



MESENCHYMAL UMBILICAL CORD STEM CELLS TREATMENT FOR AUTISM

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KEYWORDS	ABSTRACT
stem cells, autism, autism spectrum disorder, treatment, mesenchymal stem cells.	The purpose of this case is to see the effects of mesenchymal umbilical cord treatments when applied to patients with Autism. The observations are of patients attending the main clinic, "Celltech Stem Cell and Banking," in Jakarta, Indonesia. Findings on pre-treatments showed abnormally varying behaviors, physically as well as psychologically. The treatments were conducted at the Celltech Stem Cell Lab clinics in Jakarta, based on good reasons that MCSUC are well-sourced, easy to collect and preserved, besides its traits of multi-directional differentiation. Patients undergoing the treatments showed calm and friendly behaviors and of the five cases presented, all fulfilled the pre-set standard criteria of recovery. This research has implications for paving the way for the development of innovative stem cell therapies for children with autism.

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INTRODUCTION

Stem cells today represent hope for curing many incurable diseases (Hoang et al., 2022). The three main types of stem cells are placental stem cells, umbilical cord stem cells, and embryonic stem cells (Aronson, 2015). Stem cells can be divided into somatic or adult stem cells, obtained from organs and tissues, and embryonic stem cells, obtained from embryos. In addition, stem cells can be multipotent, pluripotent, and totipotent. Multipotent cells are capable of increasing to multiple cells within a lineage, pluripotent cells are capable of giving rise to all cell types in an adult, and totipotent cells are capable of giving rise to all adult and embryonic cell lineages (Tabansky & Stern, 2016). Stem cells can be obtained from various sources such as umbilical cord, umbilical cord blood, embryo tissue, fat tissue, bone marrow, placenta tissue, amniotic cells, peripheral blood, etc. (Chia et al., 2021); (Poliwoda et al., 2022).

The described procedure is performed for stem cells obtained from the umbilical cord and does not include cord blood. After cultivation, reaching the desired goal of millions of cells, they are ready for storage. Several million stem cells are stored and are in a state of sleep to wake up later when necessary and be ready for use. The optimal temperature for storing stem cells is approximately -135°C. The temperature is slowly increased when it is necessary to use stem cells. The cells are placed in a container where the temperature is approximately 20°C, after which the stem cells are ready for delivery.

This study aims to cover diseases associated with stem cell treatment, autism spectrum disorders (ASD), for which it is predicted that stem cells will gradually replace previous medical treatments and patterns of care in controlling ASD.

METHOD

When a patient's chart indicated any degree of autism, immediate action was taken to place the patient in the autism-type group for further follow-up. However, it was sometimes a good condition. Treatments were performed on average two to three times a week, and not all participants completed the program. The treatment lasted four to eight weeks in patients without comorbid conditions. Patients with comorbidities first received appropriate therapies and then underwent treatment for autism. Mesenchymal stem cells (MSCUC) were delivered to patients, consistently monitored, and documented. The results were recorded, and appropriate actions were taken when necessary.

RESULT AND DISCUSSION

Etiology of Autism

Autistic spectrum disorder is a disorder of behaviour and social interaction due to abnormalities in the brain's neurodevelopment. Autism is a condition in which learning, socializing, and communication are impaired (Health, 2023). Autism involves repetitive and restricted patterns of behaviour. Unusual behaviour or repetition of certain behaviours may include repetition of phrases or words, intense and persistent interest in specific topics such as facts, details, and numbers, overly focused interest in parts of objects or moving objects, agitation due to small changes in routine and tremors with transitions, less or more sensitivity to sensory inputs such as temperature, sound, or light about other people, irritability, and sleep problems. The term "spectrum" is used because of the heterogeneity in the presentation and severity of ASD symptoms and the skills and level of functioning of individuals with ASD (APA Dictionary of Psychology). Autism spectrum disorder refers to subtypes of autism, namely pervasive developmental disorder not otherwise specified, Asperger's disorder, and autistic disorder (Carbone & Dell'Aquila, 2023)

Epidemiology of Autism

The number of children with autism varies from region to region. WHO estimated that, on average, 1 out of 100 children globally have autism. Unfortunately, from 2019 to 2023, the exact figures stayed (WHO, 2019).

