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Stem Cell Transplantation for Ischemic Stroke

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Stroke is a leading cause of morbidity and mortality worldwide, with very large healthcare and social costs and a strong demand for alternative therapeutic approaches. Preclinical studies have shown that stem cells transplanted into the brain can lead to functional improvement. However, to date, evidence for the benefits of stem cell transplantation in people with ischemic stroke is lacking.

Objectives

This is the first update of a 2010 Cochrane review and assesses the efficacy and safety of stem cell transplantation compared with control in people with ischemic stroke.

Methods

We searched the Cochrane Stroke Group Trials Register, CENTRAL, MEDLINE, Embase, BIOSIS, and trial registers in August 2018. We also hand-searched potentially relevant conference proceedings, screened reference lists, and contacted individuals active in the field and stem cell manufacturers.

We included randomized controlled trials that recruited people with ischemic stroke, in any phase of the disease, and an ischemic lesion confirmed by computerized tomography or magnetic resonance imaging scan. We included all types of stem cell transplantation, regardless of cell source, route of cell administration, and dosage. The primary outcome was efficacy (assessed as neurological impairment or functional outcome) at longer-term follow-up (minimum 6 months). Secondary outcomes included postprocedure safety outcomes (death, worsening of neurological deficit, infections, and neoplastic transformation). If needed, we contacted study authors for additional information. We performed random-effects meta-analyses when ≥ 2 randomized controlled trials were available for any outcome. We assessed the certainty of the evidence by using the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluations).

Main Results

In this updated review, we included 7 completed randomized controlled trials with 401 participants. All tested adult human nonneural stem cells; cells were transplanted during the acute, subacute, or chronic phase of ischemic stroke; administered intravenously, intraarterially, intracerebrally, or into the lumbar subarachnoid space. Follow-up ranged from 6 months to 7 years. Efficacy outcomes were measured with the National Institutes of Health Stroke Scale, modified Rankin Scale, or Barthel Index. Safety outcomes included case fatality and were measured at the end of the trial. Overall, stem cell transplantation was associated with a better clinical outcome when measured with the National

Institutes of Health Stroke Scale (mean difference, -1.49 ; 95% CI, -2.65 to -0.33 ; 5 studies, 319 participants; low-certainty evidence), but not with the modified Rankin Scale (mean difference, -0.42 ; 95% CI, -0.86 to 0.02 ; 6 studies, 371 participants; very low-certainty evidence; Figure), or the Barthel Index (mean difference, 14.09 ; 95% CI, -1.94 to 30.13 ; 3 studies, 170 participants; very low-certainty evidence). The studies in favor of stem cell transplantation had, on average, a higher risk of bias, and a sample size of 32 or fewer participants. No significant safety concerns associated with stem cell transplantation were raised with respect to death (risk ratio, 0.66 ; 95% CI, 0.39 – 1.14 ; 6 studies, participants; low-certainty evidence). We were not able to perform the sensitivity analysis according to the quality of studies, because all of them were at high risk of bias.

Authors' Conclusions

Overall, in participants with ischemic stroke, stem cell transplantation was associated with a reduced neurological impairment, but not with a better functional outcome. These results could be consistent with a small benefit of stem cell transplantation, which could only be detected when we considered neurological impairment, not when we considered functional outcome. No obvious safety concerns were raised. However, these conclusions came mostly from small randomized controlled trials with high risk of bias, and the certainty of the evidence ranged from low to very low. Currently, there is insufficient evidence to support or refute the use of stem cell transplantation to treat ischemic stroke. More large well-designed clinical trials are needed.

This article is based on a Cochrane Review published in The Cochrane Library 2019, Issue 5. Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library should be consulted for the most recent version of the review.¹

Disclosures

None.

Reference

1. Boncoraglio GB, Ranieri M, Bersano A, Parati EA, Del Giovane C. Stem cell transplantation for ischemic stroke. *Cochrane Database Syst Rev* 2019;5:CD007231. doi: 10.1002/14651858.CD007231.pub3

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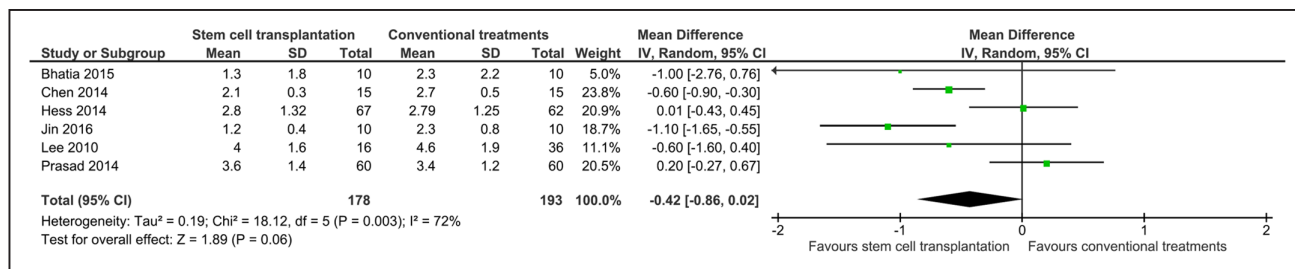


Figure. Stem cell transplantation vs control: effect on modified Rankin Scale.