EFFICACY OF THE GNRH AGONIST DESLORELIN ACETATE FOR INDUCING OVULATION IN MARES RELATIVE TO AGE OF MARE AND SEASON

Valerie J. Farquhar, BS1; Patrick M. McCue, DVM PhD1*; Dirk K. Vanderwall, DVM, PhD2; Edward L. Squires, PhD1

SUMMARY

Deslorelin acetate (Ovuplan™, Fort Dodge), a GnRH agonist, is commonly used to induce ovulation in cycling mares. Although its efficacy in hastening ovulation has been previously reported, the effects of age of mare and month of administration on percent of mares responding and interval to ovulation have not been studied.

Data was gathered from reproduction records of 376 mares receiving deslorelin acetate at the Equine Reproduction Laboratory, Colorado State University, from 1995 to 1999. Age of mare, date of administration, size of largest follicle at treatment, and interval to ovulation were recorded. Age of mare was categorized into five groups: 2-4, 5-9, 10-14, 15-19, and greater than or equal to 20 years. Date of administration was divided into four groups: March and April, May and June, July and August, and September and October.

A higher (p < 0.05) percentage of mares aged 10-14 (98.5%) ovulated in response to deslorelin acetate than mares aged 2-4 or 5-9 (90.2% or 91.0%, respectively) or mares aged 15-19 or ≥ 20 (87.9% or 83.8%, respectively). Mares ≥ 20 had the lowest ovulation rate (83.8%). However, mares ≥ 20 that responded to deslorelin acetate had a shorter (p < 0.05) interval from treatment to ovulation (1.7 ± 0.1 days) than mares 2-4 and 5-9 years of age (1.9 ± 1.0 and 1.9 ± 0.0 days, respectively).

Deslorelin acetate was more effective in inducing ovulation in the July and August (95.4%) (p < 0.01) and September and October (95.7%) (p = 0.04) than in the March and April (81.1%). Mares treated in May through October also experienced shorter (p < 0.05) intervals to ovulation than mares treated in March and April.

INTRODUCTION

The ability to induce ovulation at a predictable time is important in any equine breeding program. The two hormones routinely used to induce ovulation in cycling mares are human chorionic gonadotropin (hCG) and gonadotropin releasing hormone (GnRH).1 Human chorionic gonadotropin, a large glycoprotein structurally similar to luteinizing hormone (LH), has been used to induce ovulation in mares since the 1960's.2,3,4 However, repeated administration of hCG may result in antibody formation,5,6,7 increased intervals to ovulation, and prolonged estrous cycles.3

Deslorelin acetate (Ovuplan™), a GnRH agonist approximately 144 times more potent than native GnRH,8 has recently been approved to induce ovulation in cycling mares. The commercial product consists of a biocompatible pellet impregnated with 2.1 mg of deslorelin acetate that is slowly released over a two- to three-day period.9,10 Administration to mares in estrus with a follicle >35 mm will typically induce ovulation in approximately 42 hours.10,11,12,13

Deslorelin acetate can be used over consecutive cycles without a decrease in clinical efficacy.13 Although several studies have reported the efficacy of deslorelin acetate in inducing ovulation,10,11,12,13 the effects of age of mare and month of administration have not been reported. The purpose of this study was to examine the impact that age of mare and season exert on the efficacy of deslorelin acetate in inducing ovulation in mares.

722 JOURNAL OF EQUINE VETERINARY SCIENCE
Figure 1. Percentage of mares ovulating after administration of the GnRH agonist deslorelin acetate.

MATERIALS AND METHODS

Reproduction records for mares examined from 1995 to 1999 at the Equine Reproduction Laboratory, Colorado State University, were reviewed. The mares were primarily client-owned animals of light-horse breeding. A majority of the mares were housed indoors on a 16:8 (light:dark) photoperiod regimen. All mares were maintained on an alfalfa-grass hay mix.

Data compiled for all mares receiving deslorelin acetate included age of mare, date of administration, size of largest follicle at time of treatment, and date of ovulation. Deslorelin acetate was administered when a follicle >35 mm was detected by transrectal ultrasonography. Mares were examined once daily from the day of treatment until ovulation was detected. Age of mare was categorized into five groups: 2-4 (n=46), 5-9 (n=142), 10-14 (n=66), 15-19 (n=51), and greater than or equal to 20 (n=31) years. Six cycles were excluded from age analysis because age of mare was not available. Date of administration was categorized into one of four groups: March and April (n=30), May and June (n=144), July and August (n=123), and September and October (n=45).

