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“Stem Cell Therapy In Spinal Cord Injury”

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❖ Abstract:

Spinal cord injury is damage to the spinal cord that results in a loss of function such as mobility or feeling. This dysfunction could not be restored. To repair the spinal cord injury is through transplantation of stem cells or progenitors. On this article the promising results so far regarding stem cell therapy in Spinal cord injury will be discussed in terms of neuroprotection, axon regeneration and induced pluripotent. The ability of differentiation of Stem cells into neurons or glia in vitro, can be used for replacement of cells after Spinal cord injury. Neuroprotective and axon regeneration-promoting effects have also been credited to transplanted stem cells. There are still issues related to stem cell transplantation that need to be resolved, including ethical concerns.

1. Introduction:

1.1 Stem cell

1.1.1 **Definition:** A stem cell is defined by its ability of self-renewal and its totipotency. Self-renewal is characterized by the ability to undergo an asymmetric division in which one of the resulting cells remains a "stem cell," without signs of aging, and the other (daughter) cell becomes restricted to one of the germ layers. A stem cell may become quiescent and at later stages re-enter the cycle of cell division[1,2].

1.1.2 **Types:** A true stem cell is a totipotent cell; it can become any cell type present in an organism. Many consider the zygote to be the only true totipotent (stem) cell because it is able to differentiate into either a placenta cell or an embryonic cell. Others define the cells of the inner cell mass within the blastocyst as embryonic stem cells (ESCs). These cells are pluripotent because they cannot become a placenta cell. Besides ESCs, undifferentiated cells can be found among differentiated cells of a specific tissue after birth. These cells are known as adult stem cells, although a better term would be "somatic stem cell" because they are also present in children and umbilical cords.

1.1.3 **An important advantage** of adult stem cells over ESCs is that they can be harvested without destruction of an embryo. As a result, adult stem cells have gained ample interest for their application in a variety of disorders[3,4,5].

1.2 Spinal cord:

1.2.1 **Anatomical:** The spinal cord is a vital link between the brain and the body, and from the body to the brain. The spinal cord is 40 to 50 cm long and 1 cm to 1.5 cm in diameter. Two consecutive rows of nerve roots emerge on each of its sides. These nerve roots join distally to form 31 pairs of spinal nerves and it is divided into four regions: cervical (C), thoracic (T), lumbar (L) and sacral (S), each of which is comprised of several segments. The spinal nerve contains motor and sensory nerve fibers to and from all parts of the body[6].

1.2.2 **Spinal cord injuries (SCI):** Damage to any part of the spinal cord or nerves at the end of the spinal canal often causes changes in strength, sensation and other body functions below the site of the injury[7].

1.2.2.1 **Types of SCI:** Can be complete or incomplete. With a complete spinal cord injury, the cord cannot send signals below the level of the injury. As a result, you are paralyzed below the injury. With an incomplete injury, you have some movement and sensation below the injury[8].

2. Ability of spinal cord repair:

The endogenous regenerative events that occur After SCI, indicating that the spinal cord attempts to repair itself. Schwann cells, the myelinating and regeneration-promoting cell in the peripheral nervous system, migrate from spinal roots into the damaged tissue and myelinate spinal cord axons[9,10]. The expression of regeneration-associated genes is increased in damaged neurons[11]. There is a surge in proliferation of local adult stem cells and progenitor cells[12,13]. However, axonal growth is thwarted by growth inhibitors present on oligodendrocyte myelin debris and on cells that form scar tissue[14,15]. Also, the newborn stem cells and progenitor cells do not integrate functionally into the injured spinal cord tissue. Thus, the endogenous regenerative events that occur after injury fail to repair the spinal cord.

3. Application of stem cell therapy in SCI:

3.1 Replacement of Injured Cells:

Considering the ability of stem cells to become any cell type, their potential use for cell replacement strategies is common sense.

According to the studies in (PNAS-USA)[16], (NM journal)[17], and (Annals Neuro journal)[18], It was concluded that the appropriate combination of (growth) factors, ESCs can be used to obtain neurons and glial cells, also ES-derived neurons can survive and integrate after injection into the injured rat spinal cord. As the studies show the mouse ESCs grafted into the injured mouse spinal cord, the mouse ESCs myelinate axons in the myelin-deficient shiverer rat spinal cord and result in improved functional recovery. Importantly, ESCs were found to survive well within the injured spinal cord, suggesting that long-term treatments could be achieved using this approach.

Regarding to the previous results, that based on the Directed differentiation and transplantation of human embryonic stem cell-derived motoneurons[19], and the Human embryonic stem cell-derived oligodendrocyte progenitor cell transplants remyelinate and restore locomotion after spinal cord injury. They conclude the Human ESC can be directed toward multipotent neural precursors, motor neurons, and oligodendrocyte progenitor cells. The latter were found to differentiate into mature oligodendrocytes in vitro and in vivo.

3.2 The Protection Of Neural Cells From Death:

Regarding to the study in 2004 that based on Neural stem cells protect against glutamate-induced excitotoxicity and promote survival of injured motor neurons[20], It was shown the neural progenitor cells secrete a variety of molecules that could protect neural cells from death mechanisms other than excitotoxicity. Thus, transplantation of these cells into the injured spinal cord could in fact exert neuroprotective effects.

Based on these it may be concluded that the neuroprotective strategy implemented soon after SCI would be the first line of defense against injury-induced tissue loss and could contribute to an improved neurological outcome.

3.3 Promoting Regeneration Of Axons:

Study in 2003 shows the ability of neural progenitor cells to secrete a variety of neurotrophic factors indicates that they could promote growth of damaged axons[21].

Therefore, the Promoting axon growth in the injured spinal cord could contribute to restoring function.

3.4 The Possibility To Obtain Pluripotent Cells:

Studies based on Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors[22] and induced pluripotent stem cell lines derived from human somatic cells[23]. It was shown the possibility to obtain pluripotent cells by reprogramming differentiated cells, such as fibroblasts, through the introduction of 4 transcription factors, OCT3/4 (octamer-4), SOX2 (sex-determining region Y-box2), KLF4 (Kruppel-like factor), and MYC (induced pluripotent stem (iPS) cells.

This new technology was first described by Takahashi and Yamanaka for mouse fibroblasts and has now been applied for other mouse cells and for human somatic cells.

4. Conclusions and Recommendations:

4.1 **Conclusions:** The repair of spinal cord injury by Stem cells is possible, but their true potential has not yet clearly been shown. The associated risks of stem cell–based therapies are still unclear. Stem cell therapies still have ethical and social barriers. As with any medical intervention, the questions to be asked are whether this approach is the most likely one to achieve success or the risks justify the benefits.

4.2 **Recommendations:** Stem cell therapy have shown favorable therapeutic outcomes, it serves as new optimistic treatment for many untreatable diseases by repairing and regenerating the injured tissue, this report based on the ability of stem cell to treat spinal cord injury, but this therapy can treat numerous different diseases, from multiple sclerosis to blindness, crohn's disease, diabetes and autoimmune disease, I hope the other reports describe the role on stem cell therapy in this diseases.

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