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A novel treatment option for
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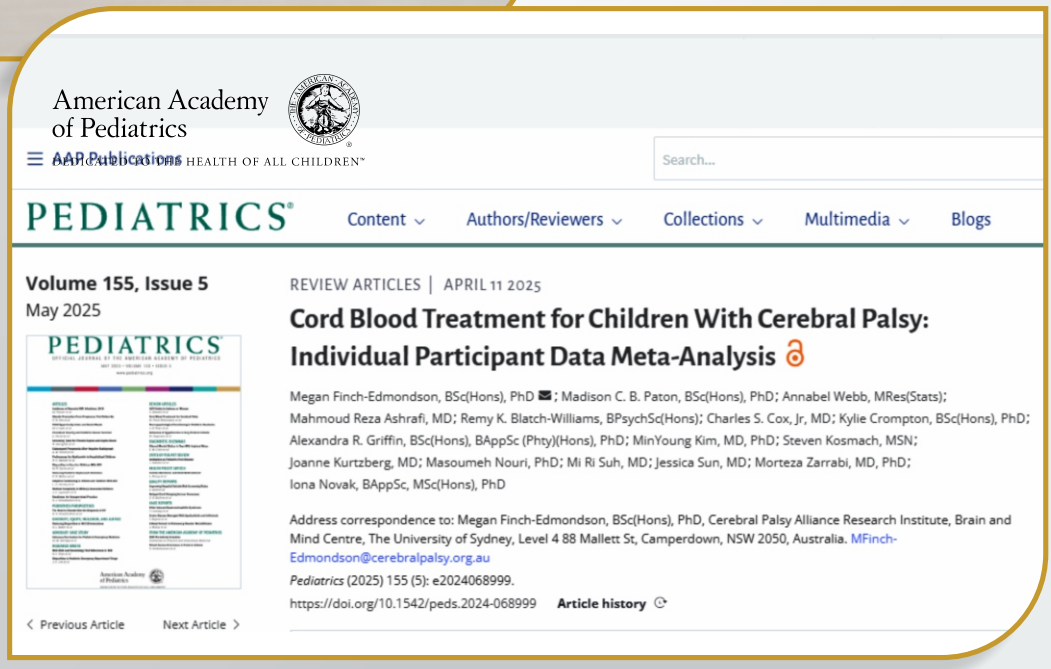

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Cord Blood Treatment for Children With Cerebral Palsy: Individual Participant Data Meta-Analysis

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What is Cerebral Palsy?

Cerebral palsy (CP) is a group of movement disorders that appear in early childhood due to brain damage. It can affect movement, posture, and coordination, and may also impact other functions like speech, vision, and hearing.

Reasons for Cerebral Palsy:

Genetic Conditions	Stroke in the Womb
Abnormal Brain Development or Damage	Premature Birth
Maternal Infections	Low Birth Weight
Brain Malformations	Infections after Birth
Lack of Oxygen (Asphyxia)	Head Injuries

Incidences:

2.95 per 1000 children in India and 1 per 345 children globally.

Clinical Trials for CP Treatment: A Concise Overview

For over 20 years several types of cells have been used under clinical trials for the treatments for CP, including umbilical cord blood (UCB) cells, bone marrow cells, mesenchymal stem/stromal cells, and neural stem cells. Of these, UCB is the most thoroughly studied cell treatment for CP, having been tested in clinical trials.

UCB contains a variety of cell types, including hemopoietic stem and progenitor cells, effector cells, mesenchymal stem/stromal cells, endothelial progenitor cells, monocyte-derived cells, and T-regulatory cells.

The Study:

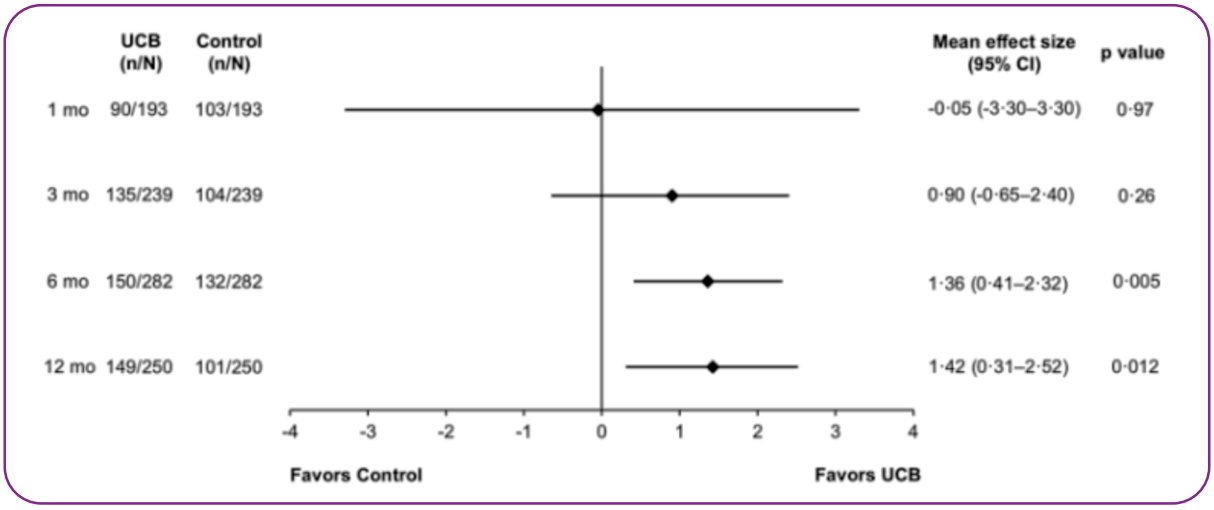
- Date of Publishing- 11th April, 2025
- PEDIATRICS Volume 155, Issue 5, May 2025

