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P-4.5. Integration Of Pharmacokinetic And Pharmacodynamic Data For Amoxicillin In Healthy And Pneumonic Calves

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Introduction: The aim of this project was to undertake pharmacokinetic-pharmacodynamic (PK-PD) integration of data for amoxicillin in healthy and pneumonic calves.

Materials and Methods: PK data for amoxicillin were established in separate groups of healthy and pneumonic calves. Amoxicillin (Betamox LA, Norbrook Laboratories) was administered intramuscularly at 15mg/kg in both studies. The first study used 10 healthy female Aberdeen Angus Holstein Friesian Cross calves aged 3-5months. The second study established serum PK, clinical response and lung pathology in a *Mannheimia haemolytica* model of calf pneumonia in 8 Holstein Friesian bull calves, aged 12 weeks. Clinical findings were compared with a group of 8 untreated control calves with induced pneumonia. Serial blood samples were collected to establish serum PK in both studies and clinical parameters were monitored over a 48h period in the second study. An LCMS method was used to determine amoxicillin concentrations in serum. For the strain of *M.haemolytica* used to induce pneumonia, minimum inhibitory concentration (MIC) was determined in Mueller Hinton Broth (MHB).

Results: PK variables and PK-PD surrogates for amoxicillin in healthy and pneumonic calves are presented in Table1. The PK variables C_{max} and AUC were significantly lower in pneumonic calves. The $T > MIC$ for calves with induced disease was $>48h$ as the sampling schedule stopped at 48h. In the pneumonia model study, significant differences were observed in rectal temperature between the treated and untreated animals and at *post mortem* there was significantly less lung consolidation (14% versus 24%) in the amoxicillin treated group compared to control animals.

Conclusions: Disease may have a significant impact on amoxicillin PK and this should be taken into account in the selection of dose schedules for clinical use.

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Table 1: PK-PD Integration for amoxicillin in healthy and pneumonic calves

Variable (units)	Healthy Calves	Calves With Induced Disease
	MHB MIC (0.15 µg/mL)	MHB MIC(0.15 µg/mL)
C_{max}/MIC	18.53	9.27
AUC_{0-24}/MIC (h)	171.9	119.6
$AUC_{0-\infty}/MIC$ (h)	238.4	187.2
C_{av}/MIC from 0-24 h	7.16	5.97
C_{av}/MIC from 24-48 h	1.71	1.79
$T>MIC$ (h)	53.11	>48

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ABSTRACTS