The efficacy of the GnRH agonist (GnRHa) in inducing ovulation was determined by calculating the percentage of mares treated that ovulated within two or three days following treatment. The interval to ovulation was calculated for each age and month group. The number of mares that ovulated greater than three days after treatment, developed persistent anovulatory follicles, or simply failed to ovulate was recorded. A total of 336 and 342 mare cycles relating age and month, respectively, to interval to ovulation were compared. Statistical analyses were completed using Least Significant Difference (L.S.D.) for the comparison of mean interval to ovulation and Fisher's Exact Test for the percentage of mares ovulating. A p < 0.05 was considered significant for all comparisons. Results are expressed as mean ± s.e.m.

RESULTS

A total of 376 mares received deslorelin acetate. The percentage of mares that ovulated within two and three days after treatment was 84.3% and 90.9%, respectively (Fig. 1). The interval to ovulation was 1.9 ± 0.5 days for all mares that ovulated within the first 3 days after treatment.

Thirty-four mares (9.0%) did not ovulate within three days after deslorelin administration. This included 20 mares that ovulated four to eight days after treatment, two mares that ovulated more than eight days later, and twelve mares that developed persistent anovulatory follicles or regressed the dominant follicle without ovulating.

A higher (p < 0.05) percentage of mares aged 10-14 (98.5%) ovulated in response to deslorelin acetate than mares aged 2-4 or 5-9 (90.2% or 91.0%, respectively) or mares aged 15-19 or ≥20 (87.9% or 83.8% respectively) (Table 1). Mares ≥20 had the lowest ovulation rate (83.8%). Older mares (≥20 years) that responded to deslorelin acetate ovulated earlier (p<0.05) (1.7 ± 0.1 days) than mares 2-4 years and 5-9 years (1.9 ± 0.1 and 1.9 ± 0.0 days, respectively).

Deslorelin acetate was more effective in inducing ovulation in the July and August (p<0.01) and September and October (p=0.04) than in March and April. Eighteen of the 37 mares treated in March and April were transitional while the remainder had ovulated at least once prior to treatment. There was no statistical difference between the ovulation rates of transitional (72.2%) versus cycling (89.5%) mares in the spring (p > 0.10) or in the interval to ovulation between the groups (2.7 ± 0.4 and 2.3 ± 0.2 days, respectively) (p>0.10). Only 81.1% of mares treated in March and April ovulated within 3 days after treatment, while 95.4% of mares treated in July and August and 95.7% of mares...
treated in September and October ovulated (Table 2). Mares treated in March and April had a longer (p < 0.05) interval to ovulation (2.1 ± 0.1 days) than mares treated in July and August (1.9 ± 0.1 days) or September and October (1.8 ± 0.1 days).

DISCUSSION

In this study, the efficacy of deslorelin acetate therapy was based on the percentage of mares that ovulated within three days after treatment. Three days was used because the mean interval to ovulation has been reported to range between 36.9 ± 13.11 and 46.8 ± 7.12 hours and 80-100% of mares ovulate within 48 to 72 hours after treatment.3,10,11,12,13,14 In addition, LH concentrations remain elevated for up to three days following deslorelin acetate administration.10,15

Season markedly influenced the efficacy of deslorelin acetate in inducing ovulation and the interval to ovulation after treatment. In the present study, mares treated in March and April with deslorelin acetate had a lower ovulation rate and a prolonged interval to ovulation than mares treated during July and August or September and October. This effect may be due to a combination of seasonal changes in pituitary function or follicular competence. Pituitary stores of FSH remain relatively constant throughout the year but LH concentrations, which are low during the winter anestrus and vernal transition periods, increase in late winter.16,17

Estradiol produced by the first steroidogenically competent transitional follicle is likely responsible for the LH surge that induces the first ovulation of the year.18 It is our hypothesis that deslorelin acetate treatment in early spring either results in a lower LH response or that transitional follicles are not as capable of responding to an LH surge as follicles that develop later in the year.

