Deslorelin as inductor of ovulation in *bos taurus x bos indicus* after previous exposure to intravaginal progesterone

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**ABSTRACT**

This study aimed to assess the efficiency of deslorelin at inducing ovulation in crossbred cows previously exposed to intravaginal progesterone (P4). A total of 43 cows (*Bos taurus x Bos indicus*) were randomly divided into two groups, G1 (treated, n = 25) and G2 (control, n = 18). Both groups received an identical hormone protocol from day (D) 0 to D8: D0 = intravaginal P4 + estradiol benzoate (2 mg) and D8 = P4 removal + cloprostenol (500 µg) + 400 IU of equine chorionic gonadotropin (eCG) + ovarian ultrasonography. The ovaries were scanned on D9. On D10, G1 received deslorelin [150 mg, intramuscularly (IM)] and G2 no treatment. The ovaries were examined ultrasonographically at 6-h intervals until ovulation on D15. The ovulation rates in G1 and G2 were 100.0 and 73.3% (p < 0.05) and the intervals between deslorelin application and ovulation was 22.3 ± 7.6 and 33.3 ± 5.3 h (p < 0.05), respectively. In conclusion, intramuscular administration of deslorelin effectively induced ovulation in cows previously treated with progesterone; deslorelin promoted ovulation within 22.3 h of its administration.

**Key words:** Deslorelin, induction of ovulation, three handlings, beef cattle.

**INTRODUCTION**

Researchers have studied the use of GnRH analogs in animal reproduction for decades. More than 2000 analogues of GnRH have been developed and tested (Padula, 2005). Since Schally et al. (1971) determined the amino acid sequence of porcine GnRH, over 1,000 synthetic analogs have been tested. One agonist of GnRH is deslorelin, which is classified as a superagonist because it is 10 to 144 times more potent than GnRH (Perrin et al., 1980; Fujino et al., 1974).

Deslorelin has been tested for its effects on the induction of ovulation in rats (Dutta et al., 1978), induction of estrus in bitches (Trigg et al., 2006), and ovarian activity in cows (Bergfeld et al., 1996; Rajamahendran et al., 1998; Silvestre et al., 2009). Cows treated with buserelin or deslorelin implants rapidly exhibited a luteinizing hormone (LH) peak, which declined after 6 h (Rajamahendran et al., 1998). Attempting to form an accessory corpus luteum, Padula and Macmillan (2005) administered deslorelin on day 6 after estrus, which resulted in an ovulation rate of 100%. Thus deslorelin was confirmed to have the strong ability to induce ovulation in cattle. Rajamahendran et al. (1998) reported that deslorelin would induce ovulation of the dominant follicle on day 5 of the estrous cycle in dairy cows. James et al. (2002) observed that deslorelin may increase the plasma concentration of LH in cows previously treated with progesterone; this validates the therapeutic value of deslorelin in the treatment of ovarian cysts, for which its mechanism of action is similar to that of GnRH.
The present study aimed to assess the efficacy of deslorelin, a superagonist of the potent GnRH agonist deslorelin on inducing ovulation of the dominant follicle in crossbred beef cows and to determine the optimum time to perform TAI using estrus synchronization protocol with 3-treatment protocol.

The study was conducted at the Experimental Farm of the Pontifical Catholic University of Parana. Cyclic, pluriparous, non-lactating, crossbred beef cows (*Bos taurus* × *Bos indicus*) aged 5–8 years with body condition scores (ECC) of 3.0–3.5 (where 1 = thin and 5 = obese; Edmonson et al., 1989) were used (n = 43). The animals were fed *Lolium multiflorum*, *Avena sativa,* *Lolium perenne,* corn silage, minerals, and water *ad libitum.* 3.5 (where 1 = thin and 5 = obese; Edmonson et al., 1989) were used (n = 43). The animals were fed with *Avena sativa,* *Lolium multiflorum,* corn silage, minerals, and water *ad libitum.* The cows were randomly divided into 2 groups (G), G1 (treated, n = 25) and G2 (placebo, n = 18). Both groups received the same hormonal treatment from day (D) 0 to D8: D0 = placement of an intravaginal progesterone (P4) device (CIDR=1.9 g; Pfizer Animal Health, São Paulo, Brazil) + 2 mg of estradiol benzoate (EB = Cronibest®, Biogenesis-Bagó Animal Health, Curitiba, Brazil) intramuscularly (IM) and D8 = removal of the P4 + 500 µg IM cloprostenol (Ciosin - MSD Animal Health) + 400 IU of equine chorionic gonadotropin (eCG)(Novohormon, Coopers, São Paulo, Brazil) (IM) + ovarian ultrasound (US). On D9 (24 h later), the ovaries were scanned by ultrasonography (Aloka model 500, 5 MHz linear transducer, Japan) to examine the follicles and/or check for ovulation.

