The effects of intravenous infusion of autologous mesenchymal stromal cells in patients with subacute middle cerebral artery infarct: a phase 2 randomized controlled trial on safety, tolerability and efficacy

ABSTRACT

Background aims Mesenchymal stromal cells (MSCs) are characterized by paracrine and immunomodulatory functions capable of changing the microenvironment of damaged brain tissue toward a more regenerative and less inflammatory milieu. The authors conducted a phase 2, single-center, assessor-blinded randomized controlled trial to investigate the safety and efficacy of intravenous autologous bone marrow-derived MSCs (BMMSCs) in patients with subacute middle cerebral artery (MCA) infarct. Methods Patients aged 30-75 years who had severe ischemic stroke (National Institutes of Health Stroke Scale [NIHSS] score of 10-35) involving the MCA territory were recruited within 2 months of stroke onset. Using permuted block randomization, patients were assigned to receive 2 million BMMSCs per kilogram of body weight (treatment group) or standard medical care (control group). The primary outcomes were the NIHSS, modified Rankin Scale (mRS), Barthel Index (BI) and total infarct volume on brain magnetic resonance imaging (MRI) at 12 months. All outcome assessments were performed by blinded assessors. Per protocol, analyses were performed for between-group comparisons. Results Seventeen patients were recruited. Nine were assigned to the treatment group, and eight were controls. All patients were severely disabled following their MCA infarct (median mRS = 4.0 [4.0-5.0], BI = 5.0 [5.0-25.0], NIHSS = 16.0 [11.5-21.0]). The baseline infarct volume on the MRI was larger in the treatment group (median, 71.7 [30.5-101.7] mL versus 26.7 [12.9-75.3] mL, P = 0.10). There were no between-group differences in median NIHSS score (7.0 versus 6.0, P = 0.96), mRS (2.0 versus 3.0, P = 0.38) or BI (95.0 versus 67.5, P = 0.33) at 12 months. At 12 months, there was significant improvement in absolute change in median infarct volume, but not in total infarct volume, from baseline in the treatment group (P = 0.027). No treatment-related adverse effects occurred in the BMMSC group. Conclusions Intravenous infusion of BMMSCs in patients with subacute MCA infarct was safe and well tolerated. Although there was no neurological recovery or functional outcome improvement at 12 months, there was improvement in absolute change in median infarct volume in the treatment group. Larger, well-designed studies are warranted to confirm this and the efficacy of BMMSCs in ischemic stroke.

Keyword: Clinical trial; Ischemic stroke; Mesenchymal stromal cells; Middle cerebral artery infarction