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SAFETY AND EFFICACY OF MESENCHYMAL STEM CELL THERAPY FOR CHILDREN AND ADOLESCENTS WITH CEREBRAL PALSY. A SYSTEMATIC REVIEW

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Background

Cerebral palsy is a condition characterized by permanent motor dysfunction that affects muscle tone, posture, and movement, which results in limitations in functional abilities. Mesenchymal stem cell (MSC) therapy has been shown in preclinical and clinical studies, to significantly improve health condition in patients with neurological disorders.

Aim

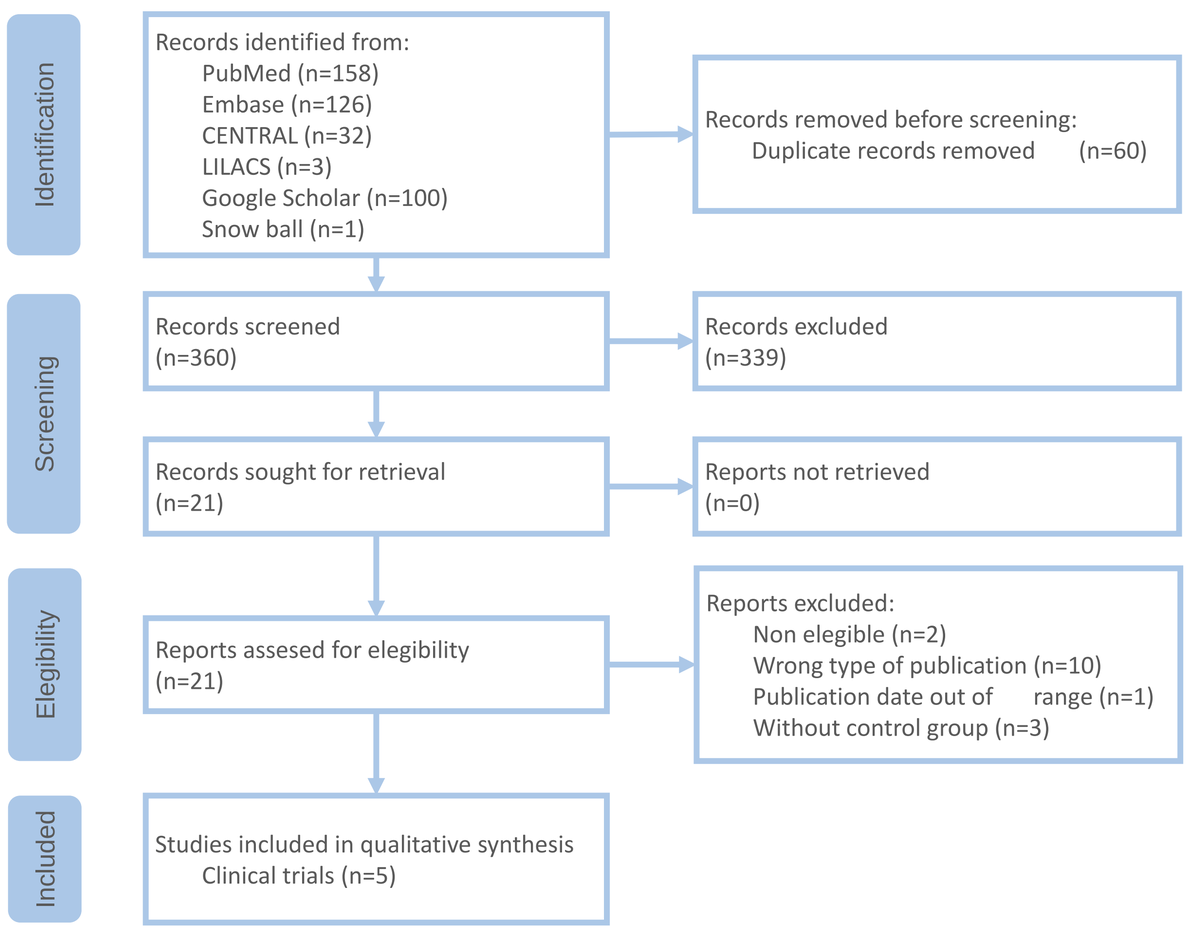
We aim to determine the safety and efficacy of MSC therapy in children and adolescents with cerebral palsy, based on currently available evidence.

