High variability of Perilymphatic Entry of Neutral Molecules Through the Round Window


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Introduction

- Perilymphatic entry characteristics of mannitol and inulin were studied.
- mannitol: 182.2 Da
- inulin: 7000 Da
Material and Methods (1)

- Osmotic minipumps was implanted in 42 guinea pigs
- The molecules administrated at a constant rate
Material and Methods (2)

- Samples from:
  - perilymph of the scala tympani
  - perilymph of the scala vestibuli
  - CSF and blood
  - was sampled at day 4 and day 7
- Radioactivity of the molecules determined
## Results

<table>
<thead>
<tr>
<th></th>
<th>PLV</th>
<th>PLT</th>
<th>CSF</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mannitol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 4</td>
<td>69±52</td>
<td>156±80</td>
<td>8±2.7</td>
<td>5±2.6</td>
</tr>
<tr>
<td>Day 7</td>
<td>35±11</td>
<td>77±24</td>
<td>8±1.3</td>
<td>10±2.0</td>
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<tr>
<td><strong>Inulin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 4</td>
<td>4±1.6</td>
<td>16±10</td>
<td>3±1.7</td>
<td>5±3.4</td>
</tr>
<tr>
<td>Day 7</td>
<td>4±1.4</td>
<td>7±5</td>
<td>2±1.0</td>
<td>1±0.8</td>
</tr>
</tbody>
</table>

1. Large inter-individual variability
2. Conc. of Inulin lower than mannitol
3. Conc. in day7 lower than day4
4. Conc. of scala vestibuli lower than tympani
Discussion: systemic spread

- Small but significant conc. in the blood and CSF
- Intratympanic therapy do not completely preclude the possibility of side effects
Discussion: conc. at day 4 and 7

- The putative decrease in conc. may result from:
  1. Displacement of the tip of catheter
  2. Postoperative inflammation
     ⇒ change of the permeability of round window
Discussion: Distribution within perilymph

- Substance reach the scala vestibuli by diffusion
- the spread characteristics depend on:
  1. Molecular weight
  2. Rate of clearance
Discussion: Inter-individual variation

- Technical factors
- Permeability of round window membrane
- Volume of the perilymphatic compartments
- Clearance rate
Conclusion

- 1. The perilymphatic entry depended on molecular weight
- 2. Distant spread of the molecules cannot be overlooked
- 3. Conc. varied widely between animals
- 4. Individual dose adaptations are necessary when treating patients.
Thanks for your attention !!