

Influence of gamithromycin and ketoprofen on the acute phase response in LPS-challenged pigs

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Lipopolysaccharide (LPS) has been widely applied as a model of immune challenge in pigs since it induces the immediate synthesis of pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β) and IL-6. These cytokines orchestrate the acute phase response by inducing fever and triggering the production of acute phase proteins such as C-reactive protein (CRP) and pig-Major Acute Phase Protein (pig-MAP). Gamithromycin is a macrolide antibiotic which has been recently developed for the treatment of bovine respiratory disease. Besides the anti-infectious properties, macrolides have frequently been reported to affect various inflammatory processes, such as the release of pro-inflammatory cytokines and mediators. Ketoprofen, on the other hand, is a non-steroidal anti-inflammatory drug which has been extensively used in veterinary medicine because of its anti-inflammatory, antipyretic and analgesic properties. The aim of the present research was to study the influence of gamithromycin and ketoprofen on the acute phase response in a standardized and reproducible LPS inflammation model in pigs.

Twenty-four 10-week-old male pigs were randomly divided in four groups. The groups received either a single bolus of respectively 12 mg/kg body weight (BW) gamithromycin (Zactran[®]; Merial) subcutaneously (GAM; $n=6$), 6 mg/kg BW ketoprofen (Ketofen 10%[®], Merial) intramuscularly (KETO; $n=6$), the combination of both drugs (GAM-KETO, $n=6$) or no drugs at all (LPS, $n=6$). One hour after the administration of the drugs, the pigs were intravenously challenged with 15 μ g/kg BW ultrapure LPS from *E. coli* serotype O111:B4 through the proximal lumen of a central venous catheter. Furthermore, two additional control animals received an equivalent volume of 0.9% NaCl. Rectal body temperature was measured and blood samples were collected from the distal lumen of the catheter at several time points until 72 h after LPS administration. Plasma samples were analyzed using ELISAs for porcine TNF- α , IL-1 β , IL-6, CRP and pig-MAP. The concentration of prostaglandin E₂ was measured using a validated high-performance liquid chromatography-tandem mass spectrometry method.

Regarding the course of the rectal body temperature, the LPS- and GAM-group undoubtedly developed fever, while the administration of ketoprofen clearly suppressed the rise in body temperature. Further analyses will elucidate the underlying mechanisms. These results and conclusions will be presented at the symposium.

Key words: gamithromycin, ketoprofen, lipopolysaccharide