Clinical application of tissue-engineered replacement for ear ossicles: PORP & TORP-shaped scaffolds cultured with human mesenchymal cells

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INTRODUCTION

Ossiculoplasty is the standard procedure to treat conductive hearing loss [1]. Depending on the type of the defects, partial or total replacement of the ossicular chain is required. Different biomaterials have been used to substitute the missing ossicles to find the best material. [1-3], but subsequent failure because of: rejections of prosthesis, synchysis to adjacent tissues, and their displacement or resorption, have not been rare [2, 4].

Other forms of replacement prosthesis are auto or hom grafts which despite lack of the aforementioned drawbacks, are difficult to sculpture and consequently increase the duration of surgery in addition to donor site complications and risk of disease transmission[2].

To solve these problems, using a compatible scaffold with autologous differentiated cells may be a promising alternative to eliminate the limitations of the current prostheses [4, 5]. To evaluate the feasibility of this theory, we used hydroxyapatite Partial Ossicular Replacement Prosthesis (PORP) and Total Ossicular Replacement Prosthesis (TORP). (Fig 1) as a scaffold with hMSCs and used them as a replacement prosthesis in ossiculoplasty in three patients.

RESULTS

The hMSCs were positive for CD10, CD44, CD166, CD106, HLA-ABC, CD90, CD54, and CD105, but were negative for CD34, CD45, CD117, and CD11b. Adipogenic and osteogenic differentiation abilities was confirmed using alizarin red S and oil red O staining for osteogenesis and adipogenesis, respectively (Fig 5 and 6).

Patients and Methods

Between April 2008 and June 2009, 3 patients were selected from those who suffered of conductive hearing loss at least 6 months after tympanomastoidectomy and therefore were candidates for ossiculoplasty.

One month before surgery, bone marrow aspirate (10 ml) was obtained from the healthy volunteer’s iliac crest. The aspirate was diluted and centrifuged. The mononuclear cell layer was separated and all cells were incubated and underwent routine cultivation and passage procedures. Patients’ own serum was used to provide cultivation and differentiation medium for hMSCs without any additional growth factors. Flowcytometry analysis and adipogenic and osteogenic differentiation were evaluated to assess the potential of hMSCs.

Cell Seeding Methods

The adherent hMSCs, with a passage number of 2 to 4, were detached from the tissue culture flask and suspended to 2×106 cells/ml in the culture medium. The cell suspension was applied to seed on scaffolds placed in 12-well tissue culture plates at a density of 2×106 cells/scaffold. Following the incubation of the cell seeded scaffolds at 37°C for 4 to 6 hours, 2 ml of culture medium was then added to each well. After 48 hours, the scaffold was set for transection (Fig 3).

Techniques and follow-up period

The study follow-up period was at least 6 months. Audiometric evaluations were carried out before and after the operation.

In all cases, a retro auricular approach was used in tympanomastoidectomy and endaural approach used for ossiculoplasty (Fig 4). The tympanic membrane perforation was reconstructed by temporals fascia in all cases.

As a summary, our research tried to show preliminary results of the clinical application of a prosthesis cultured in tissue engineered scaffold in ear surgeries.

REFERENCE

[3] Taisuke Kobayashi KG, Takayuki Shinohara, and Naoaki Yanagihara. Ossicular Reconstruction Using Hydroxyapatite Prostheses with Interposed Cartilage. Clinical application of tissue engineering technology is a potential solution for producing an optimal ossicular replacement which is tissue compatible, has a desired design and stability, and has biological integration with surrounding structures. [12, 13]. Hydroxyapatite is a well known scaffold for bone tissue engineering and is been used in several animal and human studies but the prosthesis we used in this study has not been applied as a tissue engineered scaffold in ear surgeries.

The result of ossiculoplasty is mainly dependent on disease-related factors (14) however in our study the gain in air-bone gap (17 to 25 dB) is an acceptable result in compare with the results of other studies with simple hydroxyapatite prosthesis or hydroxyapatite prosthesis combined with cartilage (12 to 23 dB).

As a summary, our research tried to show preliminary results of the clinical application of a prosthesis cultured with human mesenchymal stromal cells. There are a few reports on application of tissue engineered products in the field of otology[5] and only one report is available on producing an ossicular prosthesis without clinical usage.[6]

The idea of tissue-engineered ear ossicles is a feasible and interesting option in the replacement of the ear ossicles. Despite this early report, the safety and efficacy of this new method needs larger sample sizes and longer follow-up periods to use this new prosthesis in routine treatments of conductive hearing loss. Also other sources of stem cells should be studied in the future.