The international prevalence of autism is 0.76%. In contrast, according to the Centers for Disease Control and Prevention (CDC), the prevalence in the US is 1.68% for children aged eight years (Hodges et al., 2020). The CDC reported that the prevalence of autism in 2000 was one in 150, while in 2014, it had risen to one in 59 (Hodges et al., 2020); (Prevention, 2021). There was a drop after that in 2016 when one child diagnosed with autism was 54; in 2018, one child out of 44 children; and in 2020, one child out of 36 children. This data were recorded for eight years children (Prevention, 2021). For Indonesia, the growth rate is 1.14%, and autism is estimated to affect about 2.4 million people, where the increase is approximately five hundred people per year (Sari et al., 2020).

Management of Autism

Management of autism should be worth considering as the treatment is administered at low doses to obtain results and then adjusted gradually based on the developed condition (Centers for Control and Prevention for Autism).

For physical exercise, APA therapy is a good try. However, here again, we need to remind you that the program may affect each trainee differently, and it is the trainee's judgement to keep it in a safe condition.

Umbilical Cord Mesenchymal Stem Cell Therapy for Autism and Autism Syndromes

Umbilical cord mesenchymal stem cells represent a class of multifunctional cells isolated and then cultured from the umbilical cord. These cells possess the characteristics of high self-renewal, low immunogenicity, and potential multidirectional differentiation (Shang et al., 2021). Umbilical cord

mesenchymal stem cells (MSCUCs) could differentiate multi-directionally and have the potential to differentiate into cartilage, adipose tissue, bone, and other tissues (Yea et al., 2020); (Kfoury & Scadden, 2015); (Liu et al., 2020); (Richardson et al., 2016); (Shen et al., 2019); (Zhang et al., 2018). Research has shown that when body tissue suffers an anechoic-ischemia injury or chronic inflammation, the damaged tissue releases chemokines then mobilizes and guides the migration of mesenchymal stem cells to the site of the injury. Once at the injury site, stem cells further dedifferentiate into different cell types. Chemokines play an essential role in the maintenance and development of adaptive and innate immunity and play an important role in angiogenesis and wound healing.

Chemokines are in the cytokine family and consist of four subgroups divided according to the cysteine motif (CX3C, CXC, CC, and C). Chemokines can control the attraction of leukocytes to different tissue targets. The critical role of chemokines in neuroinflammation has been hypothesized, where chemokines can function as messengers for communication between neuroglia and neurons. Thus, chemokines may serve as intermediate players in the established relationship between autism and inflammation. The broad features of MSCUC in the recovery of many disorders with the help of raising the immunomodulatory functions of patients are presented. Additional consistency about the role of introducing more components in ASD will be provided by the subsequent applications of MSCUC in haematological diseases.

Allogeneic or autologous hematopoietic stem cell transplantation (HSCT) does not necessarily use high doses of chemotherapy agents as pretreatment. The adverse effects of damage to the bone marrow hematopoietic microenvironment and delayed immunological reconstruction can lead to poor stem cell engraftment and an increase in postoperative infection rate (Bair et al., 2020). A series of clinical and animal studies have shown that cord blood transplantation (CBT) or HSCT, when used in combination with MSCUC infusion, can promote hematopoietic engraftment and reduce the incidence of graft reactions against the host (GvHD) (Yang et al., 2020); (Liu et al., 2020). There were no adverse effects or toxicity when MSCUC was injected into laboratory animals in preclinical studies. There were also no toxicity and side effects when MSCUC was used to treat aplastic anaemia (Liu et al., 2020); (Xu et al., 2018) and leukaemia (K.-H. Wu et al., 2013); in clinical studies ((Shang et al., 2021).

In cases where it can be avoided, it is necessary to consider the graft-versus-host response related to treating autism. GvHD is an immunological disorder where the donor's immune cells attack the host's healthy tissue. It can involve the liver, gastrointestinal tract, lungs, and skin and is life-threatening (Naseeruddin et al., 2017). It has been reported that MSC infusions after allogeneic hematopoietic transplantation (Allo-HSCT) can increase Treg cells in patients, reduce memory B lymphocytes and natural killer cells, and change the Th1:Th2 ratio cell. This leads to the generation of immunological tolerance, after which inhibition of GvHD occurs and improved transplant survival rate (Gao et al., 2016). Severe aplastic anaemia can be life-threatening. The characteristics of severe aplastic anaemia are pancytopenia and bone marrow hypoplasia (Bacigalupo, 2017). Allo-HSCT is recommended in young patients where a matched donor is available as a first line. In contrast, it is recommended as a second line in older patients who have not had success with immunosuppressive therapy (Bacigalupo, 2017); (Killick et al., 2016).

