Effects of Deslorelin Administration in Vulvar Mucosa, with Removal in 2 Days, in Foal-Heat Mares

Konnie M. Wendt, DVM; Kelly L. Stich, DVM; and Terry L. Blanchard, DVM, MS

Placement of deslorelin implants in vulvar mucosa allowed easy removal 2 days later. Deslorelin treatment in the vulvar mucosa effectively induced ovulation within 2 days in foal-heat mares and resulted in normal pregnancy rates. Post-treatment follicular suppression and delayed return to estrus in mares failing to become pregnant were avoided by removing implants 2 days after placement. Authors’ addresses: Department of Large Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4475. © 2002 AAEP.

1. Introduction

Ovuplant™ was approved for the use of hastening ovulation in mares in the United States in 1999. The drug is marketed as a subcutaneous implant of the gonadotropin-releasing hormone (GnRH) agonist deslorelin. When administered to mares with an estral follicle ≥30-mm diameter, Ovuplant™ induces ovulation within 48 h in over 88% of mares.1,2 After the first year of commercial availability in the United States, a number of veterinarians reported that some deslorelin-treated mares experienced a delayed return to estrus if they failed to become pregnant.3,4,a Most affected mares experienced a 3–7 day prolongation of the interestrous interval, but some experienced intervals of >30 days.3,4 The delayed return to estrus presumably is caused by down-regulation of pituitary gonadotrophs by the GnRH agonist,5 with associated suppression of follicular growth.6 Anecdotal reports ascribe the more prolonged interestrous intervals (>30 days) to treatment too early in the breeding season (i.e., when mares are not yet ready to begin regular estrous cycles). In one report, wherein repeated administration (every other day) of deslorelin implants was used to hasten onset of the first ovulation in transitional mares, it was suggested that those treated mares that re-entered anestrus did so because ovulation was forced on them prematurely.7 Little data are available on the effects of deslorelin administration on reproductive performance during the first postpartum estrus (foal-heat) in mares. The majority of foal-heats in mares result in ovulation,8 usually within 20 days postpartum.9 Because early-foaling mares not exposed to artificial lighting may become anovulatory after their foal-heat ovulation,9,10 and delayed return to estrus may be more common in mares treated with deslorelin early in the breeding season, evaluation of reproductive performance in mares treated during foal-heat with deslorelin is war-
ranted. In a recent study, treatment of foal-heat mares with deslorelin (implants placed subcutaneously in the neck), during February and March, reduced the number of large follicles 16 days after treatment. A delayed return to estrus (e.g., 32- to 55-day interestrous intervals) in those mares failing to become pregnant on foal-heat breeding, compared with human chorionic gonadotropin-treated mares, was also reported. Whether the down-regulating effect of the drug was related to treatment on foal-heat, or was a result of season, could not be determined in that study.

Recently, several practitioners and university investigators have suggested the adverse effects of deslorelin can be avoided by removing implants 2 days after treatment. A delayed return to estrus (e.g., 32- to 55-day interestrous intervals) in those mares failing to become pregnant on foal-heat breeding, compared with human chorionic gonadotropin-treated mares, was also reported. Whether the down-regulating effect of the drug was related to treatment on foal-heat, or was a result of season, could not be determined in that study.

Goals of this study were to determine the following: 1) if placement of deslorelin implants in the vulvar mucosa would be effective in inducing ovulation in foal-heat mares, and 2) if removal of implants 2 days after administration would prevent follicular suppression and delayed return to estrus in early-foaling mares treated on their foal-heat.

