Evaluating the Ototoxicity of Aminoglycosides in an Equine Population

Alex True, DVM Candidate Class of 2023 and Dr. Monica Aleman, MVZ Cert., PhD, DACVIM (LAIM & Neurology)

Background:
- Aminoglycosides have been known to cause ototoxic effects in a wide-range of species:
  - Mice/Guinea Pigs (Sullivan et al., 1987)
  - Horses (Daurer et al., 2003)
  - Human neonates (Cooper et al., 2011)
- Aminoglycosides are frequently used in foal neonates, especially for the common condition of sepsis (Bucki et al., 2004)
- Brainstem auditory evoked response (BAER) can be used to assess the hearing capabilities of foal neonates (Aleman et al., 2014) and human neonates (Cooper et al., 2011)

Methods:
- **Vestibular System**: Performed vestibular neurological exam before aminoglycoside was administered and again 7 days after continued daily drug use on neonatal foals, and for the adult horses conducted exam at the end of their treatment
  - Clinical evaluation of vestibular deficit after detecting presence of strabismus, nystagmus, ataxia, or loss of balance when tight circling or when blindfolded
- **Auditory System**: Took BAER measurements at 90 dB and 95 dB air conduction (Fig. 2 and 3) and 55 dB bone conduction at the end of the aminoglycoside treatment in the adult horses, and for the neonatal foals performed basic hearing test before and after 7 days of treatment
  - Compared latencies and peaks of waves 1, 3, and 5 using unpaired t-tests to adult horse reference ranges
  - Bone conduction tests the auditory pathway from the cochlea to the central nervous system incoordination is noted as swaying or staggering

Results – Vestibular System:
- **Neonatal Foals**: No complete deafness noted on basic hearing test in neonatal foals
- **Adult Horses**: No statistical significance in latencies and peaks between reference and research values (Tables 1 and 2)

Results – Auditory System:
- **Neonatal Foals**: No complete deafness noted on basic hearing test in neonatal foals
- **Adult Horses**: No complete deafness noted on basic hearing test in neonatal foals

Table 1. Average Latencies with 2 Standard Deviations for Waves 1, 3, and 5 at 80dB in Both Research Horses and Reference Values. The research and reference range latencies for all the waves overlap with the standard deviations. The A1 refers to the wave from the mastoid to the vertex, and the C2 refers to the wave from C2 to the vertex.

<table>
<thead>
<tr>
<th>Wave</th>
<th>Research (ms)</th>
<th>Reference (ms)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave 1 Latency</td>
<td>2.15 ± .08</td>
<td>2.21 ± .12</td>
<td>2.12 ± .12</td>
</tr>
<tr>
<td>Wave 3 Latency</td>
<td>3.83 ± .58</td>
<td>3.61 ± .34</td>
<td>3.59 ± .38</td>
</tr>
<tr>
<td>Wave 5 Latency</td>
<td>5.56 ± .62</td>
<td>5.36 ± .32</td>
<td>5.69 ± .32</td>
</tr>
</tbody>
</table>

Table 2. Average Latencies with 2 Standard Deviations for Waves 1, 3, and 5 at 95dB in Both Research Horses and Reference Values. The research and reference range latencies for all the waves overlap with the standard deviations. The A1 refers to the wave from the mastoid to the vertex, and the C2 refers to the wave from C2 to the vertex.

<table>
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<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave 1 Latency</td>
<td>2.04 ± .70</td>
<td>2.21 ± .12</td>
<td>2.17 ± .20</td>
</tr>
<tr>
<td>Wave 3 Latency</td>
<td>3.86 ± .50</td>
<td>3.61 ± .34</td>
<td>3.66 ± .42</td>
</tr>
<tr>
<td>Wave 5 Latency</td>
<td>5.68 ± .38</td>
<td>5.36 ± .32</td>
<td>5.70 ± .34</td>
</tr>
</tbody>
</table>

Conclusions:
- **Summary of Significance**: Clinicians should feel assured that at current dosing regimens at the VMTH no significant ototoxic effects were detected
- **Future Directions**:
  - Using BAER to test ototoxicity of aminoglycosides in neonatal foals
  - Evaluating whether there is a developmental component to why neonatal humans have ototoxic effects but neonatal horses do not

References and Acknowledgements: