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Short Communication

Comparison of Efficacy of Two Dose Rates of Histrelin to Human Chorionic Gonadotropin for Inducing Ovulation in Broodmares

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ABSTRACT

Between February 15 and May 17, 2011, a total of 88 broodmares (10 maiden, 10 barren, and 68 foaling) maintained on pasture in southeast Texas were examined three times weekly (Tuesday, Thursday, Saturday) by transrectal palpation and ultrasonography. On Tuesday or Thursday, mares in estrus with uterine edema, a relaxed cervix, and a dominant follicle ≥34 mm in diameter were alternately assigned to treatment with the following: group (1) 2,500-unit human chorionic gonadotropin (hCG), intravenous; group (2) 1.0-mg BioRelease Histrelin (Biorelease Technologies, Lexington, KY), intramuscular; or group (3) 0.5-mg BioRelease Histrelin, intramuscular. Ovulation was confirmed by ultrasonographic examination. The percentage of mares ovulating within 2 days appeared to be similar between maiden, barren, and foaling mares, so responses for all mares were totaled for analysis. A nonsignificant trend for higher ovulation rates within 2 days was noted for both dose rates of histrelin compared with hCG treatment (31/37, 84%; 34/37, 92%; and 33/36, 92% for groups 1-3, respectively) ($P = .45$). Ovulatory responses appeared to improve for both products as the season progressed, yet no differences were detected between response rates to histrelin or hCG for any month ($P \geq .50$). The use of 1.0- or 0.5-mg BioRelease Histrelin was found to be at least equally effective as hCG treatment for inducing ovulation within 2 days of treatment throughout the breeding season.

1. Introduction

Gonadotropin-releasing hormone (GnRH) analogues have been routinely administered to broodmares to ensure ovulation occurs within a predictable time span, typically within 2 days of administration [1,2]. A variety of formulations containing the GnRH analogue deslorelin have been widely used for this purpose [1]. Histrelin is a more potent GnRH agonist than deslorelin or buserelin [3]. A sustained release formulation of another GnRH analogue (BioRelease Histrelin; Biorelease Technologies, Lexington, KY) has recently been prepared. Similar efficacy in promoting ovulation in mares within 2 days of treatment was described for 1.0- and 0.5-mg histrelin and 1.5-mg deslorelin [4].

Human chorionic gonadotropin (hCG) has been widely used to promote ovulation at a predictable time in broodmares [2,5]. Ovulation responses (within 2 days) following hCG treatment may be reduced when used early in the breeding season, particularly in mares in late transition [6,7]. When attempting to program ovulation early in the breeding season, the use of GnRH agonists such as deslorelin has been reported to be more reliable than the use of hCG [2].

The goal of this study was to compare the efficacy of two dose rates of histrelin (1.0 and 0.5 mg im) with hCG

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Table 1
Proportion of mares that ovulated within 2 days of treatment given 2,500-international unit hCG iv (group 1), 1.0-mg BioRelease Histrelin im (group 2), or 0.5-mg BioRelease Histrelin im (group 3) during February 15-May 17, 2011, in 110 estrous cycles of 88 maiden, barren, and foaling Quarter Horse or Quarter Horse cross mares maintained on pasture on one farm in southeast Texas

Mare Status	Number of mares	Number of cycles	hCG	1.0-mg Histrelin	0.5-mg Histrelin
Maiden	10	15	3/4 (75%)	3/4 (75%)	5/7 (71%)
Barren	10	14	6/7 (86%)	5/5 (100%)	2/2 (100%)
Foaling	68	81	22/26 (85%)	26/28 (93%)	26/27 (96%)
All[a]	88	110	31/37 (84%)	34/37(92%)	33/36 (92%)

iv, intravenous; im, intramuscular; hCG, human chorionic gonadotropin.
[a]Ovulation responses within 2 days of treatment did not differ among treatment groups ($\chi^2 = 1.617$; $P = .45$).

(2,500 IU iv) throughout the breeding season in one herd of pastured mares under ambient light conditions.

2. Materials and Methods

2.1. Mares, Examinations, and Treatments

Barren, maiden, and foaling Quarter Horse and Quarter Horse cross mares on one farm in southeast Texas during 2011 were used in this study. Mares were maintained on pasture and fed additional hay and grain to maintain good body condition. Foaling mares delivered their foals between January and May. Mares were penned and exposed to a stallion on a lead along one side of the fence line four times weekly (Monday, Wednesday, Friday, and Sunday). Between February 15 and May 17, mares detected in behavioral estrus, or expected in estrus based on previous examination findings, were brought into stocks for transrectal palpation and ultrasonographic examination on Tuesday, Thursday, and/or Saturday. Foaling mares were first examined 5-7 days after parturition.

