Steroid Effect on Hearing in Animal Models
with Cochlear Implant
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Abstract

Outcome Objectives: The present study aimed to evaluate minimal administration time of systemic steroid for long-term hearing preservation after cochlear implantation (CI) via cochleostomy approach (CSA) and round window approach (RWA).

Methods: Continuous mini-osmotic infusion pump (10μl/hr, Alzet, USA) filled with dexamethasone (4mg/ml) was inserted into subcutaneous pocket and removed 3 days or 7 days after implantation (Control group, 3 day infusion group and 7 day infusion group). Hearing thresholds (tone burst at 2, 8, 16, 24, 32 kHz) were measured by auditory brainstem response prior to implantation and at 1 week, 4 weeks, 12 weeks after implantation. Histologic evaluation of cochlea was carried out.

Results: Hearing was preserved in 7 day infusion group more than control group after 4 weeks from implantation (24 kHz in CSA and 2, 8, 16, 24, 32 kHz in RWA). Seven day infusion group maintained significantly better hearing levels over control group after 12 weeks of implantation whereas the hearing levels of 3 day group became almost identical to control group in both CSA and RWA groups. Histologic review revealed more fibrosis and inflammatory cell infiltration along the electrode insertion site of scala tympani in control group than in steroid infusion groups.

Conclusions: Systemic steroid administration was effective in long term hearing preservation in 7 day steroid infusion group in both CA and RWA groups. One of the mechanisms was the suppression of inflammation and subsequent tissue reaction by steroid according to the pathologic examination.

Introduction

Electroacoustic Stimulation (EAS)
• EAS has demonstrated auditory benefits and scaled up interest in the preservation of residual hearing during CI.
• Advantages of EAS
  ✓ Speech recognition in the noise circumstance
  ✓ Enhanced sound resolution
  ✓ Music recognition
  ✓ Enhanced sound localization

Hearing loss after CI
• Suspected mechanisms
  ✓ Inflammation
  ✓ Oxidative stress of cochlear hair cell
  ✓ Mechanical damage during electrode insertion
• Evidences for metabolic factors contributing to the hearing loss after CI other than mechanical trauma
  ✓ Delayed hearing loss
  ✓ Hearing loss at regions apical to the actual position of electrode

Systemic Steroid for Hearing Protection
• Advantages
  ✓ Flexible timing of drug delivery
  ✓ Preventing waiting periods in the operating room
• Previous animal studies
  ✓ Single injection of systemic steroid reduced the tissue response and hearing protection

Methods and Materials

Animal and Cochlea Implant
• Guinea pig, Hartley
• Wt: 350g ~ 400g
• Age: 8 wks
• dummy Electrode insertion (2.25 mm)
• Electrode diameter: 0.30 ~ 0.52mm (Melbourne)
• Cochleostomy & Round window

Steroid Systemic Delivery
• Osmotic Pump (10.0 μl/hr)
• Subcutaneous pocket with 2cm skin incision
• Alzet mini-osmotic pump (2ML) insertion

ABR recording
• Smart EP (IHS, Miami, FL)
• 2, 8, 16, 24, 32 kHz

Histologic evaluation (H&E stain)
• Fibrosis, ossification, hair cell, spiral ganglion neuron

Results

Systemically Delivered Amount of Dexamethasone

<table>
<thead>
<tr>
<th>Group</th>
<th>Dexa Concentration</th>
<th>After Dexa Filling</th>
<th>After Removal</th>
<th>Volume Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 Days</td>
<td>4.0 mg/ml</td>
<td>2.0 ml</td>
<td>0.3 ml</td>
<td>1.7 ml</td>
</tr>
<tr>
<td>3 Days</td>
<td>4.0 mg/ml</td>
<td>2.0 ml</td>
<td>1.3 ml</td>
<td>0.7 ml</td>
</tr>
</tbody>
</table>

*Human Equivalent Dose. Reagan-Shaw et al. 2007 cfj 500 – 1000 mg/day in Optic Neuritis for 3 days

Abnormal hearing thresholds were observed at frequencies above 12 kHz for the 3 days group where as the 7 day group maintained almost identical to control group in both CSA and RWA groups. Histologic analysis showed more fibrosis and inflammatory cell infiltration along the electrode insertion site of scala tympani in control group than in steroid infusion groups.

Conclusions

• Systemic steroid administration for 7 days group was effective in long term hearing preservation in both CSA and RW approaches. Although RW approach showed significant hearing preservation at more frequencies than CS approach, there was no significant difference of threshold shifts between CS and RW approach.

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References