A placental inflammatory reaction to LPS at 34 days or near-term is inhibited by the non-steroidal anti-inflammatory drug flunixin meglumine

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Infectious and inflammatory conditions are among the most common causes of pregnancy loss in the horse and have been the focus of a wide group of researchers for several decades. Through this work, the endometrial and luteal responses to infection have been well-documented, as well as the ultimate pregnancy-outcome after exposure to either bacterial or inflammatory mediators during early and late gestation. However, the role of the conceptus as an active participant in the pathogenesis of disease has not been elucidated.

We hypothesized that both embryonic and term placenta would respond to *Escherichia coli*-derived lipopolysaccharide (LPS) through production of prostaglandin (PG) in a controlled, *ex vivo* environment. We further hypothesized that the nonsteroidal anti-inflammatory drug flunixin meglumine (FM) would suppress LPS-induced prostaglandin production.

Six embryos were collected at 34 days of gestation as previously described. In addition, placentae from two near-term mares were collected surgically between 300 and 330 days. Placental tissues were incubated in triplicate for each mare for 24 hours in control medium, 1 µg/mL LPS, 10 µmol/L FM or 1 µg/mL LPS + 10 µmol/L FM. Medium samples from each well were processed for PGE and PGF2α using commercial EIA-kits (Cayman Chemical, Ann Arbor, MI).

Treatment with LPS resulted in a significant increase in PGF2α production in embryonic tissues, while FM significantly reduced PGF2α production (p=0.00001). Term tissues responded to LPS with a significant increase in PGE2 and numerical increase in PGF2α secretion, which were inhibited by FM (p=0.00001). These data indicate that placental tissues are capable of responding to the proinflammatory agent LPS through increased PG production. Interestingly, a differential secretion of PGF2α and PGE2 was seen in embryonic tissues, but not term tissues in response to LPS. This may signify selective Toll-like-receptor expression in the conceptus during early gestation, and is the first such report in the horse. Flunixin meglumine effectively inhibited LPS-induced prostaglandin secretion in all trials.

**Keywords:** Equine, pregnancy loss, inflammation, flunixin meglumine

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**Reference**