

Use of the cell-based treatment for inflammation triggered depression



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Abstract

With a variety of immunophenotypic profiles, isolation methods, modes of action, and regulatory levels, cell therapy comprises stem cell- and non-stem cell-based, unicellular, and multicellular therapies. Antidepressant-based conventional therapy is ineffective for about one-third of depressed patients. The use of mesenchymal stem cell therapy to treat depression is one of several potential non-pharmacological treatments that have been researched recently. Since it is clinically pertinent to create novel treatments to treat psychiatric patients, these therapies are reviewed here. Based on its anti-inflammatory and neurotrophic qualities, experimental findings support the idea that mesenchymal stem cell therapy could be regarded as a possible treatment for depression. However, there are several ongoing clinical trials using stem cells to treat depression, but no findings have been made public. To determine how much mesenchymal stem cells can be used in psychiatric clinics as a technique for aiding depression treatment, this review and other upcoming clinical investigations will be significant.

Keywords: Cell therapy, Depression, Inflammation, Mesenchymal stem-cell transplant.

Introduction

Cell therapy also referred to as cellular therapy, cell transplantation, or cryotherapy, is a form of treatment in which live cells are injected, grafted, or implanted into a patient to produce a therapeutic effect, such as stem cells to repair damaged tissues or T cells to fight cancer cells through cell-mediated immunity during immunotherapy. When scientists experimented by injecting animal material to treat and prevent disease in the nineteenth century, cell therapy was developed. [1] Despite the failure of these attempts, subsequent research revealed in the middle of the 20th century that human cells might be utilized to help prevent the human body from rejecting transplanted organs, eventually leading to the success of bone marrow transplantation, which is now a common procedure in treatment for patients that have compromised bone marrow after disease, infection, radiation or chemotherapy.[2] In recent decades, however, researchers have gained significant interest in stem cell and cell transplantation as a potential new therapeutic strategy for a wide range of diseases, for neurodegenerative and immunogenic pathology.

Mechanism of cell-based therapy

Cell-based therapy may be allogenic [3], autologous [4] xenogeneic [5], and the types of cells used in cell therapy are human embryonic stem cells [6], neural stem cells [7] mesenchymal stem cells [8] hematopoietic stem cells [9] differentiated or mature cells. [10] Cell therapy is targeted at many clinical indications in multiple organs and by several modes of cell delivery. Accordingly, the specific mechanisms of action involved in the therapies are wide-ranging. However, cells assist therapeutic action using two main concepts. One involves the engraftment, differentiation, and long-term replacement of injured tissue with stem, progenitor, or mature cells. In this paradigm, stem cells undergo in vitro or in vivo differentiation into a particular cell type. These cells, integrate into the wound site and help the organ or tissue function better overall. Using cells to produce cartilage matrix in intervertebral disc degeneration is an example of this mechanism. [11] Second, cells that can release soluble substances including cytokines, chemokines, and growth factors have endocrine or paracrine effects. By stimulating local (stem) cells or drawing cells to the transplantation site, these substances help the organ or area heal on its own. It has been demonstrated that early cell passes are more effective paracrine action than later passages. [12,13] The transferred cells, are viable for only a few days to a few weeks before they die. Cells that release substances that promote angiogenesis, reduce inflammation, and prevent apoptosis are examples of this. [14]

Inflammation triggered depression

Stem cell therapy has shown promise in animal trials for treating several neuropsychiatric illnesses and cognitive/social deficiencies, both during development and after neurodegeneration. Now, we have information that suggests that these stem cells may be involved in treating depression by increasing the number of neurons in the brain that can create more connections.

In recent years, there has been mounting evidence that chronic inflammatory states may play a role in the etiology of depression. This data allowed for the creation of fresh anti-inflammatory treatments that could slow the onset and progression of depression [15,16,]. One group investigated the potential application of stem cell therapy in a prior study. Their theory was based on stem cells' potential to heal the pathogenic condition that sustains depression and their anti-inflammatory and neurodegenerative characteristics. [16]

The psycho-neuroimmunological dysfunctions are emphasized as important by the inflammatory theory. This is based on a few findings: cytokines can affect neurotransmitter metabolism, neuroendocrine function, and regional brain activity, all of which are relevant to depression; acute administration of cytokines causes sickness behavior that shares features with depression; and patients receiving cytokine treatment develop depressive symptoms. Subsets of Major Depressive Disorder (MDD) patients have an altered peripheral immune system, with impaired cellular immunity and increased levels of proinflammatory cytokines. [17,18]

Stem cell therapy in depression

Neurological diseases and subacute and chronic inflammatory processes are now commonly treated using stem cell treatments. Numerous neurological disorders, including multiple sclerosis [19], autoimmune encephalomyelitis [20], Alzheimer's disease and other dementia conditions [21], Parkinson's disease [22], and epilepsy [23], may be treated with adult stem cell therapy, according to research. The encouraging outcomes of experimental investigations using mesenchymal stem cells (MSCs) and bone marrow mononuclear cells (BMMCs) in the treatment of neurological illnesses raise the possibility of creating non-pharmacological cell therapies for psychiatric disorders. The major findings from these investigations include reduced expression of pro-inflammatory cytokines, increased expression of anti-inflammatory cytokines, and decreased 8'2-deoxyguanosine in BMMCs are all anti-inflammatory effects. Treatment with adipose tissue-derived stem cells improves depressive-like behavior. By increasing miR-26a, BMSCs-derived exosomes reduced hippocampus neuron damage in depressed mice. [24]

Clinical Trials with stem cells in depression

The outcomes of various experimental studies significantly indicate stem cells' potential therapeutic application in the treatment of depression. Although data from experimental models have demonstrated beneficial effects in treating depression, there are still open questions. To determine the ideal dose, method of administration, and basic mechanisms of action, additional research is also required. Further discussion on the applicability of such experimental models to the target human population, which may include individuals who are resistive to treatment and who take multiple medications, is warranted. These deficiencies have led to the registration of the first clinical trials using exosomes or cell-based products to treat depression on international platforms. At this time, four clinical studies (phases 1 and 2) are being assessed for the security, effectiveness, and acceptability of administering MSCs and exosomes (Table 1). [25]

Table 1: Cell- therapy-based clinical trials for treating depression [25]

Study	Target population	Product	Outcomes
NCT02675556	Treatment-resistant depression; (n = 80)	Allogeneic MSCs; 108 cells. Single i.v. infusion; source not reported	Incidence of any treatment-emergent serious adverse events; Reduction of Inflammation.
NCT03522545	Treatment-resistant bipolar depression; (n = 30)	Allogeneic bone marrow-derived MSCs; dose not reported	Change in depression as assessed by the MADRS Scale.
NCT03265808	Alcohol use disorder and major depression; (n = 80)	Allogeneic MSCs; 108 cells single i.v. infusion; source not reported	An incident of treatment-emergent-serious adverse events
NCT04202770	Refractory depression; anxiety disorders; neurodegenerative diseases; (n = 300)	Focused ultrasound and exosomes	Beck depression inventory (BDI-II)

Conclusion

Treatment-resistant depression may benefit from cell therapy, including BMSC or MSC transplantation or the delivery of cell products such as exosomes. Many problems have not been resolved despite the small number of preclinical research, including how long the antidepressant effect lasts. It is an important query with implications for the viability of these treatments. The likelihood of an effective treatment for this chronic, severe, and common disorder must be investigated due to the difficulty that comes with the treatment of resistant depression. Preclinical research is still limited; hence it is recommended that clinical trials be extended further.

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