Research progress of embryonic stem cells in treatment of spinal cord injury

Deqiang Gao[1] , Xiaobo Guo[2] , Dengsheng Guo[1]

1. Changzhi Medical College, Changzhi 046000, China.

2. Spine Minimally Invasive Orthopedics Department, Jincheng General Hospital, Jincheng 048000, China.

Abstract: Spinal Cord Injury (SCI) refers to the structural and functional injury of the spinal cord under external forces. The spinal cord is an important part of the human nervous system, responsible for transmitting information between the brain and the rest of the body. Spinal cord injury may lead to varying degrees of neurological dysfunction, including impaired sensory, motor, autonomic, and vesical and intestinal functions [1]. Traditional treatments for patients often fail to fully restore their function, so it is particularly important to find a new treatment [2]. As a kind of cell with the ability of self-replication and multidirectional differentiation, stem cells have been widely used in the treatment of spinal cord injury, showing great potential in the treatment of spinal cord injury and achieving certain clinical effects [3]. This article reviews the research progress of embryonic stem cells in spinal cord injury, aiming to explore the application status, mechanism and prospect of stem cells in the treatment of spinal cord injury, and provide scientific basis for clinical treatment.

Keywords: Stem Cells; Spinal Cord Injury; Transplantation; Repair; Treatment

1. Characteristics of embryonic stem cells

Embryonic stem cells are formed during early embryonic development and have the characteristics of self-renewal and pluripotency. They can replicate themselves without limit and are able to differentiate into various cell types in the body. [4] Human embryonic stem cells (hESCs) are stable in terms of pluripotency, karyotype, global gene expression, ability to repair DNA and maintain telomerase levels, and growth characteristics. hESCs provide a renewable source of multiple cell types for research and cell-based therapies to treat disease. This makes embryonic stem cells a potential option for treating a variety of diseases. Embryonic stem cells can be transplanted into the damaged spinal cord area to promote nerve regeneration. Once transplanted, these cells can differentiate into nerve cells, replace damaged nerve cells, and rebuild damaged neural networks. [5] Research has shown that cell replacement therapy using stem cells or their derivatives has become a very promising approach to promoting motor recovery in this regard. Embryonic stem cell transplantation can improve motor and sensory function in patients and improve quality of life. [6]Jones I, et al transplanted embryonic stem cells into acute and chronic rat models of cervical spinal cord injury, promoting remodeling of descending spinal projection and contributing to partial recovery of forelimb motor function. The results obtained in this proof-of-concept study suggest that human embryonic stem cell-derived neural crest cells warrant further investigation as cell-based therapeutic candidates for spinal cord injury. Second, embryonic stem cells have the ability to secrete a variety of growth factors and cytokines, which can promote the regenerative environment of the damaged spinal cord. [7] Stem cells are induced by nutritional factors in vivo and in vitro to differentiate into other types of cells, including neurons. Scientists have isolated various stem cells from different organs and tissues in the human body and demonstrated that these cells are effective in regenerative medicine. The use of these cells offers a non-surgical approach to treating neurological disorders such as neurological defects. These molecules can stimulate the growth and connections of nerve cells, promoting repair and regeneration of damaged areas. The study found that embryonic stem cells can promote nerve cell regeneration and improve functional recovery after spinal cord injury.

2. Mechanism of stem cells promoting spinal cord injury repair

The mechanism by which stem cells promote spinal cord injury repair is an area of great interest. Research has shown that stem cells can promote spinal cord injury repair in a variety of ways, including promoting neuronal regeneration, reducing inflammation, promoting neuronal regeneration and forming new synaptic connections. These mechanisms provide a theoretical basis for the application of stem cells in the treatment of spinal cord injury, and also provide an important research direction for future clinical treatment.

Release of secretory factors: Stem cells can release a variety of growth factors, neurotrophic factors and neuroprotective factors, such as nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neuron-oriented factor (NT-3), etc. These factors can promote the growth, regeneration and connectivity of nerve cells, provide nutrition and support, and improve the environment of damaged areas. [8]Luo H et al. transplanted RADA16-PRG self-assembled nanopeptide scaffolds (SAPNSs), bone mesenchymal stem cells (BMSCs), and brain-derived neurotrophic factor (BDNF) expressing adeno-associated virus (AAV) into rats with acute spinal cord injury (SCI). To investigate the effects of these transplants on acute spinal cord injury (SCI) repair and explore the mechanisms, results showed: Co-transplantation of RADA16-PRG-SAPNS with BMSCs and BDNF-AAV can prolong the survival time of BMSCs in rats, reduce postoperative scar formation caused by glial cell proliferation, promote the migration and proliferation of neurons in the injured area, and promote functional repair after acute spinal cord injury.

Immune regulation: Stem cells have the function of immune regulation, which can inhibit the inflammatory response, reduce the infiltration and activation of immune cells, reduce the release of inflammatory factors, reduce the inflammatory damage in the injured area, and promote repair and regeneration [9].

Spinal cord environmental regulation: Stem cells can change the environment at the site of spinal cord injury, including improving blood circulation, increasing angiogenesis, promoting the migration and localization of neurons and glial cells, and providing suitable growth environment and support [10].

These mechanisms interact to promote the repair and functional recovery of spinal cord injury. However, there are still some controversies and unanswered questions about the specific mechanism, and further research and experiments are needed to further understand it.