2. Materials and Methods

Palpation and breeding records were examined for 39 first-postpartum estrus (foal-heat) crossbred (Quarter Horse type) broodmares maintained on pasture in southeast Texas. Mares were teased daily and examined three times weekly by transrectal ultrasonography beginning 5–6 days postpartum. To avoid effects of season, mares in estrus with a follicle ≥35-mm diameter were alternately assigned to the following: treatment 1, 2.1 mg deslorelin; or treatment 2, control. Immediately before treatment, the vulva was scrubbed and dried. Lidocaine (2%, 1–2 ml) was injected beneath the dorsal vulvar mucosa, and either one Ovuplant® (treatment 1) or no implant (treatment 2) was injected beneath the desensitized bleb. Two days after implant placement, a 0.5-to 1-cm incision was made through the vulvar mucosa directly over the implant, and the implant was removed. Mares were also re-examined by transrectal ultrasonography at this time to detect ovulation and again 14 days after ovulation to assess follicular activity and pregnancy status.

Following treatment, mares were bred every other day until either ovulation was confirmed or until they ceased behavioral signs of estrus. The majority of mares were bred by natural service, with a few mares being bred artificially. Eight stallions, all of which passed a breeding soundness examination in January 2002, were used for breeding. Pregnancy rates per cycle did not vary among these stallions for the previous breeding season. Interestrous interval for mares not becoming pregnant was calculated from the last day of the treated estrus to the last day of the next estrus.

Days postpartum at the time of treatment, date of treatment, diameter of the dominant follicle at time of treatment, number of 20- to 29-mm and ≥30-mm diameter follicles at time of treatment and at 14 days postovulation, and interestrous intervals were analyzed by analysis of variance procedures. Categorical data were analyzed by chi-square procedures.

3. Results

Results are presented in Table 1. Mean date at treatment, size of the dominant follicle at treatment, and day of postpartum ovulation did not differ be-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Deslorelin-Treated Mares (n = 19)</th>
<th>Control Mares (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foaling date</td>
<td>Feb 11 ± 14 d</td>
<td>Feb 12 ± 13 d</td>
</tr>
<tr>
<td>Date of treatment</td>
<td>Feb 21 ± 13 d</td>
<td>Feb 19 ± 16 d</td>
</tr>
<tr>
<td>Day postpartum</td>
<td>9.7 ± 3.0 d</td>
<td>8.3 ± 1.9 d</td>
</tr>
<tr>
<td>Follicle size at treatment</td>
<td>40 ± 6 mm</td>
<td>41 ± 6 mm</td>
</tr>
<tr>
<td>Interval to ovulation from treatment</td>
<td>2.6 ± 1.7 d°</td>
<td>4.5 ± 1.3 d°</td>
</tr>
<tr>
<td>Ovulations within 2 d of treatment</td>
<td>84% (16/19)°</td>
<td>10% (2/20)°</td>
</tr>
<tr>
<td>Date of ovulation</td>
<td>Feb 23 ± 13 d</td>
<td>Feb 25 ± 13 d</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>74% (14/19)</td>
<td>65% (13/20)</td>
</tr>
<tr>
<td>Number of covers after treatment</td>
<td>1.3 ± 0.7 a</td>
<td>2.1 ± 0.6 b</td>
</tr>
<tr>
<td>Number of 20- to 29-mm follicles 16 d after treatment</td>
<td>1.3 ± 1.4</td>
<td>1.0 ± 1.1</td>
</tr>
<tr>
<td>Number of ≥30-mm follicles 16 d after treatment</td>
<td>0.5 ± 0.5</td>
<td>0.4 ± 0.5</td>
</tr>
<tr>
<td>Interestrous interval in mares not pregnant</td>
<td>21.2 ± 2.5 d</td>
<td>20.8 ± 2.0 d</td>
</tr>
</tbody>
</table>

*a,b* Means are significantly different (p < 0.01).
between deslorelin-treated and control mares (p > 0.05). Interval to ovulation was shorter, fewer covers were required, and more mares ovulated within 2 days of treatment in deslorelin-treated than in control mares (p < 0.01). Pregnancy rates did not differ between deslorelin-treated and control mares (p > 0.05). Number of follicles 20- to 29-mm or ≥30-mm diameter present 14 days after ovulation and interesting intervals for mares failing to become pregnant on foal-heat breedings did not differ between deslorelin-treated and control mares (p > 0.05).