The Study Design:

- Systematic review and meta-analysis of individual participant data, who were assessed through GMFM-66 rating from 11 studies.
- The study collected data on a total of 498 treatments over 447 participants. Out of which 170 participants were treated with cord blood and 171 under controls, participants that received erythropoietin were excluded from the study.
- Participants included in the main analysis were 60% of boys.
- In 84% of the treatments, the cord blood did not come from the patient (autologous), but from a donor (related or unrelated allogeneic).
- Efforts were made to exclude genetic disorders that cause symptoms like CP.
- The mean age of the treated children at baseline was 57 months (range 8 to 227).
- 52% of the participants were term born and moderate-to-late preterm.
- The cord blood cells was delivered by systemic infusion and intrathecal.
- The median pre-thaw dose of the infusions was 56.1 million TNC/kg (range 9.7 to 210.3).
- Individuals were assessed at 1-, 3-, 6- and 12- months for identifying safety and efficacy.

Observation & Analysis

- The analysis identified best responders as children with CP that are under age five years and who have some ability to walk, either independently or with assistance, before the therapy.



- There appeared to be a significant difference in GMFM-66 effect size when comparing studies from an unrelated allogeneic source compared with autologous cells at both 6- and 12-month follow-up (Table S17), favouring unrelated allogeneic source. However, investigation revealed that allogeneic UCB received, on average was more than double the cell dose compared with autologous UCB (Table S5).

