

Comparison of deslorelin and histrelin for induction of ovulation in mares

Jennifer Morrissey, Ryan Ferris, Patrick McCue
Department of Clinical Sciences
College of Veterinary Medicine and Biomedical Sciences
Colorado State University, Fort Collins, CO

Abstract

Ovulation induction agents are used to synchronize ovulation to optimize reproductive management in breeding programs. The goal of this retrospective study was to compare interval from treatment to ovulation in mares given deslorelin acetate versus histrelin. Reproductive records of 134 estrous cycles from 91 privately owned mares managed for insemination with frozen semen were evaluated. Deslorelin acetate (1.8 mg) or histrelin (0.5 mg) were given as an intramuscular injection when a dominant follicle was ≥ 35 mm in diameter, in the presence of uterine edema. Average interval from deslorelin administration to ovulation (34.8 ± 11.4 hours) tended ($p = 0.054$) to be shorter than the average interval from histrelin administration to ovulation (38.0 ± 8.1 hours). For both hormones, the highest percentage of ovulations occurred between 37 and 44 hours after treatment. When an ultrasonographic examination was done at or prior to 36 hours post treatment, ovulation was detected in 36.6 and 18.3% of mares given deslorelin and histrelin, respectively. In conclusion, interval from treatment to ovulation and percentage of mares that ovulated within 48 hours were not significantly different between mares receiving 1.8 mg of deslorelin acetate versus 0.5 mg of histrelin. Furthermore, sequential scheduled ultrasonographic examinations are recommended after any GnRH agonist treatment, as some mares ovulate earlier than anticipated.

Keywords: Mare, induction, ovulation, deslorelin, histrelin

Introduction

Ovulation inducing agents are frequently administered to mares to optimize reproductive management in live-cover and artificial insemination programs and to synchronize ovulation of embryo donors and recipient mares.¹⁻⁷ Common products for inducing ovulation include human chorionic gonadotropin (hCG) and gonadotropin releasing hormone (GnRH) agonists, such as buserelin, deslorelin and histrelin.

Native GnRH, a 10-amino acid peptide produced in the hypothalamus, stimulates secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary.⁸ Agonists of GnRH such as deslorelin and histrelin are synthetic 9 amino acid peptides with enhanced potency compared to native GnRH. In previous studies, 84 - 100% of mares ovulated within 48 hours after administration of deslorelin acetate^{4,7,9-11} and 82 - 100% ovulated within 48 hours after administration of histrelin.¹²⁻¹⁴

The goal of this retrospective study was to compare interval from treatment to ovulation in mares given deslorelin acetate or histrelin.

Materials and Methods

Reproductive records of 134 estrous cycles from 91 privately owned mares managed for insemination with frozen semen in the 2015 and 2016 breeding seasons were evaluated. Transrectal ultrasonographic examinations were performed on each mare, including evaluation of ovarian follicle development, presence or absence of a corpus luteum, uterine edema score and presence or absence of uterine fluid. Diameter of all follicles ≥ 30 mm on each ovary were measured with electronic calipers and recorded. Edema score was graded on a scale ranging from 0 (no edema), 0.5 (trace edema), 1 (mild edema), 2 (moderate edema), to 3 (marked edema).

In 2015, all mares were given deslorelin acetate, whereas in 2016, all mares were given histrelin. Deslorelin acetate (SucroMate™, Thorn-Biosciences, Louisville, KY) or histrelin (Doc Lane's Veterinary

Pharmacy, Lexington, KY) were given as intramuscular injections at a dose of 1.8 mg or 0.5 mg, respectively, when there was a dominant follicle ≥ 35 mm in diameter in the presence of uterine edema. All GnRH agonist treatments were given at 8:00 pm, with the goal of inducing ovulation approximately 40 hours later at 12:00 (noon). Ultrasonographic examinations were performed at ~ 6 hour intervals after hormone administration until ovulation was detected. All protocols and procedures used were approved by the University Institutional Animal Care and Use Committee (16-6876A).

A Student's t-test was used to compare, between the two hormones, follicular size, uterine edema score and intervals from treatment to ovulation, whereas a Fisher's Exact test was used to compare percentage of mares that ovulated at each time point. For all analyses, $p < 0.05$ was considered significant. Values are reported as mean \pm SD.

Results

There was no significant difference between mares given deslorelin versus histrelin for diameter of the dominant follicle at treatment or edema scores (Table). Although ovulation tended ($p = 0.054$) to occur earlier in mares given deslorelin versus histrelin (34.8 ± 11.4 versus 38.0 ± 8.1 hours, respectively), there was no difference in the percentage of mares that ovulated at any time interval after treatment (Figure). In both groups, the highest percentage of ovulations occurred between 37 and 44 hours after treatment. All mares treated with deslorelin ovulated within 48 hours. However, 6 mares given histrelin failed to ovulate within 48 hours; 4 mares formed hemorrhagic follicles and 2 mares given 2,500 IU of hCG at 48 hours after the initial dose of histrelin ovulated within 2 days.

