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Case Report

Treatment of a Population of 32 Patients with ALS and Spine Injury Grafting Stem Cells through Neuroendoscopy

Alvaro Cordoba[1]* and Dra Mariela Alza[2]

[1]*Department of Neurology, British Hospital Montevideo Uruguay, Uruguay*

[2]*Department of ENT surgery, Police´s Hospital Montevideo Uruguay, Uruguay*

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***Corresponding author**

Alvaro Cordoba,Department of Neurology, British Hospital Montevideo Uruguay, Uruguay

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Introduction

Considering the devastating effects of the ALS (Amyotrophic lateral sclerosis) we have designed a trial in order to treat a series of 24 patients implanting their own stem cells, in the spinal cord and in the cerebrospinal fluid, through a neuroendoscopic procedure. We utilized stem cells implants in 4 patients with traumatic spine injury combining haemathopoietics types of precursors. Neuronal death and degeneration occurs prematurely in spinal cord trauma and in neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), among others. The low CNS repair potential has led to the development of therapeutic strategies focused on maintaining the viability of damaged tissue, limiting the area of injury or halting the progression of a neurodegenerative disease.

Materials and Methods

We have designed a treatment protocol for these patients who have autologous stem cells implanted in the spinal cord and CSF, immediately after being selected and purified [1-5]. To improve functional rehabilitation and quality of life in the injured spinal cord by means of the repetitive grafting hematopoietic stem cells.

Methods

24 patients with (ALS) and 4 patients with traumatic spine injury in the last 6 months met the inclusion criteria for this study. Mean follow up of 18months. Spirometry not inferior to 60% was required. All patients were measured with an (ALS) scale. No patients with less than 17 points were included. Bone Marrow was stimulated with Filgrastim 10mg/kg Peripheral blood stem cells were collected $CD34^+$cells were tested and selected under general anesthesia. A spinal needle in the intervertebral space L_4-L_5 is introduced to obtain four milliliters of Cerebrospinal fluid and to suspend 2ml of Stem Cells in it, injecting in the subarachnoid space. Then between D_8 and D_9 we introduce percutaneously a semiflexible 0.9mm Neuroendoscope 1ml. of concentrated stem cells are transplanted. 2ml of concentrated stem cells are injected in the perispinal space. The remaining Stem Cells were injected through the central venous catheter. The last 4 patients were included in the haemathopoietics stem cells grafting group.

Results

No complications were observed. Periodically assessment of the evolution of the score points of the ALS function and ASIA scale revealed at 18 months that 15 patients improve their initial scores while 9 keep the same condition with no progressive deterioration. A decrease of the muscular fasciculations was observed. Two patients with long survival more than 6 months were considered to be re-transplanted withsame results. Three patients died with pulmonary insufficiency in the first 18 months. Patients with spine injury showed improvement of motor and sensitive-vegetative performances in 3 cases with no changes in one patient, (improve of ASIA scale from A to B and C) and will be considered to be part of a new protocol combining OEC and haemathopoyetics SC.

Discussion

The term "stem cell" (SC) was coined in 1868 by Ernst Haeckel, a German biologist who used "Stammzelle" (stem cell in German) to designate the single-celled organism as the ancestor of all multicellular organisms. Today, SC also called progenitor, mother or Stem Cells are a group of cells characterized by their capacity for self-renewal throughout life, developing functions of cellular homeostasis and in the repair and regeneration of tissues and for responding to signals or stimuli present in the microenvironment where they are found, inducing their differentiation towards cell lines with specialized characteristics and functions [6-8]. To date, there is no ideal SC for regenerative medicine, since they present great heterogeneity [9-11]. It has been considered that the ideal SC for tissue regeneration are those obtained from internal cells of the blastocyst. However, its use in human therapy is ethically complex since it involves the destruction of donor embryos and has potential risks, since there is evidence of development of teratomas in vitro and in vivo. On the other hand, adults SC have the ability to differentiate into cells of different lineages, without developing teratomas and without ethical impediments [12-14]. Until two decades ago, it was thought that there was no neuronal replacement in adult mammals. However, today we know that neurogenesis exists from SC located in the neurogenic niches of the subgranular zone of the hippocampus, the subventricular area of the olfactory bulb and the subependymal area of the spinal cord. Neurogenesis is limited and depends on the activity of the astrocytes that secrete factors and cytokines, generating a microenvironment that induces neuronal development and differentiation in the hippocampus area, but that at the same time would fulfill an inhibitory role in the proliferation of Neural CT´s in the rest of the central nervous system (CNS). This dual effect translates into a restricted CNS repair response to injury and neurodegenerative diseases. One of the most interesting effect was observed in the disappearance of the fasciculations immediately after the procedure. Same as observed with pharmacological treatment with Riluzol and Gabapentin [15]. We suppose a cytokinerelated effect over the target.

The enveloping cells of the olfactory bulb (CEO), possess regenerative capacities, are part of the glía limitans of the olfactory nerve and have the ability to distribute both along the olfactory epithelium in the SNP, and within the CNS, in the layers of fibers olfactory and glomerular [16-18] they share phenotypic characteristics with astrocytes and Schwann cells [19-21] and within the olfactory nerve, they stimulate the differentiation of neural precursors towards olfactory neurons, enabling them to reconnect with the olfactory bulb in the CNS, after injury [22,23]. CEO transplants have been used as an alternative in the repair and regeneration of CNS anisomorphic lesions (with destruction of the blood-brain barrier and the glia limitations),

mainly at the level of the spinal cord, caused by: dissection, hemisection and contusion mechanics. The results obtained demonstrate neuroprotection, regeneration and partial functional recovery of the affected area [24,25]. The use of cells of the olfactory bulb to promote the repair and regeneration of damaged tissues in various neurological pathologies is proposed, for which curative therapies are currently lacking, including, among others, ischemia, Parkinson's and medullary trauma, in which both structural and functional benefits were obtained [26,27]. There is evidence of the ability to self-renew and differentiate SC as well as their ability to secrete trophic factors, induce signals of cell survival, and interfere in the long term with the mechanisms responsible for neuronal apoptosis. Furthermore, they directly inhibit cell death by inducing anti-apoptotic and anti-oxidant proteins. Until now, there is no effective and bloodless treatment to reverse the functional sequelae of the spinal cord injury due to traumatic spinal injury.

Acknowledgement

To: Prof Dr Roberto de Bellis In Memoriam.

Conclusion

The procedure was safe, feasible and easy to reproduce. Improvement of neurological condition was registered and stabilization of the progressive disease in others. In spite of the short follow up we think is a encouraging new approach in restorative neurosurgery.

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