Methods

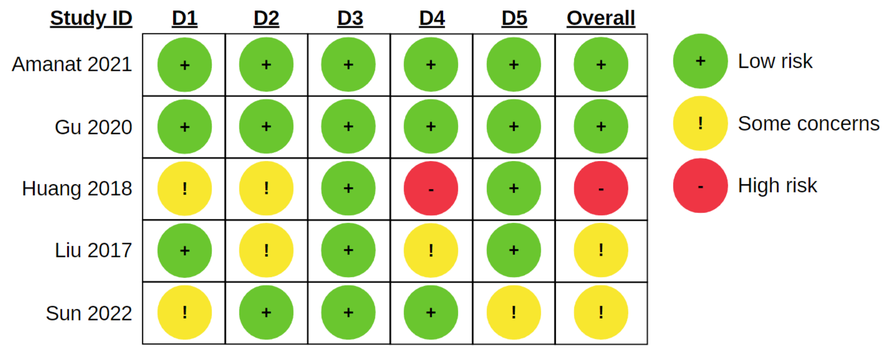
Systematic review in indexed databases and grey literature. Search strategy was composed of free terms and exploited controlled vocabulary. Review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement. Two independent reviewers performed the screening, selection, bias evaluation, and a qualitative synthesis of the included studies. PROSPERO ID: CRD42022384467