3. Application of embryonic stem cells in spinal cord injury

Spinal cord injury (SCI) is one of the serious neurological diseases that occur in young people with high rates of morbidity and disability. However, effective treatments are still lacking. Stem cell (SC) therapy for SCI has gradually become a new research hotspot in the past decades. [11]Zeb H, Khan IN, et al., mention that in the last century, scientific advances have created a new paradigm for the medical treatment of SCI. Basic and translational research has flourished, so much so that a variety of protective and regenerative therapies can be used in clinical trials. In particular, the mechanisms underlying the pluripotent state of human embryonic stem cells (hESCs) proved crucial in identifying the intended role of SCI in regenerative medicine. Knowledge of SCI related neurogenesis and hESC is essential for critical evaluation of existing translational therapy strategies for SCI. [12] To date, more than 200 clinical studies have been registered applying various stem cell approaches to treat neurological disorders (Clinicaltrials.gov), most of them for multiple sclerosis, stroke, and spinal cord injury. In total, we identified 17 neurological indications that are in clinical development. By transplanting embryonic stem cells into damaged areas of the spinal cord in the hope that they will differentiate into nerve cells and repair the damage, [13] A large number of studies have focused on SCI treatment of SCI, most of which have shown good results with both in vivo and in vitro induction. The transplantation routes include intravenous, transarterial, nasal, intraperitoneal, intrathecal and intramedullary injection. Most SC treatments for SCI use many cells, ranging from tens of thousands to millions. Researchers can do this by taking a patient's own adult stem cells, differentiating them into nerve cells, and transplanting them to the site of the spinal cord injury. [14]Dalamagkas K et al mentioned NeuralStem Inc. Phase I clinical trials are currently underway using human spinal cord stem cells (NSI-566) derived from the spinal cord of a single 8-week-old fetus and continuously expanded by epigenetic means only. Although no publicly available data is available, the company reports that no serious adverse events have occurred, that stem cell implantation is feasible in patients with chronic SCI, and that implantation of NSI-566 FSC in patients with SCI is safe and well-tolerated. The last surgery was completed in June 2015, and the patient recently completed the 2015 month post-observation period (NeuralStem Inc., 566). [15]Tsuji O et al. found that when ES cells are applied to the treatment of SCI, it is preferred to transplant ES derived cells that have formed nerve stem/progenitor cells, which can produce glial cells and neurons, rather than nerve stem/progenitor cells that almost only produce neurons. These findings are therefore extremely important for future attempts to implement ES cell and iPS cell transplantation therapies. This approach avoids the problem of immune rejection;

4. Challenges and prospects of embryonic stem cells in clinical application

Although embryonic stem cells have made some progress in the treatment of spinal cord injury, there are still some challenges. Such as cell transplantation survival and differentiation efficiency, cell source selection, immune rejection and safety. In response to these problems, researchers are constantly working to find solutions to improve the effectiveness and safety of stem cell therapy. Embryonic stem cells face several challenges in clinical applications, including the following:

Safety concerns: [16] Heng BC et al mentioned indirect evidence that the observed therapeutic effect was due to various secretory factors produced by transplanted cells. This therefore raises the exciting prospect of using human embryonic stem cells as a “catalyst” to promote bioremediation and regeneration in transplant therapy. However, the immune barrier against allotransplantation and the teratogenic potential of human embryonic stem cells present significant technical challenges. Stem cell transplantation may trigger safety issues such as immune rejection or tumor formation after xenotransplantation, and these potential risks need to be addressed to ensure the safety of treatment. 2. Quality control: [17] Hashii N et al mentioned the limited availability of cell therapy products and the need for more sensitive and specific quality testing methods. Quality control of cell therapy products requires a more sensitive and specific approach, as in many cases only a small number of cell products, approximately 1×106 to 1× 108, should be available for quality testing. Quality control of stem cells is an important challenge to ensure that the source, culture, differentiation and quality of stem cells meet clinical requirements. 3. Ethical issues: Due to ethical and legal restrictions on the use of embryonic stem cells, their clinical application still needs further research and discussion.

Despite the challenges, stem cells still hold great promise in clinical applications:

Therapeutic potential: [18]Gazdic M et al. mentioned that hESC is pluripotent both in vitro and in vivo. Since hESC can differentiate into ectodermal cells such as neurons and glial cells, it has been used as a new treatment option for SCI in many clinical studies. Transplantation of HESC-derived oligodendrocyte progenitor cells into SCI models in this paper resulted in cell survival and clinically relevant recovery of neural function without evidence of harmful effects. Embryonic stem cells are pluripotent and self-renewing, can differentiate into a variety of cell types, has a wide range of therapeutic potential, can be used to treat a variety of diseases and injuries, such as cardiovascular and cerebrovascular diseases, neurodegenerative diseases, tissue damage and so on. 2. Individualized treatment: Embryonic stem cells can be derived from patients themselves, which has a low risk of immune rejection, and can realize individualized treatment strategies and improve treatment effects.

Tissue Engineering and regenerative medicine: Embryonic stem cells can be used in tissue engineering and regenerative medicine to help repair and regenerate damaged tissues and organs, offering new possibilities for clinical treatment. 4. Innovative therapies: Embryonic stem cell therapy is an innovative treatment method that can develop new therapeutic strategies and drugs and promote the progress of medical science.

To sum up, stem cells face some challenges in clinical application, but they still have broad prospects and application value, and are a field of concern and research. With the continuous progress of science and technology, these challenges will gradually be overcome, and stem cell therapy is expected to bring more well-being to human health.

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