Bioactivity of 5α-Dihydroprogesterone in Mares: Endometrial Response and Maintenance of Early Pregnancy

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These data provide the first definitive evidence that 5α-dihydroprogesterone is a bioactive progestogen capable of activating the endometrium, eliciting progesterone-responsive uterine secretion, and maintaining early pregnancy in mares. Understanding the role of this progestin in early pregnancy may provide a basis for novel diagnostic, prophylactic, or therapeutic options for minimizing early pregnancy loss. Authors’ addresses: Department of Population Health and Reproduction (Scholtz, Ball, Conley) and K.L. Maddy Equine Analytical Chemistry Laboratory, California Animal Health and Food Safety Laboratory (Stanley, Moeller), School of Veterinary Medicine, University of California, Davis, California 95616; e-mail: elscholtz@ucdavis.edu (Scholtz). © 2009 AAEP.

1. Introduction
The purpose of this study was to examine the progestogenic effect of 5α-dihydroprogesterone (5α-DHP) on the endometrium and to assess its ability to maintain early pregnancy in the mare.

2. Materials and Methods
In experiment 1, ovariectomized mares (n = 4) were treated daily with 5α-DHPa (300 mg, IM) or vehicle for 10 days in a crossover design. Endometrial biopsies were taken immediately before the first administration of 5α-DHP and 24 h after the last administration for routine histology and detection of the progesterone-responsive protein, lipocalin (P19). In experiment 2, mares with confirmed day 12 pregnancies (n = 9) were treated daily with 5α-DHP (0.7 mg/kg, IM) or vehicle (n = 5), beginning on day 13. On day 14, mares were given PGF2αb (10 mg, IM) to eliminate endogenous progesterone. Plasma concentrations of progesterone and 5α-DHP were measured daily by liquid chromatography–mass spectrometry (LC-MS).

3. Results and Discussion
In experiment 1, 5α-DHP stimulated a progestogenic response in the endometrium characterized by increased glandular activity and by the presence of P19, which was not detected in vehicle control mares. In experiment 2, conceptus development progressed to day 27 (study endpoint) in seven of nine mares treated with 5α-DHP but in none of five control mares (p < 0.05, Fisher’s exact test). Circulating concentrations of 5α-DHP maintained by exogenous administration were similar to those measured in diestrous mares. These results indicate that 5α-DHP is a bioactive progestogen capable...
of activating the endometrium, eliciting progesterone-responsive uterine secretion, and maintaining early pregnancy in mares.

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Footnotes

\(^a\)Steraloids, Inc., Newport, RI, 02840-0600.
\(^b\)Lutalyse®, Pharmacia & Upjohn, Kalamazoo, MI, 49001-0199.