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Comparing the effect of bone marrow mono-nuclear cells with mesenchymal stem cells after acute myocardial infarction on improvement of left ventricular function: a meta-analysis of clinical trials

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Abstract

Background: The effect of transplantation of bone-marrow mononuclear cells (BM-MNCs) and mesenchymal stem cells (MSCs) on ejection fraction (LVEF) has been studied in patients with acute myocardial infarction (AMI) in clinical trials. This raises the question that which type of cell may help improve LVEF better in AMI patients. No meta-analysis of clinical trials has yet addressed this question.

Methods: Electronic databases were searched thoroughly to find eligible trials on the effects of transplantation of BM-MNCs and MSCs in patients with AMI. The primary outcome was improvement in LVEF. Data were synthesized using random-effects meta-analysis. For maximizing the credibility of subgroup analysis, we used the instrument for assessing the Credibility of Effect Modification of Analyses (ICEMAN) for meta-analyses.

Results: A total of 36 trials (26 on BM-MNCs and 10 on MSCs) with 2489 patients (1466 were transplanted [1241 with BM-MNCs and 225 with MSCs] and 1023 as controls) were included. Both types of cells showed significant improvements in ejection fraction in short-term follow-up (BM-MNCs: WMD = 2.13%, 95% CI = 1.23 to 3.04, $p < 0.001$; MSCs: WMD = 3.71%, 95% CI = 2.32 to 5.09, $p < 0.001$), and according to ICEMAN criteria, MSCs are more effective. For selected population of patients who received stem cell transplantation in early course after AMI (less than 11 days), this effect was even more pronounced (BM-MNC: WMD = 3.07%, 95% CI = 1.97 to 4.17, $p < 0.001$, $I^2 = 40.7\%$; MSCs: WMD = 5.65%, 95% CI = 3.47 to 7.84, $p < 0.001$, $I^2 = 84.6\%$).

Conclusion: Our results showed that transplantation of MSCs after AMI might increase LVEF more than BM-MNCs; also, based on ICEMAN, there was likely effect modification between subgroups although uncertainty still remained.

Keywords: Stem cells, Acute myocardial infarction, Bone-marrow mononuclear cells, Mesenchymal stem cells

Background

Inadequate blood flow and oxygen supply secondary to formation of thrombus in coronary arteries activate a series of complications leading to myocardial injury, leading to ventricular failure. It is noteworthy that the repair mechanisms following reperfusion in the setting of acute myocardial infarction (AMI) causes irreversible damage

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regarding LVEDV and also LVESV although since only one MSC trial was included in the analysis, no definite effect can be assumed (based on ICEMAN) and conduction of future MSC trials are crucial to confirm the possible outperformance of MSCs compared to BM-MNCs. Also, for hospitalization for HF both groups did not show a significant difference compared to their control group, and there seemed to be no effect modification based on ICEMAN.

Since ventricular dysfunction and the subsequent decompensated heart failure carry the most cardiac-related precipitating factor for mortality of AMI patients [52], preventing ventricular dysfunction is of great importance in these patients. As utilization of the stem cells in acute myocardial infarction is becoming more established in clinical trials, a great endeavor should be made to find the most effective type of cell for AMI patients. In the present systematic review and meta-analysis, we found that MSCs improve ejection fraction more than BM-MNCs although a level of uncertainty should be reminded. For other outcomes in our review (LVEDV, LVESV, and hospitalization), it is noteworthy that our findings were equivocal since for LVEDV and LVESV mononuclear cells had better results although their difference remained insignificant, and for hospitalization both of stem cells did not change the hospitalization rate due to CHF.

This study also had several limitations. We included a non-randomized clinical trial for MSCs since trials of MSCs included a total of 451 patients, which were limited compared to BM-MNCs that had a total of 2038 patients. Different modalities were used for measuring ventricular indices such as echocardiography, CMR, SPECT, and LV angiography, and this can cause some differences in interpretations. Another issue was that the baseline ejection fractions for patients were different and ranged from 33 to 62, and this can significantly change the results of trials.

Conclusion

This meta-analysis provided evidence that both BM-MNCs and MSCs enhanced ventricular function by improving LVEF and MSCs appeared to be superior to BM-MNCs regarding the improvement of ejection fraction although these results cannot be interpreted without a level of uncertainty. Other ventricular parameters including LVEDV and LVESV and the rate of hospitalization for heart failure had equivocal results.

Abbreviations

AMI: Acute myocardial infarction; HF: Heart failure; CHF: Congestive heart failure; BM-MNC: Bone marrow mononuclear cell; MSC: mesenchymal stem cell; IL-1: interleukin-1; IL-6: interleukin-6; TNF-α: tumor necrosis factor-α; PSC: progenitor stem cell; LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; STEMI: ST elevation myocardial infarction; SD: standard deviation; RR: risk ratio; CI: confidence interval; WMD: weighted mean difference; ICEMAN: instrument for assessing the credibility of effect modification of analyses; CMR: cardiac magnetic resonance; SPECT: single-photon emission computed tomography; PCI: percutaneous coronary intervention.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13287-022-02883-3.

Additional file 1. Summary of the risk of bias in the included studies.

Additional file 2. Forest plot of the effect sizes of changes in LVEF from baseline during the short-term follow-up (4-6 months) measured by echocardiography in acute MI patients who received an intracoronary injection of either BM-MNCs or MSCs before 11 days after diagnosis of acute MI compared to the control group who received standard therapy with or without placebo injection.

Additional file 3. Forest plot of LVEDV changes measured by echocardiography in acute MI patients receiving either standard therapy (with or without placebo injection) or autologous intracoronary injection of stem cells before 11 days of diagnosis based on the type of cell (BM-MNCs or MSCs).

Additional file 4. Forest plot of comparison of changes in LVESV over the follow-up period measured by echocardiography in patients with acute MI who received intracoronary injection of stem cells based on the type of cells (BM-MNCs or MSCs) before 11 days after diagnosis of MI compared to the control group.

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Author contributions

AA contributed to concept and design of the study. AK assisted in statistical analysis and administrative support. The first draft of the manuscript was written by AH. AA, AH, and FK contributed to manuscript writing and preparing the final version of the manuscript. All authors read and approved the final manuscript.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate

This study has been approved by the local ethical committee of Shiraz University of Medical sciences and the protocol of this systematic review and meta-analysis was previously registered in PROSPERO (CRD42022296966).

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interests.

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