

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

© The Authors 2019;

This article is published with open access at Licensee Open Journal Systems of Kazimierz Wielki University in Bydgoszcz, Poland
Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 25.08.2019. Revised: 31.08.2019. Accepted: 22.09.2019.

Treatment of cerebral palsy using stem cells

**Magdalena Hołowczuk¹, Dominika Janeczko¹, Anna Orzeł¹, Barbara Klatka¹,
Michał Terpiłowski¹**

1. Students of Medical University of Lublin

Abstract:

Cerebral palsy is a wide group of diseases whose common feature are motor disorders. Patients affected by this condition show abnormalities of movement and posture.

Various possible causes of damage were identified. Hypoxia, ischemia, infection, injury and congenital defects are one of the conditions that increase the risk of the disease. The first signs of cerebral palsy noted by parents are: incorrect head and torso stabilization, inability to sit and walk at the right age. There are currently no treatments available that would indicate good efficacy. . In recent years, stem cell therapies have enjoyed considerable interest. The encouraging results of many preclinical studies have indicated that stem cell therapy may have benefits in neonatal diseases.

Despite many encouraging reports, data on the effectiveness of stem cell therapy in cerebral palsy are still insufficient. Scientists should continue to research the success of the therapy.

Key words: stem cells; cerebral palsy

Cerebral palsy is a wide group of diseases whose common feature are motor disorders. The illness is caused by damage to brain tissue during its early development. Patients affected by this condition show abnormalities of movement and posture. The group of children with cerebral palsy is very diverse. Some of patients have only minor motor disorders such as unstable walking corrected by specialist footwear, however some require equipment to replace independent movement [1].

This neuromuscular disease is caused by injury in infant's brain [2]. Damage occurs before the birth of the child. Most often this happens during delivery or shortly after birth. It is hard to estimate which factor specifically cause a brain damage, though its action leaves a mark in the form of scars in the nervous tissue. Various possible causes of damage were identified. Hypoxia, ischemia, infection, injury and congenital defects are one of the conditions that increase the risk of the disease. Symptoms of the condition at the beginning are difficult to observe. They increase in intensity with the child's age. The first signs noted by parents are: incorrect head and torso stabilization, inability to sit and walk at the right age. Inappropriate muscle tone should also get the attention of both doctors and parents. Other symptoms that may indicate cerebral palsy include: improper positioning of the child, spontaneous motor different from peers, abnormal reflexes and fixed asymmetry. Very often children affected by cerebral palsy are accompanied by other diseases. This group of patients require multi-specialist medical care and extraordinary supervision. Hearing and sight impairment, intellectual disability, seizure disorders, pain or feeding problems may also occur with cerebral palsy [1].

Brain tissue in the course of the disease is irreversibly damaged. There are currently no treatments available that would indicate good efficacy. We do not have adequate medicines that could undo damage in brain tissue. Some plasticity of the child's brain is used during therapy. The effects of the treatment used depend primarily on the severity of the disease. The better the brain function is preserved, the better the response to treatment. Therapy is based primarily on various forms of rehabilitation. In the case of increased muscle tone, injections containing botulinum toxin are used [1].

Due to the fact that cerebral palsy is an incurable disease, research is constantly ongoing on new therapeutic options. In recent years, stem cell therapies have enjoyed considerable interest. Stem cells are characterized by the ability to differentiate into specific cell types. Therefore scientist began to examine their effectiveness in the case of cerebral palsy. From these cells specific cells can be formed for tissues in which there is a need for constant production of new cells e.g. bone marrow, intestine or epidermis. They are capable of a countless number of divisions. They are the starting point for the formation of all body tissues. Stem cells are found in human body during his entire individual life. Their presence is

found in peripheral blood and umbilical cord blood, as well as in some tissues such as nerve tissue and retina [3]. Cells derived from umbilical cord blood have greater proliferative dynamics compared to stem cells obtained from an adult from bone marrow or peripheral blood [4]. Currently, stem cells are used to treat diseases such as Fanconi anemia or chronic myelogenous leukemia [3].