Co-transplantation with donor-derived MSCUC can be used in hematologic malignancies as well as in refractory or recurrent hematologic malignancies to reduce post-engraftment as well as to reduce GvHD (Y. Wu et al., 2013) (Zhao et al., 2019). In addition, there are key facts that need to be seriously considered that show that MSCs can act as a double-edged sword. Patients suffering from haematological malignancies who underwent bone marrow MSC (BM-MS) and HSC co-transplantation after chemotherapy exhibited a higher tumour recurrence rate than patients treated with HSC transplantation alone. Another investigation showed that BS-MS treatment tended to increase

relapse, while MSCUC treatment tended to decrease relapse (Zhao et al., 2019). These results indicate that BM-MSCs are not a viable candidate for GvHD prophylaxis compared to MSCUC. It is also important to note that MSCUCs promote the proliferation of Teji cells in vitro as well as in vivo (Li et al., 2020).

Immune Thrombocytopenic Purpura (ITP), which belongs to the autoimmune disease where the antibody-mediated destruction of platelets and variable platelet production may occur, is also one of the symptoms that MSCUC may seek of helped (Justiz et al., 2020); (Tinazzi et al., 2020). It is known that ITP is an immune system where blood cells (platelets) are destroyed, leading to the formation of blood clots. A low platelet count leads to easy bleeding and bruising, which can be seen as purple areas on the skin, organ linings, or mucous membranes (Syndrome, 2016). The results showed that when MSCUC were co-cultured with splenocytes from an ITP patient, they could stimulate spontaneous antiplatelet antibody (PAIgG) healing. Under platelet-inducing conditions, MSCUC inhibits PAIgG production when the ratio of splenocytes to MSCUC is low. Furthermore, MUSC inhibits the proliferation of platelet-reactive T helper cells in a close-dependent manner. Therefore, MSCUC can regulate the secretion of antiplatelet antibodies in vitro (Shang et al., 2021).

Case Study

Specific treatments of young patients with ASD and their progress will be reviewed here as a case study. The age of the studied group is from 4 to 9 years, and all symptoms of ASD were detected near the beginning of the development of the disorder. Each patient should undergo allele testing to determine their actual condition. Other essential conditions of the typical characteristics of the laboratory evaluated outcomes are satisfying the GMW standard. Below is the collected patient data.

Patient #1: A 4-year-old boy with ASD was diagnosed at two years old. There is a lack of contact with the fathers, and the conversation is delayed. He can express his wishes fluently, such as "I want to open the door" or ride a motorbike." Allele exclusion and MSCUC transplantation during three treatments.

Patient #2: A 7-year-old girl with ASD was diagnosed at four. She cannot speak and is hyperactive. She was treated with quantum MSCUC. There is no collected data on the results, except that hyperactive behaviour seems to be under control. Other results have not yet been revealed. It is necessary to monitor the patient for another 1-2 weeks to notice the effects of the treatment.

Patient #3: A 3-year-old girl with ASD was diagnosed when she was two. She has a speech delay and unrecognizable sound expressions because she talks with his mouth closed. Not a single word or noticeable sound is recognized. She is thirsty most of the time and likes to drink. After the treatment, there was a surprising improvement in cognitive abilities. She has started to open her mouth when she speaks and follows clearly with almost clear understanding. Cognitive abilities improve rapidly.

Patient #4: A 7-year-old boy with ASD was diagnosed at 1.5 years old. He is hyperactive, speaks when imitating, cannot focus, and emotional control is defective. He underwent quantum stem cell treatment.

Patient #5: A 4-year-old boy born through in vitro fertilization. At six months, he knew how to say "mom" and "dad," at one year, he was walking, even running, and did not respond to calls. During the treatment, he was diagnosed with ASD.

The boy's older sister is ten years old and in normal health. The sister was also born from in vitro fertilization. All patients were provided with a different number of MSCUCs, and the optimal results were positive.

CONCLUSION

MSCUC treatments applied to patients with ASD have shown, after follow-up, the potential reliability of stem cells to contribute to improving the effectiveness of ASD treatment. From an epidemiological point of view, ASD has shown a statistically consistent development, slow but steady. Therefore, additional efforts are needed to improve the epidemiological picture of ASD. Close consistency is assured by the ongoing trend, which is based on competent authorities in Indonesia and WHO data and other regions of the world. Stem cells have shown excellent efficiency in treating various hitherto incurable diseases. According to the results of theoretical research and research findings, stem cells could be used as a treatment for ASD. However, further research to safeguard its reliability is expected and welcome.

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