM	Auto	1	12
Cheng et al. (24)	2015	Singapore	RCT	NR	56	2828	2828	35 ± 10	35.5 ± 10.5	1414	1414	BM	Auto	1	24
Lee et al. (25)	2015	China	RCT	II	60	4800	4800	35.9 ± 3.1	35.1 ± 6.8	1426	1157	BM	Auto	1.66	12
Indudhara et al. (26)	2016	India	RCT	II/III	40	1924	1924	31.7 ± 9.2	34.7 ± 5.3	1207	1109	BM	Auto	3.02	6
Cheng et al. (27)	2016	India	RCT	III	60	4020	4020	38.16 ± 8.37	34.96 ± 8.27	1228	416	BM	Auto	2.5-15	12
Bauer et al. (28)	2019	Israel	RCT	II/III	47	3017	3017	38.16 ± 8.37	35.9 ± 10.4	1515	0908	BM	Auto	4	12
Makino et al. (29)	2002	Japan	RCT	II	24	1212	1212	35.7 ± 7.4	NR	NR	NR	BM	Auto	1	16

## DISCUSSIONS:

We comprehensively and systematically reviewed all the available literature of which are multinational, published RCTs to assess the efficacy and safety of MSC treatment for knee OA patients. Our review found that all functional outcome indicators, revealed a statistically significant improvement after MSC transplantation when compared to their corresponding controls over time. The ability of MSCs to regenerate cartilage and restore it to the articular surface is intriguing. Our analysis findings showed that MSC therapy might dramatically relieve pain, minimize symptoms, and enhance knee OA patient's function. MSC therapy has also been proved to be safe.

## CONCLUSION:

Our review establishes the efficacy and safety of BM-MSC injection in the management of osteoarthritis of the knee. Hence, these results suggest that MSC therapy has great potential as an efficacious treatment for patients with knee OA. As for the suggested dosage would be of  $4 \times 10^7$  cells as it is already sufficient for significant functional advantages of MSC therapy.

## REFERENCES:

- Vega A, Martín-Ferrero MA, del Canto F, Alberca M, García V, Munar A, et al. Treatment of Knee Osteoarthritis With Allogeneic Bone Marrow Mesenchymal Stem Cells.