The encouraging results of many preclinical studies have indicated that stem cell therapy may have benefits in neonatal diseases. In the case of cerebral palsy, the impact of mesenchymal stromal cells (MSC) was studied [5] Application of MSC in animal models of intraventricular hemorrhage increases behavioural outcomes and improves development of oligodendrocytes. Reduction of inflammation was also observed [6, 7]. What is more it has been shown in human studies that cord blood stem cells are safe to administer. Improvement of motor symptoms were observed for up to two years after administration [5,8]. The main purpose of using stem cells in the treatment of cerebral palsy is to use their regenerative capacity to rebuild damaged brain tissue. Scientist have tested numerous techniques of cell delivery in the patients with different course of illness and etiologies of the disease [9]. Some of researchers established that patients who are in acute phase of cerebral palsy e.g. with hypoxic-ischemic brain injuries may have better response to the treatment due to the occurrence of the chemotactic signals and higher vascular permeability [9]. It was also observed that the use of therapy at a young age gives better results [10]. Some studies have also shown the effect of stem cells on processes such as loss motor control, speech control, muscle tone disorders and cognitive problems [11].

Previously available therapy methods focus mainly on relieving symptoms. Stem cell therapy gives a chance to repair brain damage. Despite many encouraging reports, data on the effectiveness of stem cell therapy in cerebral palsy are still insufficient. Scientists should continue to research the success of the therapy. It is crucial to estimate the advantage over any potential therapy risk. Cerebral palsy as a incurable disease is a huge burden for both the patient and his family. Improving the quality of life of patients should be a priority.

References

1. <https://www.mp.pl/pacjent/pediatric/choroby/choroby-neurologiczne/141866,mozgowe-porazenie-dzieciece>
2. The Role of Stem Cells in the Treatment of Cerebral Palsy: a Review. Kiasatdolatabadi A, Lotfibakhshaiesh N, Yazdankhah M, Ebrahimi-Barough S, Jafarabadi M, Ai A, Sadroddiny E, Ai J; Mol Neurobiol. 2017 Sep;54(7):4963-4972. doi: 10.1007/s12035-016-0030-0. Epub 2016 Aug 13.
3. Stem Cells... friend or enemy? Paweł Kowalczyk, Katarzyna Hulka, Dorota Dziuban, Maciej Filocha; Borgis - Nowa Medycyna 3/2012, s. 52-55
4. Generation of germline-competent induced pluripotent stem cells. Okita K, Ichisaka T, Yamanaka S; Nature 2007; 448 (7151): 313-317. 5. Goodell, M. J Exp Med 1996; 183: 1797-1806.

5. Stem cell therapy for preventing neonatal diseases in the 21st century: Current understanding and challenges. Christopher R. Nitkin, Johnson Rajasingh, Courtney Pisano, Gail E. Besner, Bernard Thébaud and Venkatesh Sampath; *Pediatric Research* (2019), ; <https://doi.org/10.1038/s41390-019-0425-5>
6. Mesenchymal stem cells prevent hydrocephalus after severe intraventricular hemorrhage. Ahn, S. Y. et al.; *Stroke* 44, 497–504 (2013).
7. Improvement of human umbilical cord mesenchymal stem cell transplantation on glial cell and behavioral function in a neonatal model of periventricular white matter damage. Zhu, L. H. et al.; *Brain Res* 1563, 13–21 (2014).
8. A Randomized, placebo-controlled trial of human umbilical cord blood mesenchymal stem cell infusion for children with cerebral palsy. Huang, L. et al.; *Cell Transpl.* 27, 325–334 (2018).
9. The Role of Stem Cells in the Treatment of Cerebral Palsy: a Review, Anahita Kiasatdolatabadi, Nasrin Lotfibakhshaiesh, Meysam Yazdankhah, Somayeh Ebrahimi-Barough, Mina Jafarabadi, Arman Ai, Esmaeil Sadroddiny, Jafar Ai; *Mol Neurobiol* DOI 10.1007/s12035-016-0030-0; Springer Science+Business Media New York 2016
10. Non-haematological uses of cord blood stem cells. *Br J Haematol* Harris DT (2009) 147(2):177–184. doi:10.1111/j.1365-2141.2009.07767.x
11. Current proceedings of cerebral palsy. Fan HC, Ho LI, Chi CS, Cheng SN, Juan CJ, Chiang KL, Lin SZ, Harn HJ (2015) *Cell transpl* 24(3):471–485. doi:10.3727/096368915x68693119