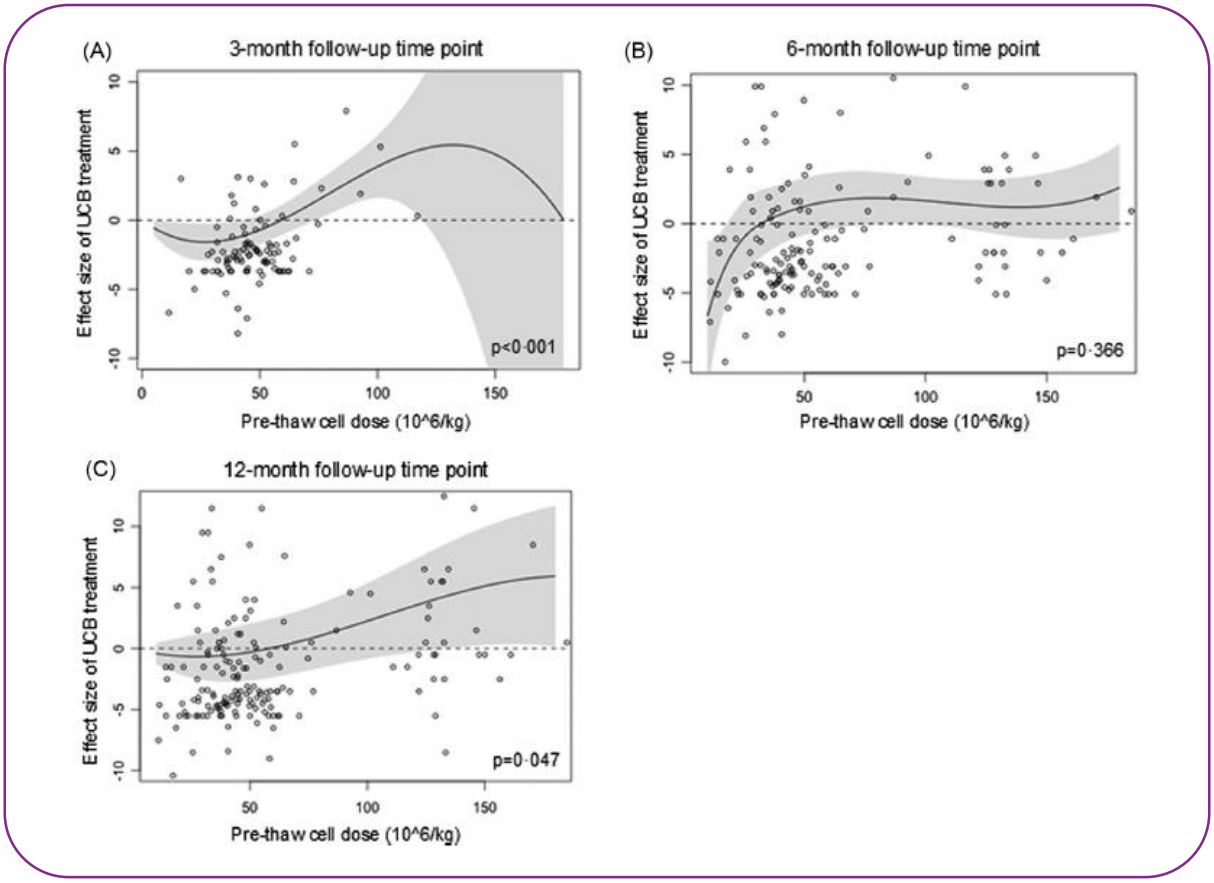


FIGURE 2.

Effect of UCB cell dose on GMFM-66 effect size. The figures depict the mean GMFM-66 effect size after UCB treatment compared with controls, by dose, at 3- (A), 6 (B), and 12-month (C) follow-up time points, with 95% Cls (shaded areas). Dose data include imputed pre-thaw dose values and represent total nucleated cell counts. Open circles represent individual participant data points. The P values represent test for an association between effect size and pre-thaw cell dose. Number of participants was n = 259 (A), n = 282 B), n = 250 (C). Erythropoietin-treated participants (either alone or with UCB) were excluded. GMFM, Gross Motor Function Measure, UCB, umbilical cord blood.

- This IPDMA additionally identified participant characteristics of responders to UCB treatment. Namely, participants who were younger at baseline (before age ≈5 years) with milder CP (GMFCS I-III) had the most improved gross motor function after UCB treatment.

- The hypothesized mechanism of action of UCB for treating the underlying brain injury in CP—namely, reduced neuroinflammation and stimulation of endogenous tissue repair via paracrine effects, leading to increased brain connectivity—the time taken to see clinical effect is justified. Improvements in brain connectivity are not immediate, and subsequent clinical improvements likely rely on the principles of neuroplasticity, with neural pathways strengthened by physical therapy over weeks to months. This is supported by analysis showing that UCB treatment increased normalized whole-brain connectivity in children with CP 1 year after treatment.

- UCB is postulated to provide therapeutic benefit via its paracrine effects and immune modulation, findings support that UCB may be targeting elevated systemic inflammation in younger patients to provide the greatest benefit.

- The GMFM-66 effect sizes after UCB treatment indicate medium-to-large MCIDs, particularly for the responder subgroups (e.g., younger and milder), and 6–12 months after infusion. Importantly, UCB treatment may be a preferred intervention choice by patients and families compared with time-intensive rehabilitation or highly invasive surgical procedures, with a similar financial cost.

- The findings on this study, positioned banked UCB as a feasible, readily available treatment for improving gross motor function in CP and proposes a new indication for the existing stocks of high-quality UCB units in cord blood banks around the world.

