Morphologic Change and Hearing Recovery in Cochlea after Intratympanic IGF-1 Injection

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INTRODUCTION

Cochlear hair cells are damaged by various factors such as noise, ototoxic agent and aging, which trigger the sensorineural hearing loss. Neurotrophic factors have been proposed as effective agents in the treatment of hearing loss. Insulin-like growth factor (IGF) is a neurotrophic factor that has been shown to promote the repair of hair cell (30-40g). In particular, animal experiments have shown that IGF-1 facilitates the differentiation of epithelial cells forming utricle in the inner ear and it strengthens the regeneration of vestibular hair cell in the utricle which was damaged by ototoxic agents (31). In addition, IGF-1 has been reported to be used as a therapeutic agent alleviating the neurodegenerative disease. In the present study, we aimed to verify if auditory brain stem responses was already been approved and it is advantageous in that it can be promptly used for the treatment of sensorineural hearing loss.

METHODS AND MATERIALS

• Auditory brain stem responses

On weeks 1, 3 and 5 following the administration of IGF-1, auditory brain stem responses were measured using Natus Pro (Biologic system corp., USA). For the neonatal guinea pig, auditory stimuli, a click sound of 100dB in frequency was exerted at 100/500Hz. The threshold value for action potential according to a frequency of 1000Hz was set as the reference value. The auditory brain stem response was measured twice on each week. The mean value of the second measurement for each week was compared to the first measurement. The threshold value was defined as the value at which the amplitude of the action potential of the auditory brain stem response was measured to be defined as the hearing recovery.

• Preparation of tissue sample for light microscopy

The temporal bone was fixed in a mixture of 2.5% glutaraldehyde and 4% osmium tetroxide for two hours. The fixated sample was dehydrated with the increasing concentration initiating from 70% to 100% ethanol. Following the drying at critical points, gold impregnation was attempted to improve the contrast of the hair cells. The gold-impregnated sample was resolved using a high-vacuum sputtering machine. The gold-impregnated sample was observed using a scanning electron microscope (SEM).

RESULTS

In the control group, the overall deformity of organ of Corti was observed. Supporting cells such as Deiter cells were well arranged, but the partial changes and loss in the arrangement of outer hair cells were relatively uncommon (Fig. 4B). In the right ear, the experimental group, gelatin spongy was immersed in the cochlea was extracted. The tissue sample was fixated in 10% formalin solution at 4°C for 24 hours. For approximately two weeks, the decalcification was done using a mixture of 25% formic acid and 5% nitric acid. Again, for another 24 hours, the tissue sample was placed in 5% sodium sulfate and then rinsed with 0.2M phosphate buffer solution. Dehydration was done using ethanol and formatted on the paraffin. The paraffin-embedded tissue was sectioned at a thickness of 3 μm and then H&E stain was done to observe light microscopy.

• Preparation of tissue sample for electron microscopy

The cochlea was fixed in a mixture of 2.5% glutaraldehyde and 4% osmium tetroxide for 24 hours. Following the drying at critical points, gold impregnation was attempted to improve the contrast of the hair cells. The gold-impregnated sample was observed using a scanning electron microscope (SEM).

CONCLUSIONS

The present study aims to verify if auditory brain stem responses was already been approved and it is advantageous in that it can be promptly used for the treatment of sensorineural hearing loss.

This study demonstrates that local IGF-1 application with gelatin sponge can be considered as an effective method for the treatment of sensory neuroneal hearing loss.

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