Discussion

In this study, mares were given a GnRH agonist to induce ovulation to facilitate insemination of a single dose of frozen-thawed semen immediately after detection of ovulation. Treatment at 8:00 pm was done in an attempt to induce ovulation approximately 40 hours later, at 12:00 (noon) to optimize availability of trained personnel. Mares were examined the morning after GnRH agonist therapy and at ~ 6 hour intervals thereafter until ovulation was detected. Mares that did not ovulate within 48 hours after GnRH agonist therapy were subsequently given hCG in a further attempt to induce ovulation.

The objective of this retrospective study was to compare efficacy of a commercial deslorelin acetate preparation with that of a compounded histrelin preparation. The deslorelin product was used at the manufacturer's recommended dose of 1.8 mg. Previous work at our facility indicated that doses of histrelin from 0.5 to 1.0 mg had the same efficacy for inducing ovulation;¹⁴ therefore, 0.5 mg was given in the present study.

All mares were privately owned and had been presented for reproductive management in breeding program using frozen-thawed semen. Consequently, it was not possible to have an untreated or placebo-treated control group.

The highest percentage of mares ovulated between 37 and 44 hours after administration of either product. Interestingly, there was a statistical trend for an earlier ovulation following deslorelin administration. Perhaps the higher dosage of deslorelin used (1.8 versus 0.5 mg) elicited an earlier and higher LH response.

The average interval from deslorelin to ovulation in this study (34.8 ± 11.4 hours) seemed shorter than the 38.6 hours and 41.4 hours previously reported.^{4,7} It is also noteworthy that ovulation was detected in 36.6% of mares given deslorelin and 18.3% of mares given histrelin on an ultrasonographic examination performed prior to the 37 - 44 hour time window. Variability in interval to ovulation may have been due to differences between mares in their proximity to spontaneous ovulation at the time of GnRH agonist administration. These 'early ovulations' emphasized the need for close monitoring of mares given a GnRH agonist, to facilitate insemination with a single dose of frozen semen in the immediate post-ovulation period.

All 41 mares given deslorelin ovulated within 48 hours, whereas six of the 93 mares (6.5%) given histrelin failed to ovulate within 48 hours. Presumably sample size had an effect, as previous studies using deslorelin to induce ovulation reported ovulation failure rates ranging from 1.2 to 9.0%.^{4-6,10}

Conclusions

Interval from hormone administration to ovulation and percentage of mares that ovulated within 48 hours after treatment were not significantly different between mares receiving 1.8 mg of deslorelin acetate versus 0.5 mg of histrelin. In addition, sequential scheduled ultrasonographic examinations are recommended after any GnRH agonist treatment, as some mares ovulate earlier than anticipated.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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Table. Reproductive end points in mares given deslorelin versus histrelin to induce ovulation.

End point	Deslorelin	Histrelin
Number of cycles	41	93
Follicle diameter (mm)	42.0 ± 5.1	42.1 ± 4.8
Edema score	1.9 ± 0.6	1.9 ± 0.7
Interval to ovulation (hours)	34.8 ± 11.4 ^a	38.0 ± 8.1 ^b

^{a,b}within a row, values without a common superscript tended to differ (p = 0.054)

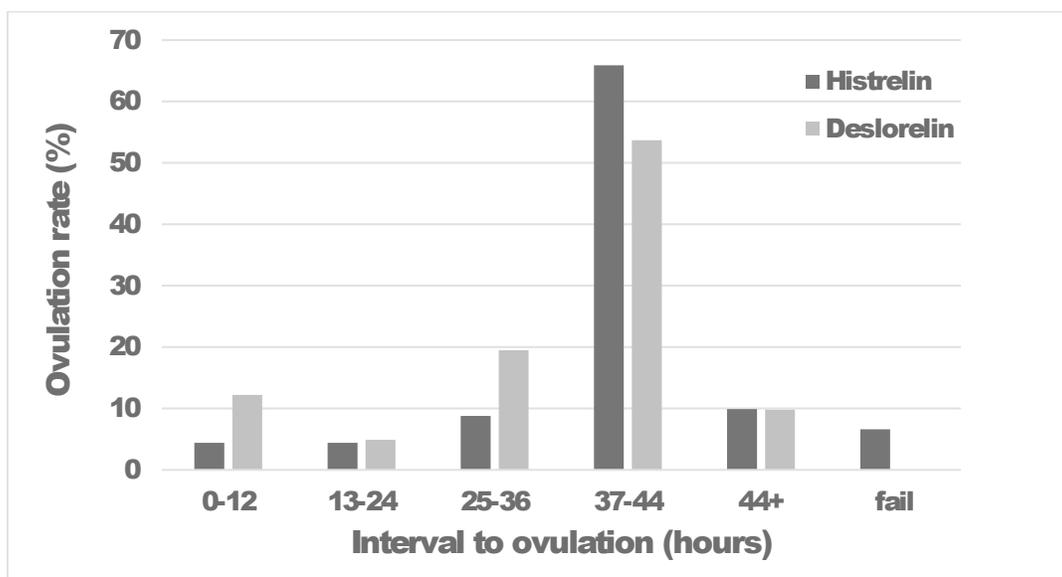


Figure. Intervals from treatments (deslorelin or histrelin) to ovulation.