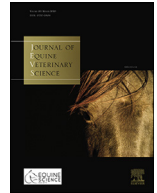




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Cortisol and DHEA as markers of placentitis in pregnant mares: a preliminary study

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Placentitis in mares is a subclinical cause of abortion, highlighting the importance of early detection for successful treatment. Sexual steroids could serve as biomarkers, but cross-reactivity and a limited detection range of immunoassays may hinder accurate measures. This study evaluated some steroids as potential markers of placentitis using liquid chromatography coupled to mass spectrometry (LC-MS), known to improve detection and quantification of steroids with good selectivity, specificity, and allowing multiplexing capabilities (Conley et al., *Reproduction*. 2019;158:197-208; Ledeck et al., *Theriogenology*. 2022;189:86-91). From the 7th month of pregnancy, mares were transrectally scanned to measure the combined thickness of the uterus and placenta (CTUP), and blood samples were collected at a fixed time of day. Ten healthy mares (HM) and nine mares diagnosed with non-experimentally-induced placentitis (PM) between 8 and 10 months were enrolled, based on ultrasonographic placentitis signs: heterogeneous echogenicity and/or thickened CTUP. *Post-partum* allantochorion examination confirmed the diagnosis. Subsequently, PM were further excluded from the study as they received treatments for placentitis. Serum concentrations of progesterone, 17α -hydroxyprogesterone (17α OHP), dehydroepiandrosterone (DHEA), and cortisol were assayed using LC-MS. Non-normally distributed data were presented as medians, and groups were compared at the same month of pregnancy using the Mann-Whitney test. There were no significant differences in 17α OHP and progesterone concentrations between groups at any month.

DHEA concentrations were significantly higher ($p=0.0297$) at 8 months in PM ($3.552\mu\text{g/L}$) compared to HM ($2.240\mu\text{g/L}$). A similar trend was observed at 9 months, with DHEA concentrations of $2.126\mu\text{g/L}$ and $1.445\mu\text{g/L}$ in PM and HM, respectively ($p=0.0604$). In contrast, HM had significantly higher ($p=0.022$) cortisol concentrations at 7 months ($71.75\mu\text{g/L}$) compared to PM ($38.62\mu\text{g/L}$). This difference tended ($p=0.0529$) to be observed at 8 months with cortisol concentrations of $52.25\mu\text{g/L}$ (HM) and $37.28\mu\text{g/L}$ (PM). The DHEA/cortisol ratio was significantly higher in PM than in HM at 9 months ($p=0.013$) and tended to be increased at 7 and 8 months (respectively, $p=0.0659$ and $p=0.0529$). Placentitis has been shown to increase pregnenolone production (Ousey et al., *Theriogenology*. 2005;63:1844-1856). In this preliminary study, PM were observed to metabolize pregnenolone into DHEA rather than cortisol, without changes in 17α OHP concentrations. Reduced cortisol concentrations at 7 months could be an early but non-specific biomarker of placentitis. Conversely, elevated DHEA levels only appear together with ultrasonographic signs at 8 months but could become a more specific biomarker, which differs from previous findings in mares with experimentally-induced placentitis (Canisso et al., *Equine Veterinary Journal*. 2017;49:244-249). These changes result in a higher DHEA/cortisol ratio in PM at 9 months. However, further research should explore modifications of steroids' pathways in PM to confirm the value of DHEA and cortisol for early diagnosis of placentitis in mares.