Effectiveness of Umbilical Cord Derived Mesenchymal Stem Cell Transplantation in Cochlear Implantation

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Introduction

- Mesenchymal stem cells (MSCs) have promising therapeutic potential in neural cell regeneration due to their multipotent ability.

- Umbilical cord blood (UCB) & Wharton’s jelly (WJ) in umbilical cord have mesenchymal stem cells that can differentiate into various tissue cell types.

Umbilical cord
Objectives

- This study was performed to confirm the effect of transplantation of human umbilical cord derived MSCs on the functional & morphological regeneration of spiral ganglion neurons (SGNs) in deaf animal model.
Materials and Methods

1. Isolation of UCB-MSC & WJ-MSC

- centrifuge gradient method with the use of histopaque (UCB-MSC) (Sigma-Aldrich, ST Louis, MO)

- mechanical & enzymatic cell separation (WJ-MSC)

- 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 MSC
   - SPF Guinea Pig (wt : 250 – 300 g) (5 cases in each group)
     (control, saline injection, MSC injection)
   - Intra-tympanic Injection of 25mM ouabain octahydrate and neomycin solution in 10% of total volume
   - Injection of MSC via brachial vein (1x10^7 cells in 100μL)
   - Hearing test with ABR (HIS Smart EP System)
     (before deafening, after 1, 3, 5 weeks after MSC injection)
   - P –value < 0.01

3. Morphologic Study
   Light Microscopy & SGN cell count
   - Toluidine blue staining
   - Image processing & analysis with Java (Image J; NIH)
Results (1)

1. Neurosphere Formation from UCB-MSC & WJ-MSC

A - differentiation term for 5 days
B - differentiation term for 7 days
C - differentiation term for 14 days
D - differentiation term for 18 or 19 days
E - differentiation term for 20 days
F - differentiation term for 23 and 25 days
2. Characterization of UCB-MSC & WJ-MSC

FACS analysis of MSCs derived from UCB & WJ
3. Regeneration of Spiral Ganglion after UCB-MSC & WJ-MSC Transplantation

(A) Severe loss of SGNs from the basal to the apical turn of the cochlea was observed in the deaf group.

(B) Five weeks after transplantation of UCB & WJ-MSCs, SGNs were regenerated in all the turns of the cochleae.
3. Regeneration of Spiral Ganglion with UCB-MSC & WJ-MSC Transplantation

(C) Average neuron counts in each turn of the spiral ganglion for each treatment after transplantation. The average numbers of SGNs were significantly greater in the stem cell transplantation group than in the deaf group (\(p < 0.01\), normal model vs. SNHL model; \(p < 0.01\), SNHL vs. after 1, 3, and 5 weeks).
4. Hearing Restoration with UCB-MSC & WJ-MSC Transplantation
Conclusion

• Intravenous transplantation of umbilical cord derived MSCs can regenerate spiral ganglion neurons and restore hearing in deaf animal model.

• Therefore, autologous umbilical cord derived MSC transplantation may improve the functional result of cochlear implantation.
Thank you for your attention!