Effect of Altrenogest on Luteinizing Hormone Concentrations in Mares During the Transition Period

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Altrenogest administration suppressed both baseline luteinizing hormone (LH) secretion and gonadotropin-releasing hormone (GnRH)-induced LH secretion in transitional mares. There was no evidence that administration of altrenogest to transitional mares resulted in accumulation of LH in the pituitary, or that LH release is enhanced when altrenogest treatment is discontinued, as had been previously hypothesized. Authors’ address: Animal Reproduction and Biotechnology Laboratory, Colorado State University, Ft. Collins, CO 80523. © 2001 AAEP.

1. Introduction

Seasonally anestrous mares have low plasma concentrations of luteinizing hormone (LH). Baseline concentration of LH increases as the mare progresses through the transition period toward the physiologic breeding season. Elevated levels of LH are essential to induce follicular maturation and ovulation at the end of the transition period.

Administration of exogenous progesterone inhibits secretion of LH, and this effect has been used clinically in an attempt to manipulate pituitary stores of LH in transitional mares. The hypothesis has been that administration of exogenous progesterone to transitional mares results in a blockage of LH secretion while synthesis of LH continues. This would result in an accumulation of LH in the pituitary. Consequently, when administration of progesterone is discontinued, a surge of LH secretion would occur that results in stimulation of follicular development and ovulation.

The objective of this study was to determine the effects of prolonged administration of the synthetic progestin altrenogest in combination with gonadotropin-releasing hormone (GnRH) on baseline concentration of LH and the release of LH in response to a GnRH challenge in transitional mares.

2. Materials and Methods

Twenty-four light horse mares were used between April 18 and May 18. Mares were examined by palpation and ultrasonography per rectum 2–3 times per week for 2 months before the onset of the experiment. A reproductive examination was performed on April 16, and mares with follicles between 20 mm and 25 mm in diameter were randomly assigned to 1 of 4 treatment groups of 6 mares each. Mares in Group 1 received 1 ml of a saline placebo subcutaneously q 12 h, mares in Group 2 received 22 mg of altrenogest orally q 24 h, mares in Group 3 received 250 μg of native GnRH subcutaneously q 12 h, and mares in Group 4 received 22 mg...
of altrenogest orally q 24 h and 250 μg of native GnRH subcutaneously q 12 h.

On the day before the first exogenous hormone treatment and the day after the last treatment, mares were challenged with a pharmacologic dose of native GnRH. An intravenous catheter was inserted into the jugular vein 2 hours before the first blood collection. Blood samples were collected at −2 hours, −1 hour, and immediately before (0 h) intravenous injection of 1 mg of native GnRH. Blood samples were then collected at 0.5, 1.0, 1.5, 2, 3, and 4 hours post-GnRH in 10 ml vacutainer tubes with no anticoagulant. Blood samples were allowed to clot at room temperature, centrifuged, and the serum frozen (−20°C) until assayed for concentrations of LH. Levels of serum LH were measured in a single radioimmunoassay in which the intra-assay coefficient of variation was 1.2% and the assay sensitivity was 0.38 ng/ml.

Comparisons of LH concentrations between treatment groups were made by repeated measures analysis of variance (SAS). Comparisons of area under the curve between GnRH challenges within treatment groups were made using a paired t-test.

To determine the date of the first ovulation of the year, ovarian follicular development was monitored by transrectal ultrasonography a minimum of 2–3 times per week for up to 2 months after the end of the treatment period.

3. Results

Concentration of LH before the first GnRH challenge or exogenous hormone administration did not differ among treatment groups (p > 0.05). Furthermore, there was no difference in the GnRH-induced LH response among treatment groups before the onset of exogenous hormone therapy (p > 0.05).

A significant difference (p = 0.04) was detected in baseline levels of LH during the 12 day treatment period between the control (Group 1) and the altrenogest-treated group (Group 2), as well as between the GnRH-treated (Group 3) and the altrenogest-treated group (p = 0.04). Concentrations of LH were lower in altrenogest-treated mares than in either control or GnRH-treated mares. At the conclusion of the 12 day treatment period LH release was significantly greater in control and GnRH-treated mares than in altrenogest (p < 0.05) and altrenogest plus GnRH-treated (p < 0.05) mares.

Mares treated with altrenogest or altrenogest plus GnRH had significantly greater LH release in the first challenge than in the second challenge (p = 0.01 and p = 0.05, respectively). There was no difference between pre- and post-treatment challenges for mares treated with saline or GnRH.

The mean intervals from end of treatment to first ovulation of the year for mares in Group 1 (control), Group 2 (altrenogest), Group 3 (GnRH), and Group 4 (altrenogest and GnRH) were 24.0 ± 20.5, 10.8 ± 7.4, 19.6 ± 20.9, and 15.6 ± 16.0, respectively. There was no difference in interval from end of treatment to ovulation between groups (p > 0.05).

4. Discussion

Progesterone has been used in conjunction with GnRH to shorten the onset of the breeding season with some reported success.10,11 The present study examined the effects of treatment with the synthetic progestin altrenogest on the release of LH in transitional mares. Before initiation of treatment, baseline levels of LH and the LH release in response to a GnRH challenge did not differ among groups. During the subsequent 12 days of treatment, mares administered altrenogest alone had lower serum concentrations of LH than control and GnRH-treated mares, indicating that LH synthesis and/or release had been inhibited. This finding was in agreement with previous observations that levels of LH decreased when a progestagen-treated vaginal sponge was inserted into mares.5 Serum concentrations of LH in mares treated with a combination of altrenogest plus GnRH was intermediate between those of mares receiving altrenogest alone or GnRH alone.

Mares that received exogenous altrenogest for 12 days had a lower GnRH-induced release of LH in the second challenge compared with the first. Mares receiving altrenogest plus GnRH had a lower GnRH-induced release of LH in the second challenge than in the first challenge, indicating that the administration of GnRH did not offset the suppressive effects of altrenogest. Failure of altrenogest plus GnRH treatment to increase the GnRH-induced LH release in the second challenge suggests that q 12 h administration of GnRH did not stimulate the synthesis of additional LH that was then stored in the pituitary while the mare was receiving altrenogest. It is uncertain whether altrenogest acts at the level of the hypothalamus to inhibit synthesis and/or secretion of GnRH or at the level of the anterior pituitary to inhibit the synthesis and/or release of LH.

In summary, altrenogest suppressed both baseline LH levels and GnRH-induced LH secretion in transitional mares. Cotreatment with GnRH was not effective in offsetting the inhibitory effect of altrenogest. There was no evidence in this study that administration of altrenogest to transitional mares results in accumulation of LH in the anterior pituitary or that LH release is enhanced when altrenogest treatment is discontinued, as had been previously hypothesized.

References and Footnotes


3. Fitzgerald BP, Affleck KJ, Barrows SP, et al. Changes in LH pulse frequency and amplitude in intact mares during the


*aRegumate®, Intervet, Millsboro, DE 19966.

*bLuteinizing Hormone Releasing Hormone (LHRH), Bachem, Torrance, CA 90505.*