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

David Burch[1], Ulrich Klein[2]
[1]Octagon Services Ltd, Old Windsor, Berkshire, UK; [2]Novartis Animal Health Inc., Basel, Switzerland

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 (C_{max}) were 1.64 and 0.77µg/ml for plasma and joint fluid, respectively and concentration steady state (Css) were 0.73 and 0.47µg/ml for plasma and joint fluid, respectively (see Figure 1).

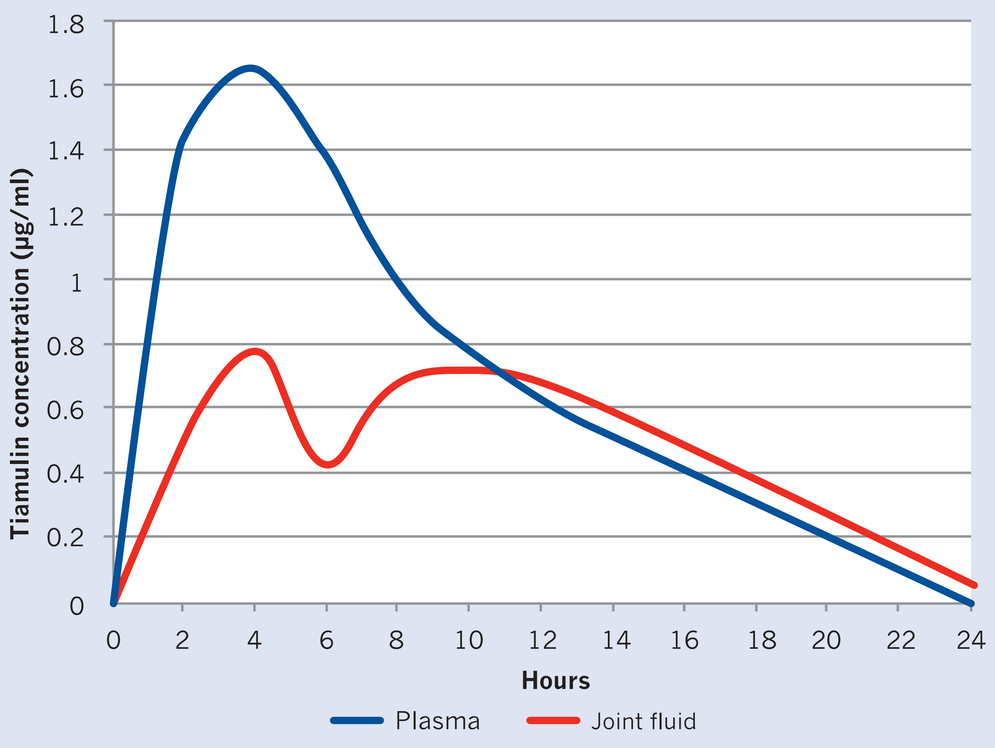

Figure 1. Tiamulin concentrations in plasma and joint fluid after an injection at 15mg/kg bwt (Klein *et al*., 2012 a & b)

Pharmacodynamics:
The MIC_{90} for *Mycoplasma hyosynoviae* and *Mycoplasma hyorhinis* were reported at 0.025 and 0.25µg/ml, respectively (Hannan *et al*., 1997) (see Table 1). The MIC_{50} and MIC_{90} for *Streptococcus suis*, a common bacterial joint pathogen in piglets, were 1.0 and 2.0µg/ml (Martel *et al*., 2001) and for *Haemophilus parasuis* (UK isolates) were 4.0 and 16µg/ml (Martin de la Fuente *et al*., 2007), respectively.

Organism	No of isolates	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)	MIC range (µg/ml)
M. hyosynoviae	18	0.005	0.025	0.0025-0.01
M. hyorhinis	20	0.1	0.25	0.025-0.5
S. suis	87	1.0	2.0	0.12-16
H. parasuis	30	4.0	16	4.0-32

Table 1. MIC_{50}, MIC_{90} and MIC range of tiamulin against a variety of porcine joint pathogens

Results and conclusions:

The MIC_{90}s for *M. hyosynoviae* and *M. hyorhinis* were well below the Css for tiamulin in joint fluid and with AUC/MIC_{90} figures of 448 and 45h, respectively, showing a strong inhibition of both *Mycoplasma* spp, especially of *M. hyosynoviae* (see Figure 2). It is considered unlikely that tiamulin would reach inhibitory joint concentrations for the tiamulin MIC_{50}s or MIC_{90}s against *S. suis* and *H. 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 MIC_{50} of 0.125µg/ml and MIC_{90} of 0.5µg/ml.

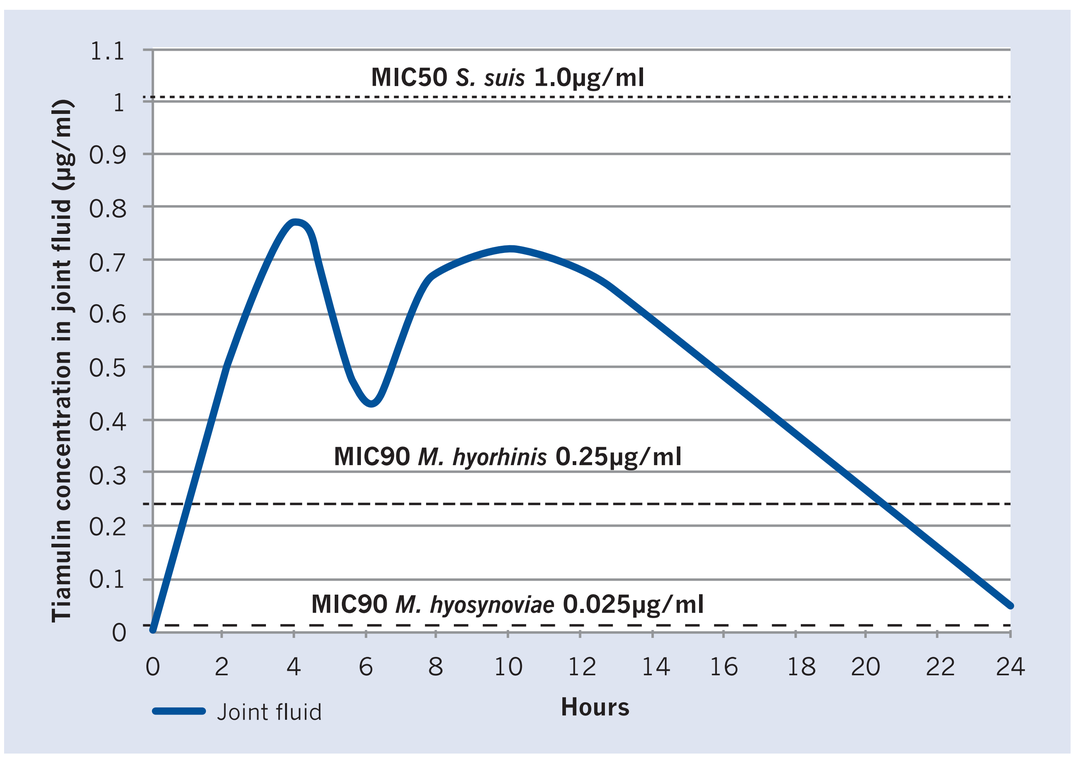

Figure 2. Comparison of tiamulin concentration in joint fluid with the tiamulin MIC_{90} against *M. hyosynoviae* and *M. hyorhinis* and tiamulin MIC_{50} against *S. suis*

References:

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