Regenerative Stem Cell Therapy with Umbilical Cord Mesenchymal Stromal Cells In Deaf Animal Model

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Abstract

Introduction

Hearing loss is one of the most common diseases. The majority of human sensorineural hearing loss (SNHL) results from primary neuronal loss involving the degeneration of neurons in the absence of hair cell degeneration or secondary to the loss of hair cells that normally provide trophic support to spiral ganglion neurons (SGNs). Mesenchymal stem cells (MSCs) have the capacity for self-renewal and proliferation and are multipotent; thus, they can differentiate into various specific cell types such as muscle, epithelium, and liver cells. Recent studies have also demonstrated that neuronal cells such as Schwann cells (supporting cells) can differentiate from the endogenous stem cells in the inner ear and from MSCs. This study was performed to confirm the effect of transplantation of human umbilical cord blood mesenchymal stem cells (UCB-MSCs) on hearing restoration in a sensorineural hearing loss (SNHL) animal model.

Materials and Methods

1. Isolation of UCB-MSC
- centrifuge gradient method with the use of histopaque (Sigma-Aldrich, ST Louis, MO)
- 4°C, for 20 minutes, at 2500 rpm,
- a layer of mononuclear cells between the serum and RBC layer was extracted.
- Flow Cytometry (FACS Caliber, Becton Dickson, San Diego, CA)

Marker for hematopoietic stem cells; CD34, CD45 for mesenchymal stem cells; CD73, CD90

2. Deaf animal Model & Transplantation of UCB-MSC
- SPF Guinea Pig (wt : 250 – 300 g) (5 cases in each group)
- Saline injection, MSC injection

DPOAEs and increased ABR threshold were noted. And ABR hearing thresholds were unconverted and were similar to those observed in deafness. The transplanted UCB-MSC group showed a significant improvement in hearing threshold(40dB).

Result: In SNHL group, decreased DPOAEs and increased ABR threshold were noted. And ABR hearing thresholds were unconverted and were similar to those observed in deafness. The transplanted UCB-MSC group showed a significant improvement in hearing threshold(40dB).

Conclusions: Intravenous transplantation of UCB-MSCs can enhance hearing thresholds, and regenerate inner ear hair cells and spiral ganglion neurons (SGNs).

Results

1. Hearing restoration with UCB-MSCs transplantation

A) Auditory brain response (ABR) results compared between normal hearing, SNHL, and UCB-MSC transplantation groups. Click-evoked ABR waves were recorded up to 10 dB in guinea pigs with normal hearing. After intravenous injection, the UCB-MSC group showed a significant improvement in hearing threshold compared to that for the SNHL group.

B) The SNHL group showed disappearance of DPOAE expression. After UCB-MSC transplantation, the DPOAE re-expressed.

Conclusion

- Based on these results, intravenous transplantation of UCB-MSC can restore hearing of deaf animal.
- Transplantation of UCB-MSC can regenerate the damaged SGN & hair cells.
- In the current study, it was demonstrated that UCB-MSC could be used in stem cell based therapy for the deaf in the future.