Results

PRISMA flowchart

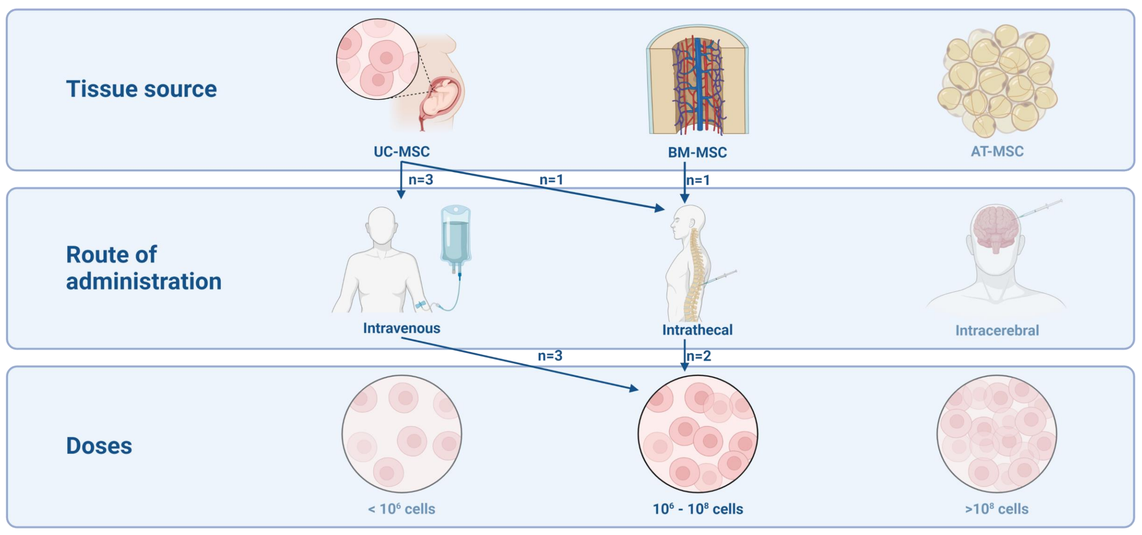


Risk of Bias Assessment: RoB 2 tool



Synthesis

Of the 5 selected studies, 339 children between 6 months and 14 years of age were enrolled, of which 70 received intravenous MSC therapy and 71 received intrathecal MSC therapy. Main outcomes were efficacy according to the gross motor function measure (GMFM) and comprehensive function assessment (CFA); and safety by the incidence of adverse events (AEs) associated with MSC therapy. We observed follow-ups up to 24 months post treatment. Based on the results of the included studies in this review, changes in GMFM total and CFA total scores for MSC therapy groups, were significantly higher than in the control groups at all post-treatment follow-ups. In addition, no serious AEs were observed, and there was no difference between the intervention and control groups.



Author, country, year	Design	Age	Pathology	N (int/ cont)	Intervention	Control	Dose, administration	Outcomes assessment	Follow up time
Amanat, Iran, 2021	RCT Double blind Controlled with sham	4 - 14 years	Spastic CP, GMFCS level II - V	72 (36/ 36)	Allogenic UC-MSC Unique dose (+ rehabilitation)	Sham (+rehabilitation)	$2x10^7$, IT	Efficacy: GMFM-66, MAS, PEDI, CP-QoL Security: AE, SAE and NSAE	12 months
Gu, China, 2020	RCT Double blind Controlled with placebo	2 - 12 years	CP	40 (20/ 20)	Allogenic UC-MSC 4 doses (+ rehabilitation: conductive and Bobath)	Placebo (50ml Sln 0.9% con 1% albumin) (+rehabilitation)	$5x10^7$, IV	Efficacy: GMFM-88, ADL and CFA Security: AE, SAE and NSAE	12 months
Huang, China, 2018	RCT Single blind Controlled with placebo	3 - 12 years	CP	54 (27/ 27)	Allogenic UCB-MSC 8 doses (+ rehabilitation)	Placebo (50ml Sln 0.9%) (+rehabilitation)	$5x10^7$, IV	Efficacy: GMFM-88 and CFA Security: AE, SAE, NSAE and AE grade 1-5	24 months
Liu, China, 2017	RCT Double blind (only for BM-MSC and BM-MNC groups)	6 months - 12.5 years	Spastic CP, GMFCS level II - V	105 (35/ 35/ 35)	Group autologous BM-MSC Group autologous BM-MNC 4 doses	Rehabilitation	$1x10^6$/kg, IT	Efficacy: GMFM and FMFM Security: AE, SAE and NSAE	12 months
Sun, USA, 2022	RCT Phase II Open label	2 - 5 years	Hypertonic CP, GMFCS level I - IV	68 (20/ 23/ 25)	Group TNC (AlloCB) Group allogenic UC-MSC 3 doses	Natural history group	$2x10^6$/kg, IV	Efficacy: GMFM-66, PDMS-2 Security: AE, SAE and NSAE	12 months

ADL: Activities of daily living; **AE:** Adverse events; **BM-MNC:** Bone marrow-derived mononuclear cells; **BM-MSC:** Bone marrow-derived mesenchymal stem cell; **CFA:** comprehensive function assessment; **CP:** Cerebral palsy; **CP-QoL:** CP quality of life; **FMFM:** Fine motor function measure; **GMFCS:** Gross motor function classification system; **GMFM:** Gross motor function Measure; **MAS:** Modified Ashworth scale; **NSAE:** Non-serious adverse events; **PEDI:** Pediatric evaluation of disability inventory; **PDMS-2:** Peabody developmental motor scales – 2; **RCT:** Randomized clinical trial; **SAE:** Serious adverse events; **UC-MSC:** Umbilical cord-derived mesenchymal stem cell; **UCB-MSC:** Umbilical cord blood-derived mesenchymal stem cell

Conclusion

MSC therapy intrathecally or intravenously, is safe and could improve gross motor and comprehensive functions in children and adolescents with cerebral palsy, mainly when combined with basic rehabilitation.

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