Although age influenced the efficacy of deslorelin acetate in inducing ovulation in mares, its effects were less notable than those produced by season of treatment. The highest and lowest ovulation rates in response to treatment were noted in mares 10–14 and in mares ≥ 20 years of age, respectively. However, the ovulation rate for older mares was not statistically different from that of younger mares. It is possible that a statistical difference may have been detected if a larger number of older mares had been treated.

In conclusion, deslorelin acetate may be used as an alternative to hCG to induce ovulation in estrous mares. Efficacy is greatest in mares 10–14 years old and mares treated in July through October. Efficacy is lower in older mares and mares treated in March through June. The GnRH agonist may be especially useful in mares that are refractory to hCG. However, a recent report has indicated that some mares receiving deslorelin acetate may have reduced follicular development and a prolonged interval to the next ovulation following treatment.19 Additional controlled studies must be completed to verify the frequency and cause(s) of this phenomenon, and given the results of the present study, these studies should take into account the effects of age and season of administration.

FOOTNOTES


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**CALL FOR PAPERS**

**ORAL OR POSTER PRESENTATIONS AND WORKSHOPS**

**SIXTH INTERNATIONAL CONFERENCE ON EQUINE EXERCISE PHYSIOLOGY (ICEEP)**

Marriott Griffin Gate Hotel

Lexington, Kentucky, USA

**CONFERENCE LOCATION**

The conference will be held **22-28 September 2002** at the Marriott Griffin Gate Hotel in Lexington, Kentucky, USA. The hotel is 10-15 minutes from the airport in Lexington. International air service to and from Lexington is usually through one of several hubs including Cincinnati, Chicago, Pittsburgh, and Atlanta. The hotel is located on the northern outskirts of Lexington on 100 acres with a golf course, tennis courts, and swimming pools. It is located near many of the famous horse farms of the area and is 10 minutes from the Kentucky Horse Park, site of the Rolex Kentucky CCI Three-Day Event, headquarters of the American Horse Shows Association, United States Pony Clubs, and the American Association of Equine Practitioners.

**CONFERENCE ORGANIZATION**

The conference will be structured similarly to previous International Conferences but with a few new features. There will be three main types of presentation: Oral, Poster and Workshops.

Submission of abstracts dealing with the full spectrum of equine exercise physiology is encouraged. It is anticipated that there will be up to 100 presentations of which around 50 are expected to be oral presentations (i.e. two minutes of presentation in the lecture hall with three minutes of discussion). There will also be a display of posters throughout the conference.

**Categories** for papers ICEEP Conference have been:

- Respiratory responses to exercise
- Cardiovascular responses to exercise
- Biomechanics of exercise in horses
- Muscular response to exercise in horses
- Electrolytes, acid-base, and thermoregulation in horses
- Nutrition of the performance horse
- Applied physiology of athletic horses

The committee reserves the right to introduce new categories or to combine previously used categories depending on the abstracts available for selection.

**CONFERENCE WORKSHOPS**

Workshop topics are sought. It is important the workshop proposals have a clear indication of objectives and proposed outcomes. The workshop will be specialized sessions with between 15 and 30 attendees. Workshops will be held during the afternoon sessions and not during the evenings.

**CONFERENCE DETAILS**

The abstract **deadline for abstracts of papers, posters, and workshop proposals is 1 August 2001**.

Details of the submission process will be published in March, 2001. Successful presenters will be **notified by 1 September 2001**. Acceptance of the invitation to presenters will be required by **1 October 2001**.

Manuscripts of accepted abstracts must be submitted by **1 December 2001**.

**COMMUNICATIONS WITH ICEEP**

This first call for papers and further announcements regarding ICEEP 6 may be found at the ICEEP home page at: www.iceep.org. Communications to the National or International Committees may be made through that web site or:

**Professor Skip Hintz**
Chair, International Committee
Department of Animal Science
345 Morrison Hall
Cornell University, Ithaca, NY 14853 USA

**Professor K.W. Hinchcliff**
Chair, National Organizing Committee
Department of Veterinary Clinical Sciences
College of Veterinary Medicine
The Ohio State University 601 Vernon Tharp Street
Columbus, OH 43210-1089

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