On Tuesdays and Thursdays, mares in estrus with uterine edema, a relaxed cervix, and a dominant follicle ≥34 mm in diameter were alternately assigned to treatment with the following: group (1) 2,500-unit hCG (Chorulon, Intervet/Schering Plough Animal Health, Summit, NJ), intravenous; group (2) 1.0-mg BioRelease Histrelin (Biorelease Technologies, Lexington, KY), im (intramuscular); or group (3) 0.5-mg BioRelease Histrelin, im. Mares were bred at 1-2-day intervals to one of eight stallions by either natural service or artificial insemination with fresh or cooled, transported semen. Ovulation was confirmed by ultrasonographic examination, and mares were examined for pregnancy approximately 2 weeks after detection of ovulation. If more than one ovulation occurred, the interval to the first ovulation was used for assessing response in 2 days. If a mare was not pregnant, she was reentered into the treatment rotation, and typically assigned to a different treatment than the one she had previously received.

2.2. Data Analysis

Difference in mean follicle size (diameter) on day of treatment among groups was evaluated by analysis of variance. The proportion of ovulations occurring within 2 days among all three groups was evaluated by χ^2 test, and the proportion of ovulations occurring within 2 days during each month of treatment with histrelin (1.0 and 0.5 mg) or hCG was evaluated by Fisher exact tests.

2.3. Animal Use

All experimental procedures were performed according to the United States Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (http://history.nih.gov/research/downloads/US_Principles.pdf).

3. Results and Discussion

During the season, 88 mares (10 maiden, 68 foaling, 10 barren) were treated over 110 estrous cycles on Tuesdays or Thursdays to induce ovulation. The number of cycles of treatment for each treatment group was group (1) hCG = 37, group (2) 1.0-mg histrelin = 37, and group (3) 0.5-mg histrelin = 36. Mean (± SD) follicle size on day of treatment did not differ among groups (41.2 ± 4.6 mm, 40.0 ± 4.2 mm, and 40.5 ± 3.8 mm for groups 1-3, respectively; $P = .51$).

The percentage of mares ovulating within 2 days appeared to be similar between maiden, barren, and foaling mares, so responses for all mares were totaled for analysis (Table 1). Although there was a trend for higher ovulation responses with both dose rates of histrelin compared with hCG treatment, ovulation responses within 2 days of treatment did not differ among treatment groups (31/37, 84%; 34/37, 92%; and 33/36, 92% for groups 1-3, respectively) ($\chi^2 = 1.617$; $P = .45$). The use of 1.0- or 0.5-mg BioRelease Histrelin was found to be at least equally effective as hCG treatment for inducing ovulation within 2 days. The ovulation rates within 2 days we obtained with histrelin were similar to those obtained in the same herd during the 2010 breeding season when 1.5-mg BioRelease deslorelin was administered (113/128, 88%).

Response rates (ovulation in 2 days) appeared to be similar for both doses of histrelin, so response rates in each month to both dose rates of histrelin were compared with those achieved with hCG treatment. Ovulations within 2 days of treatment were 89%, 90%, 96%, and 100% for histrelin, compared with 75%, 83%, 89%, and 100% for hCG, during the months of February, March, April, and May, respectively (Fig. 1). Although ovulatory response appeared to improve for both products as the season progressed, no differences were detected between response rates to histrelin or hCG for any month ($P \geq .50$). The failure to detect a significant improvement in ovulatory responses in mares treated with histrelin early in the season may have been because of small numbers of mares available each month for comparison. Owing to the use of eight stallions and different methods of breeding, no attempt was made to

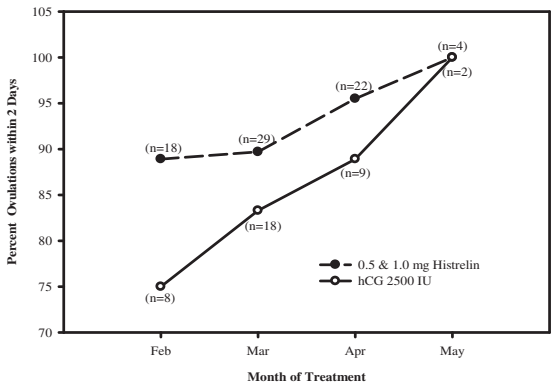

Fig. 1. Percent of ovulations (by month of treatment) within 2 days between February 15 and May 17. Treatment with 1.0- or 0.5-mg BioRelease Histrelin (intramuscular) (denoted by •) or 2500-international unit human chorionic gonadotropin (intravenous) (denoted by ○) was administered when each mare was in estrus with uterine edema and a dominant follicle ≥ 34 mm in diameter. Number (n) of cycles of treatment for each month is indicated in parentheses. Data represent 110 cycles of treatment in 88 Quarter Horse or Quarter Horse cross mares maintained on pasture in southeast Texas during 2011.

evaluate effects of treatment on fertility (pregnancy rate). However, pregnancy rates per cycle were similar to those obtained in previous years at this farm, and appeared similar among groups (68%, 68%, and 61% for groups 1-3, respectively).

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