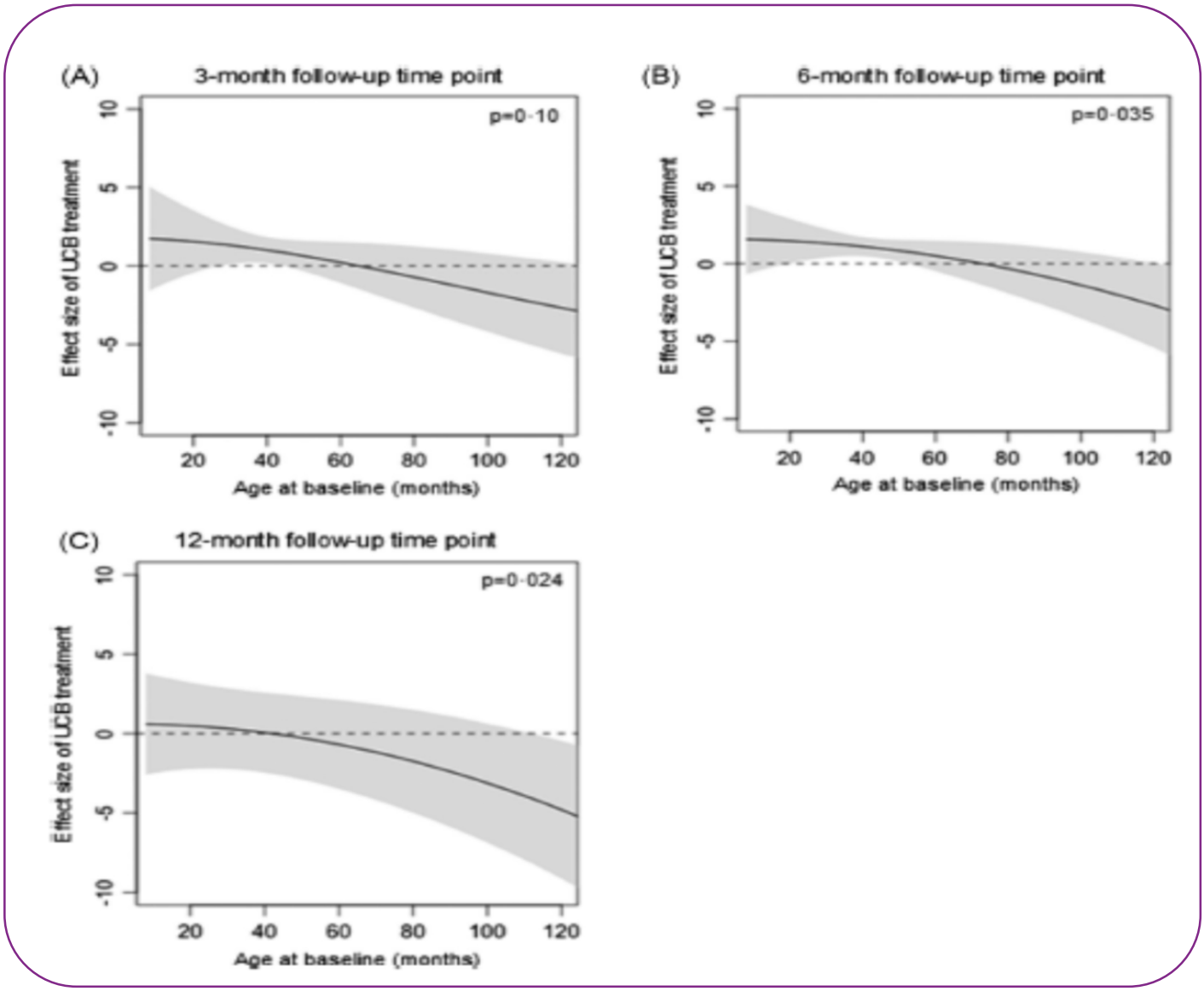


FIGURE 4.
Effect of baseline age on GMFM-88 effect size. The figures depict the mean GMFM-65 effect size after UCB treatment compared with controls, by age, at baseline (months) at 3- (A), 6 (8), and 12-month (C) follow-up time points, with 95% Os (shaded areas). Values are adjusted for severity (Grass Motor Function Classification System). The Pvalues represent a test for an association between age at baseline and effect size. Number of participants was n = 239 (A), n = 282 (B), and n = 250 (Q. Erythropoietin-treated participants (either alone or with UCB) were excluded. GMFM, Gross Motor Function Measure; UCB, umbilical cord blood.

Conclusion

- It is hypothesized that children with genetic and cryptogenic etiologies of CP may not benefit from UCB treatment.

- Nevertheless, in the future, UCB is unlikely to be administered as a stand-alone treatment, as UCB paired with an intensive rehabilitation after infusion may harness greater neuroplasticity.

- The peak in response was observed at 6 to 12 months after treatment and was consistent with the hypothesized mechanism of action: that the cord blood works through a paracrine effect that reduces neuro-inflammation, stimulates endogenous tissue repair, and thus leads to increased brain connectivity.

- For the overall treatment effect of UCB, mean GMFM-66 scores were significantly higher in UCB-treated participants compared with controls at 6 and 12 months after intervention (6 months: 1.36 points [95% CI, 0.41–2.32; P = .005]; 12 months: 1.42 points [95% CI, 0.31–2.52; P = .012]; Figure 1).

- It is observed that the children with milder CP and of younger age showed improved response to UCB.

Annexure:

Understanding GMFM:

- The GMFM-66 is a 66-item subset of the original GMFM-88, designed to evaluate gross motor function in children with cerebral palsy. It's a clinical measure that assesses how much a child can do in terms of gross motor movements, rather than the quality of those movements. The GMFM-66 uses a free computer program, the Gross Motor Ability Estimator (GMAE), to calculate the total score.

- The GMFM-66 provides a valuable tool for clinicians and researchers to assess and monitor gross motor function in children with cerebral palsy, offering a more concise and clinically relevant measure compared to the original GMFM-88.

- Children with CP often present with spasticity, muscle weakness, and motor planning deficits that impair gross motor performance. Enhancing gross motor function is a primary therapeutic goal, as it:

Promotes Independence
Improves Quality of Life
Reduces Secondary Complications

References:
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