

## SEREBRAL PALSİDE KÖK HÜCRE TEDAVİSİ

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## GİRİŞ

Serebral palsi (SP), gelişmekte olan fetüs veya bebek beyinde meydana gelen ilerleyici olmayan hasara bağlı, aktivite sınırlanmasına neden olan, hareket ve duruş gelişimindeki bir grup kalıcı bozukluğu tanımlar. SP çocukluk çağında motor yetersizliğin en sık nedeni olan kronik nörogelişimsel bir bozukluktur. SP, etiyoloji, klinik özellikler, işlevsel seviye, eşlik eden durumlar, tedavi seçenekleri, bireysel özellikler ve sonuçları bakımından heterojen bir özellik göstermektedir. SP'nin motor bozukluklarına sıklıkla duyu, algı, bilişsel, iletişim ve davranış bozuklukları, epilepsi ve ikincil kas-iskelet sistemi sorunları eşlik eder.<sup>6</sup>

<sup>6</sup> SP prevalansı dünyada 1000 canlı doğumda 1,3-3; erkek/kız oranı 1,3-1,4, ülkemizdeki sıklığı ise 2-16 yaş arasındaki çocuklarda binde 4,4 olarak bildirilmiştir.<sup>7</sup> SP etiyojisinde konjenital malformasyonlar, perinatal inme, düşük doğum ağırlığı, doğum asfiksisi, gestasyonel yaş, çoklu doğum ve enfeksiyon gibi çok sayıda faktör rol oynar.<sup>1,2</sup> SP'nin geniş bir yelpazeye yayılan etiyojisi nedeniyle, beyindeki patolojik bulgular da değişkenlik göstermektedir.<sup>1,2</sup> SP farklı klinik ve fenotipleri ile heterojen bir bozukluktur, motor

yetersizliklerine göre 4 grupta sınıflandırılmıştır.<sup>2</sup> Spastik tip SP, SP'nin en sık klinik tipi olup derin tendon reflekslerinde artış, spastisite, klonus ve babinski yanıtı görülür.<sup>2,8,9</sup> Diskinetik SP'de kore, atetoz ,distoni gibi istemsiz hareketlerin gözleendiği ekstrapiramidal sistem bulguları baskındır. Ataksik veya serebellar tipte koordinasyon güçlüğü, mikst tipte ise bu özelliklerin birden fazlası bulunmaktadır.<sup>2,8,9</sup>

Çocuklarda SP, yaşam kalitesini ciddi şekilde etkileyen, çocuğun ailesi ve ulusal mali kaynaklar üzerinde yük oluşturan önemli bir halk sağlığı sorunu haline gelmiştir.<sup>10</sup> Serebral palsili bireylerin güncel tedavisinde bu bireylerin işlevsel özelliklerini ve yaşam kalitesini en üst seviyeye çıkarmayı amaçlayan fizyoterapi, uğraşı ve konuşma terapisi, ortezleme, beslenme ve uyarlanabilir cihazlar gibi farmakolojik olmayan yöntemlerden; oral farmakolojik ajanlar, botulinum nörotoksin A enjeksiyonları, oral veya intratekal baklofen gibi farmakolojik yöntemlerden; dorsal rizotomi, çeşitli ortopedik işlemler gibi cerrahi yöntemlerden yararlanılmaktadır.<sup>11</sup> SP'li bireylerin yaşam kalitesini iyileştirmek ve fiziksel işlevlerini desteklemek için yeni tedavi seçenekleri araştırılmaktadır. Kök hücre tedavisinin (KHT) çeşitli klinik uygulama