4. Discussion
Vulvar mucosal administration of deslorelin implants with subsequent removal 2 days later was easily accomplished. Whereas absorption characteristics and luteinizing hormone response were not studied, the efficacy of deslorelin implants used in this manner was apparent. The 84% ovulation rate within 2 days of deslorelin treatment in this group of foal-heat mares was similar to that reported for cyclic mares treated with deslorelin in the United States. An ovulation rate of 93% within 2 days of treatment was reported for 85 lactating mares. The 84% ovulation rate within 2 days of treatment was also similar to that reported for foal-heat mares treated with deslorelin implants placed subcutaneously in the neck (82%). Our results indicate that ovulatory response and fertility seem normal for mares treated with vulvar mucosal deslorelin implants on their foal-heat.

Mares that foal early in the year (January and February) have been noted to be more likely to revert to ovarian inactivity after their foal-heat ovulation than mares foaling later in the year. Mares in this study foaled between January 19 and March 7. In this same herd during a similar period in 2001, the number of large follicles present 14 days after ovulation was reduced with deslorelin treatment (subcutaneous implants) compared with human chorionic gonadotropin treatment on foal-heat. In addition, return to estrus was delayed in mares failing to become pregnant after deslorelin (subcutaneous implants) treatment on foal-heat (i.e., 32- to 55-day interestrous intervals). Based on the results of this study, it seems that prolonged absorption of the GnRH agonist is occurring when implants are not removed, and this demonstrates that removal of deslorelin implants 2 days after placement will avoid these problems.

For breedings on the foal-heat, conception and early pregnancy development must occur at the same time uterine involution is progressing. In a landmark study performed on foal-heat mares, demonstrated that Thoroughbred mares ovulating ≤10 days postpartum achieved a 45% pregnancy rate, whereas those ovulating ≥11 days postpartum achieved a 59% pregnancy rate. In our study, 9 of 15 mares ovulating before 11 days postpartum became pregnant (60% pregnancy rate), whereas 18 of 24 mares ovulating ≥11 days postpartum became pregnant (75% pregnancy rate; p > 0.01). Evaluation of pregnancy rates achieved in mares foaling later in the spring, when a higher proportion of ovulations occur earlier in the postpartum period, would be necessary to determine if Loy’s observation holds true in Quarter Horse-type mares.

While not a goal of this study, we did note that the number of covers did not seem to influence pregnancy rate achieved on foal-heat breedings (i.e., 1 cover = 10/16, 63% pregnancy rate; 2 covers = 10/15, 67% pregnancy rate; 3 covers = 5/6, 83% pregnancy rate; 4 covers = 2/2, 100% pregnancy rate). Because mating results in transient postbreeding endometritis, repeated contamination from multiple matings during the process of uterine involution could result in lowered fertility. Perhaps the uterus of normal foaling mares is quite resistant to repeated contamination from multiple matings. A number of factors might explain the high foal-heat fertility in this herd. Mares in this herd have a traditionally high seasonal pregnancy rate (typically exceed 90%). Mares are kept in good to excellent body condition and are maintained on large pastures, ensuring adequate exercise. These combined factors might result in an improved postpartum uterine condition and level of fertility that negated any potential adverse effects of repeated matings.

In summary, placement of deslorelin implants in the vulvar mucosa was an easily performed, safe procedure that reliably induced ovulation in foal-heat mares within 2 days of treatment. Normal pregnancy rates were achieved with deslorelin-induced ovulations on foal-heat. Removal of the implants 2 days after insertion avoided follicular suppression and delayed return to estrus.

The authors thank the Texas Department for Criminal Justice for providing the horses and facilities used in this study, and Fort Dodge Animal Health for graciously providing the Ovuplant™ for this study.

References and Footnotes
6. Farquhar VJ, McCue PM, Nett TM, et al. Effect of deslorelin acetate on gonadotropin secretion and ovarian fol-


“Ovuplant®; Fort Dodge Animal Health, Fort Dodge, IA 50501