PHARMACOKINETICS AND PHARMACODYNAMICS OF TIAMULIN ADMINISTERED BY INJECTION AGAINST COMMON SWINE JOINT PATHOGENS

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Introduction:
Tiamulin (Denagard 200 Injectable – Novartis Animal Health Inc.) was shown to be highly effective in the treatment of mycoplasmal arthritis caused by Mycoplasma hyosynoviae (Burch & Goodwin, 1984). It is only recently that the comparative plasma and joint fluid concentrations have been reported in young piglets (Klein et al., 2012).

Objective:
The objective of this review paper was to compare and contrast the pharmacokinetics (PK) of tiamulin administered by injection and the concentrations achieved in joints with its pharmacodynamics (PD) related to various common joint pathogens.

Materials and methods:
Pharmacokinetics:
The PK of tiamulin given by injection at 15mg/kg bodyweight in the plasma and joint fluid of young piglets were previously reported (Klein et al., 2012 a & b). Areas under the curve (AUC 24h) of 17.4 and 11.2µg.h/ml (64% of plasma) were calculated for plasma and joint fluid respectively. The concentration maximum (Cmax) were 1.64 and 0.73µg/ml for plasma and joint fluid, respectively (see Figure 1).

The MIC90s for tiamulin against Mycoplasma hyorhinis (being well below the Css for tiamulin in plasma and joint fluid at this dosage rate in young piglets, however some authors have reported lower tiamulin MICs against S. suis (Fodor et al., 2007) with an MIC50 of 0.125µg/ml and MIC90 of 0.5µg/ml). The MIC90 for M. hyorhinis were well below the Css for tiamulin in plasma and joint fluid and with AUC/MIC50 figures of 448 and 45h, respectively, showing a strong inhibition of both Mycoplasma spp, especially of M. hyorhinis (see Figure 2). It is considered unlikely that tiamulin would reach inhibitory joint concentrations for the Haemophilus parasuis at this dosage rate in young piglets, however some authors have reported lower tiamulin MICs against S. suis (Fodor et al., 2004) with an MIC50 of 0.125µg/ml and MIC90 of 0.5µg/ml.

Table 1. MIC50, MIC90 and MIC range of tiamulin against a variety of porcine joint pathogens

<table>
<thead>
<tr>
<th>Organism</th>
<th>No of isolates</th>
<th>MIC50 (µg/ml)</th>
<th>MIC90 (µg/ml)</th>
<th>MIC range (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. hyorhinis</td>
<td>20</td>
<td>0.1</td>
<td>0.25</td>
<td>0.025-0.5</td>
</tr>
<tr>
<td>M. hyorhinis</td>
<td>20</td>
<td>0.1</td>
<td>0.25</td>
<td>0.025-0.5</td>
</tr>
<tr>
<td>S. suis</td>
<td>87</td>
<td>1.0</td>
<td>2.0</td>
<td>0.12-16</td>
</tr>
<tr>
<td>H. parasuis</td>
<td>30</td>
<td>4.0</td>
<td>16</td>
<td>4.0-32</td>
</tr>
</tbody>
</table>

References:

Figure 1. Tiamulin concentrations in plasma and joint fluid after an injection at 15mg/kg bw (Klein et al., 2012 a & b)

Figure 2. Comparison of tiamulin concentration in joint fluid with the tiamulin MIC₉₀ against M. hyosynoviae and M. hyorhinis and tiamulin MIC₉₀ against S. suis