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## KAYNAKLAR

- Rosenbaum B, Paneth N, Allen L, Goldstein M, Bax M. A report: The definition and classification of cerebral palsy. *Dev Med Child Neurol* 2007;(Suppl No 109)49:8-14.
- Yarar C. Serebral palsi'de tanı ve tedavi. Kumandaş S, Canpolat M, editörler. *Temel Pediatrik Nöroloji Tanı ve Tedavi*. 1. Baskı. Ankara: Akademisyen Kitabevi; 2022. p1587-1612.
- Yarar C. Serebral palside karşılaşılan diğer sorunlar ve yaklaşım. İçağasıoğlu DF, Sönmez FM, editörler. *Serebral Palsi*. 1. Baskı. Ankara: Türkiye Klinikleri; 2021. p.86-94.
- Korzeniewski SJ, Slaughter J, Lenski M, Haak P, Paneth N. The complex aetiology of cerebral palsy. *Nat Rev Neurol*. 2018; 14(9):528-543.
- Brandenburg JE, Fogarty MJ, Sieck GC. A critical evaluation of current concepts in cerebral palsy. *Physiology (Bethesda)*. 2019;34:216-229.
- Pearson TS, Pons R, Ghaoui R, Sue Cm. Genetic mimics of cerebral palsy. *Mov Disord*. 2019;34(5): 625-636.
- Serdaroğlu A, Cansu A, Ozkan S, Tezcan S. Prevalence of cerebral palsy in Turkish children between the ages of 2 and 16 years. *Dev Med Child Neurol*. 2006;48(6):413-416.
- Surveillance of Cerebral Palsy in Europe (SCPE). Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. *Dev Med Child Neurol*. 2000;42:816-24.
- Michael-Asalu A, Taylor G, Campbell H, Lelea LL, Kirby RS. Cerebral palsy: diagnosis, epidemiology, genetics and clinical update. *Adv Pediatr*. 2019;66:189-208.
- Whitney DG, Kamdar NS, Ng S, Hurvitz EA, Peterson MD. Prevalence of high-burden medical conditions and health care resource utilization and costs among adults with cerebral palsy. *Clin Epidemiol*. 2019;11:469-481.
- Sun JM, Kurtzberg J. Stem cell therapies in cerebral palsy and autism spectrum disorder. *Dev Med Child Neurol*. 2021;63(5):503-510.
- Ankrum J, Karp JM. Mesenchymal stem cell therapy: Two steps forward, one step back. *Trends Mol Med*. 2010;16(5):203-209.
- Fan HC, Ho LI, Chi CS, et al. Current proceedings of cerebral palsy. *Cell Transplant*. 2015;24:471-485.
- Jantzie LL, Scafidi J, Robinson S. Stem cells and cell-based therapies for cerebral palsy: a call for rigor. *Pediatr Res*. 2018;83:345-355.
- Jiao Y, Li XY, Liu J. A new approach to cerebral palsy treatment: discussion of the effective components of umbilical cord blood and its mechanisms of action. *Cell Transplant*. 2019;28:497-509.
- Dong H, Li G, Shang C, et al. Umbilical cord mesenchymal stem cell (UC-MSC) transplantations for cerebral palsy. *Am J Transl Res*. 2018;10(3):901-906.
- Eggenberger S, Boucard C, Schoeberlein A, et al. Stem cell treatment and cerebral palsy: Systemic review and meta-analysis. *World J Stem Cells*. 2019;11(10):891-903.
- Thore CB, Sudheer S, Janke D, Jagodzinska J, Jung M, Adjaye J. The origins of human embryonic stem cell: a biological conundrum. *Cells Tissues Organs*. 2008;188 (1-2): 9-22.
- Sharma A, Sane H, Gokulchandran N, et al. A clinical study of autologous bone marrow mononuclear cells for cerebral palsy patients: a new frontier. *Stem Cells Int*. 2015;905874.
- Huang L, Zhang C, Gu J, et al. A randomized, placebo-controlled trial of human umbilical cord blood mesenchymal stem cell infusion for children with cerebral palsy. *Cell Transplant*. 2018;27:325-334.
- Forraz N, McGuckin CP. The umbilical cord: a rich and ethical stem cell source to advance regenerative medicine. *Cell Prolif*. 2011;44 Suppl 1:60-69.
- Liu X, Fu X, Dai G, et al. Comparative analysis of curative effect of bone marrow mesenchymal stem cell and bone marrow mononuclear cell transplantation for spastic cerebral palsy. *J Transl Med*. 2017;15:48.
- Trounson A, McDonald C. Stem cell therapies in clinical trials: progress and challenges. *Cell Stem Cell*. 2015;17:11-22.
- Chen L, Huang H, Xi H, et al. Intracranial transplant of olfactory ensheathing cells in children and adolescents with cerebral palsy: a randomized controlled clinical trial. *Cell Transplant*. 2010;19:185-191.
- Xue E, Milano F. Are we underutilizing bone marrow and cord blood? Review of their role and potential in the era of cellular therapies. *F1000Res*. 2020;9:F1000 Faculty Rev-26.
- Rah WJ, Lee YH, Moon JH, et al. Neuroregenerative potential of intravenous G-CSF and autologous peripheral blood stem cells in children with cerebral palsy: a randomized, double-blind, cross-over study. *J Transl Med*. 2017;15:16.
- Lv ZY, Li Y, Liu J. Progress in clinical trials of stem cell therapy for cerebral palsy. *Neural Regen Res*. 2021;16(7):1377-1382.
- Chen G, Wang Y, Xu Z, et al. Neural stem cell-like cells derived from autologous bone mesenchymal stem cells for the treatment of patients with cerebral palsy. *J Transl Med*. 2013;11:21.
- Mancías-Guerra C, Marroquín-Escamilla AR, González-Llano O, et al. Safety and tolerability of intrathecal delivery of autologous bone marrow nucleated cells in children with cerebral palsy: an open-label phase I trial. *Cytotherapy*. 2014;16:810-820.
- Min K, Song J, Kang JY, et al. Umbilical cord blood therapy potentiated with erythropoietin for children with cerebral palsy: a double-blind, randomized, placebo-controlled trial. *Stem Cells*. 2013; 31:581- 591.
- Kim H, Na DL, Lee NK, Kim AR, Lee S, Jang H. Intrathecal injection in a rat model: a potential route to deliver human Wharton's jelly-derived mesenchymal stem cells into the brain. *Int J Mol Sci*. 2020; 21:1272.
- Sherman LS, Romagano MP, Williams SF, Rameshwar P. Mesenchymal stem cell therapies in brain disease. *Semin Cell Dev Biol*. 2019;95:111-119.

33. He S, Luan Z, Qu S, et al. Ultrasound guided neural stem cell transplantation through the lateral ventricle for treatment of cerebral palsy in children. *Neural Regen Res.* 2012;7:2529-2535.
34. Donega V, van Velthoven CT, Nijboer CH, et al. Intranasal mesenchymal stem cell treatment for neonatal brain damage: long-term cognitive and sensorimotor improvement. *PLoS One.* 2013; 8:e51253.
35. Lv Z, Li Y, Wang Y, et al. Safety and efficacy outcomes after intranasal administration of neural stem cells in cerebral palsy: a randomized phase 1/2 controlled trial. *Stem Cell Res Ther.* 2023;14(1):23.
36. Sun JM, Song AW, Case LE, et al. Effect of autologous cord blood infusion on motor function and brain connectivity in young children with cerebral palsy: a randomized, placebo-controlled trial. *Stem Cells Transl Med.* 2017;6 (12):2071-2078.
37. Gu J, Huang L, Zhang C, et al. Therapeutic evidence of umbilical cord-derived mesenchymal stem cell transplantation for cerebral palsy: a randomized, controlled trial. *Stem Cell Res Ther.* 2020;11(1):43.
38. Wang X, Cheng H, Hua R, et al. Effects of bone marrow mesenchymal stromal cells on gross motor function measure scores of children with cerebral palsy: a preliminary clinical study. *Cytotherapy.* 2013;15:1549-1562.
39. Luan Z, Liu W, Qu S, et al. Effects of neural progenitor cell transplantation in children with severe cerebral palsy. *Cell Transplant.* 2012;21 Suppl 1:S91-98.
40. Alotaibi M, Long T, Kennedy E, Bavishi S. The efficacy of GMFM-88 and GMFM-66 to detect changes in gross motor function in children with cerebral palsy (CP): a literature review. *Disabil Rehabil.* 2014;36(8):617-627.
41. Nguyen LT, Nguyen AT, Vu CD, Ngo DV, Bui AV. Outcomes of autologous bone marrow mononuclear cells for cerebral palsy: an open label uncontrolled clinical trial. *BMC Pediatr.* 2017;17(1):104.
42. Zali A, Arab L, Ashrafi F, et al. Intrathecal injection of CD133-positive enriched bone marrow progenitor cells in children with cerebral palsy: feasibility and safety. *Cytotherapy.* 2015;17(2):232-241.
43. DaCosta JC, Portuguez MW, Marinowic DR, et al. Safety and seizure control in patients with mesial temporal lobe epilepsy treated with regional superselective intraarterial injection of autologous bone marrow mononuclear cells. *J Tissue Eng Regen Med.* 2018;12(2):e648-e656.
44. Milczarek O, Jarocha D, Starowicz-Filip A, Kwiatkowski S, Badyra B, Majka M. Multiple autologous bone marrow-derived CD271(+) mesenchymal stem cell transplantation overcomes drug-resistant epilepsy in children. *Stem Cells Transl Med.* 2018;7(1):20-33.
45. McIntosh CC, Crino RD, O'Neill K. Treating problem gambling samples with cognitive behavioural therapy and mindfulness-based interventions: a clinical trial. *J Gambl Stud.* 2016;32(4):1305-1325.
46. Jin J. Stem cell treatments. *JAMA.* 2017; 317(3):330.
47. Duncan T, Valenzuela M. Alzheimer's disease, dementia, and stem cell therapy. *Stem Cell Res Ther.* 2017;8(1):111.
48. Burman J, Tolf A, H gglund H, Askmark H. Autologous haematopoietic stem cell transplantation for neurological diseases. *J Neurol Neurosurg Psychiatry.* 2018;89(2):147-155.
49. Naji A, Eitoku M, Favier B, Deschaseaux F, Rouas-Freiss N, Sukanuma N. Biological functions of mesenchymal stem cells and clinical implications. *Cell Mol Life Sci.* 2019;76:3323- 3348.
50. Huang L, Zhang L. Neural stem cell therapies and hypoxic-ischemic brain injury. *Prog Neurobiol.* 2019;173:1-17.
51. Finch-Edmondson M, Paton MCB, Honan I, et al. Are we getting it right? A scoping review of outcomes reported in cell therapy clinical studies for cerebral palsy. *J Clin Med.* 2022;11(24):7319.
52. Motavaf M, Dehghan S, Ghajarzadeh M, et al. Stem cell treatment and cerebral palsy: A Systematic review and meta-analysis. *Curr Stem Cell Res Ther.* 2022;19(2):210-219.
53. Qu J, Zhou L, Zhang H, et al. Efficacy and safety of stem cell therapy in cerebral palsy: A systematic review and meta-analysis. *Front Bioeng Biotechnol.* 2022;10:1006845.