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[Intervention Review]

Stem cell therapy for chronic ischaemic heart disease and congestive heart failure

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ABSTRACT

Background

A promising approach to the treatment of chronic ischaemic heart disease and congestive heart failure is the use of stem cells. The last decade has seen a plethora of randomised controlled trials developed worldwide, which have generated conflicting results.

Objectives

The critical evaluation of clinical evidence on the safety and efficacy of autologous adult bone marrow-derived stem/progenitor cells as a treatment for chronic ischaemic heart disease and congestive heart failure.

Search methods

We searched CENTRAL in the Cochrane Library, MEDLINE, Embase, CINAHL, LILACS, and four ongoing trial databases for relevant trials up to 14 December 2015.

Selection criteria

Eligible studies were randomised controlled trials comparing autologous adult stem/progenitor cells with no cells in people with chronic ischaemic heart disease and congestive heart failure. We included co-interventions, such as primary angioplasty, surgery, or administration of stem cell mobilising agents, when administered to treatment and control arms equally.

Data collection and analysis

Two review authors independently screened all references for eligibility, assessed trial quality, and extracted data. We undertook a quantitative evaluation of data using random-effects meta-analyses. We evaluated heterogeneity using the I² statistic and explored substantial heterogeneity (I² greater than 50%) through subgroup analyses. We assessed the quality of the evidence using the GRADE approach. We created a 'Summary of findings' table using GRADEprofiler (GRADEpro), excluding studies with a high or unclear risk of selection bias. We focused our summary of findings on long-term follow-up of mortality, morbidity outcomes, and left ventricular ejection fraction measured by magnetic resonance imaging.

Main results

We included 38 randomised controlled trials involving 1907 participants (1114 cell therapy, 793 controls) in this review update. Twentythree trials were at high or unclear risk of selection bias. Other sources of potential bias included lack of blinding of participants (12 trials) and full or partial commercial sponsorship (13 trials).

Cell therapy reduced the incidence of long-term mortality (\ge 12 months) (risk ratio (RR) 0.42, 95% confidence interval (CI) 0.21 to 0.87; participants = 491; studies = 9; I² = 0%; low-quality evidence). Periprocedural adverse events associated with the mapping or cell/placebo injection procedure were infrequent. Cell therapy was also associated with a long-term reduction in the incidence of non-fatal myocardial infarction (RR 0.38, 95% CI 0.15 to 0.97; participants = 345; studies = 5; I² = 0%; low-quality evidence) and incidence of arrhythmias (RR 0.42, 95% CI 0.18 to 0.99; participants = 82; studies = 1; low-quality evidence). However, we found no evidence that cell therapy affects the risk of rehospitalisation for heart failure (RR 0.63, 95% CI 0.36 to 1.09; participants = 375; studies = 6; I² = 0%; low-quality evidence) or composite incidence of mortality, non-fatal myocardial infarction, and/or rehospitalisation for heart failure (RR 0.64, 95% CI 0.38 to 1.08; participants = 141; studies = 3; I² = 0%; low-quality evidence), or long-term left ventricular ejection fraction when measured by magnetic resonance imaging (mean difference -1.60, 95% CI -8.70 to 5.50; participants = 25; studies = 1; low-quality evidence).

Authors' conclusions

This systematic review and meta-analysis found low-quality evidence that treatment with bone marrow-derived stem/progenitor cells reduces mortality and improves left ventricular ejection fraction over short- and long-term follow-up and may reduce the incidence of non-fatal myocardial infarction and improve New York Heart Association (NYHA) Functional Classification in people with chronic ischaemic heart disease and congestive heart failure. These findings should be interpreted with caution, as event rates were generally low, leading to a lack of precision.

PLAIN LANGUAGE SUMMARY

Stem cell treatment for chronic ischaemic heart disease and congestive heart failure

Review question

Are adult stem/progenitor cells derived from bone marrow safe and effective as a treatment for chronic ischaemic heart disease and heart failure?

Background

The current treatment for people suffering from heart disease and heart failure is drugs and, when possible, restoration of the blood supply in the heart (revascularisation) either by opening the arteries with a tiny balloon in a procedure called primary angioplasty (or percutaneous coronary intervention) or by heart surgery (or coronary artery bypass graft). Revascularisation has reduced the death rate associated with these conditions. In some people, heart disease and heart failure symptoms persist even after revascularisation. Recently, bone marrow stem/progenitor cells have been investigated as a new treatment for people with heart disease and heart failure, whether or not they also undergo revascularisation.

Search date

We searched electronic databases for relevant randomised controlled trials to December 2015.

Study characteristics

We included 38 randomised controlled trials involving more than 1900 participants in this review, with 14 trials of chronic ischaemic heart disease, 17 trials of ischaemic heart failure secondary to heart disease, and seven trials of refractory or intractable angina. The mean age of participants ranged from 55 to 70 years, and the proportion of male participants ranged from 51% to 100%.

Key results

Results indicated that treatment with bone marrow-derived cells can lead to a reduction in deaths in participants followed for at least 12 months. Adverse events occurring around the time of treatment were generally rare. Participants who received cell treatment also experienced fewer heart attacks and arrhythmias when compared to those who received no cells. However, cell therapy does not appear to reduce the risk of rehospitalisation for heart failure or the combined risk of death, non-fatal heart attack, or rehospitalisation, and did not result in any improvement over standard treatment in tests of heart function. These results suggest that cell therapy may be of benefit in people with chronic ischaemic heart disease or heart failure, or both.

Quality of the evidence

The quality of the evidence was low, as the number of included studies and participants is not currently high enough to draw robust conclusions. Thirteen studies received commercial funding, of which four were fully commercially sponsored, and 12 studies did not report



that participants were blinded to the treatment they received. Further research involving a larger number of participants is required to confirm our results.