Effects of estradiol on uterine blood perfusion in reproductively healthy mares and mares affected with uterine vascular elastosis

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Uterine vascular elastosis is a degeneration of the uterine vasculature that is associated with aged, multiparous, infertile or subfertile mares. In previous experiments, we associated this degeneration with reduced uterine blood perfusion (UBP). Histologically, these lesions consist of enlargement, duplication and thickening of the membrana elastica interna of the uterine blood vessels. We hypothesize that vasodilatation is impaired in affected uterine vasculature. To test the functionality of these vessels we evaluated the effects of 17\(^{\beta}\) estradiol (E\(_2\)) on UBP in reproductively healthy mares and mares affected by uterine vascular elastosis.

Mares with normal uterine vascular architecture or mild changes were used as controls and further divided by stage of cycle (determined by ultrasound examination and confirmed by circulating serum progesterone levels; <0.5 ng/mL for estrus and >1.0 for diestrus) into control-estrus (n=3) and control-diestrus (n=3). Mares affected with severe uterine vascular degeneration were used for elastosis groups, also divided into elastosis-estrus (n=3) and elastosis-diestrus (n=3). Fluorescent microspheres (FM; 15µm diameter, Triton Technology, Inc, San Diego CA) were injected directly into the left ventricle of the heart of anesthetized mares and were used to determine baseline levels of UBP using a reference blood sample method using four different arterial blood samples to ensure adequate mixing and sampling, followed by the administration of 1.0 mg/kg of E\(_2\) (IV). After an onset period of 90 minutes, FM with a different fluorescent dye were also injected and used to determine changes in UBP induced by E\(_2\). Mares were euthanized and reproductive tract removed. Concentrations of the two different FM (with different excitation and emission wavelengths) were determined, by digesting the tissue, recovering the FM, reading the fluorescent intensity (proportional to the number of FM and used to calculate UBP levels. Repeated measures were used for comparison of baseline levels and post-estradiol levels and a 2x2 ANOVA was used for comparison between vascular grade and stage of cycle.

Results are expressed as baseline levels of UBP and post-E\(_2\) UBP levels (mL of blood/min/100 g of uterine tissue ± SD). Control mares during estrus had an overall increase in UBP (p < 0.05). Baseline UBP levels were 18.8 ± 2.9 mL/min/100 g vs. post-E\(_2\) UBP levels 28.3 ± 2.9 mL/min/100g. No other group had an overall significant increase when comparing baseline UBP levels vs. post- E\(_2\) UBP levels (control-diestrus: 12.1 ± 2.9 vs. 14.0 ± 3.1, elastosis-estrus: 6.8 ± 1.2 vs. 6.7 ± 2.6, elastosis-diestrus: 7.2 ± 2.4 vs. 7.4 ± 2.4). The baseline UBP of the control-estrus group was also significantly different of all other groups. Additionally, data were analyzed by uterine region (uterine horns, uterine body and cervix) and expressed as per cent of change of UBP from baseline levels ((post- E\(_2\) UBP – baseline UBP / baseline UBP) x 100 ± SD. In the control-estrus group, there was an increase in UBP in both uterine horns 52.4 ± 36% (p=0.065), 54.4 ± 20% (p < 0.05) and uterine body 54.2 ± 17% (p <0.05). In the control-diestrus group, there was an increase in both uterine horns; 25.4 ± 5% (p < 0.05) and 32.9±5 % (p < 0.05). No uterine region had a significantly increased of UBP after E\(_2\) administration in mares affected by uterine vascular elastosis.

The difference in vasodilatory response induced by estradiol between reproductively healthy mares and mares affected with elastosis of the uterine vascular bed indicates that the vasodilation of the affected vessels is compromised.

Keywords: Uterine blood perfusion, elastosis, infertility, mare, estradiol.