On D10, G1 received 150 mg of deslorelin (single dose, IM) and G2 1.0 ml of physiological saline solution (placebo; IM). From D10 onwards, the ovaries were examined ultrasonographically at 6 h intervals to monitor the ovulatory follicle (OF) until the confirmation of ovulation or until D15 for cows that had not ovulated.

### Statistical analysis

The mean diameters of the OF and time intervals from the administration of deslorelin or placebo to ovulation were compared using the Mann–Whitney test. The ovulation rates were compared between the groups using Fisher’s exact test (GraphPad Software, Inc., Prism 3, San Diego, USA). The level of significance was set at p < 0.05.

### RESULTS AND DISCUSSION

The effects of the potent GnRH agonist deslorelin on ovulation have been studied in dairy cows (Rajamahendran et al., 1998; Bartolome et al., 2004; Padula and Macmillan, 2002, 2005; Santos et al., 2004) and in heifers (Bartolome et al., 2004). The present study focused on the efficacy of deslorelin, a drug several times more potent than other GnRH agonists—buserelin, gonadorelin, and triptorelin (Nestor et al., 1982)—for inducing ovulation in cows. Induction of ovulation improves the pregnancy rates achieved in cattle at the end of a breeding season by reproductive biotechnologies such as TAI and embryo transfer in fixed time (FTET). All cows (100%) exposed intravaginally to P4 for 8 days and treated with deslorelin ovulated before day 15, a significantly higher rate than that observed in the control animals (73.3%) (Table 1). This result is consistent with that obtained by Padula and Macmillan (2005), who treated cows with deslorelin on D6 after estrus to induce ovulation of the dominant follicle (DF) of the 1st follicular wave of the estrous cycle and observed 100% ovulation. Rajamahendran et al. (1998) used subcutaneous deslorelin implants in cows to target ovulation of the DF to D5 of the estrous cycle, with good results.

We found that deslorelin administration decreased the time of ovulation (22.3 ± 7.6 h) for the treated group vs.

### Table 1. Diameter of the ovulatory follicle (OF), ovulation rate, and administration/ovulation interval in crossbred beef cows (*Bos taurus* × *Bos indicus*; n = 43) treated with deslorelin (G1) or placebo (G2).

<table>
<thead>
<tr>
<th>Group</th>
<th>Ø OF (mm)(x±s)</th>
<th>Ovulation (n, %)</th>
<th>Ovulation after treatment hours (x±s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 (n = 25)</td>
<td>15.5±0.08a</td>
<td>22/22(100)a</td>
<td>22.3 ± 7.6a</td>
</tr>
<tr>
<td>G2 (n = 18)</td>
<td>15.0±0.11a</td>
<td>11/15(73.3)b</td>
<td>33.6 ± 5.3b</td>
</tr>
</tbody>
</table>

Different letters in the same column indicate significant differences (p < 0.05).

Santos et al. (2004) tested the use of deslorelin implants for timed artificial insemination (TAI) of dairy cows and demonstrated that it could induce ovulation as part of the Ovsynch protocol. Bartolome et al. (2004) used deslorelin implants in non-lactating cows and heifers and concluded that the superagonist induced ovulation and stimulate the development of a corpus luteum.

Ambrose et al. (1998) compared the effects of deslorelin implants and cistorelin on synchronization of ovulation for TAI in lactating dairy cows and observed a higher pregnancy rate in the deslorelin group (62.5%) than in the cistorelin group (12.5%).

The present study aimed to assess the efficacy of deslorelin at inducing ovulation of the dominant follicle in crossbred beef cows and to determine the optimum time to perform TAI using estrus synchronization protocol with 3-treatment protocol.

### MATERIALS AND METHODS

The study was conducted at the Experimental Farm of the Pontifical Catholic University of Parana. Cyclic, pluriparous, non-lactating, crossbred beef cows (*Bos taurus* × *Bos indicus*) aged 5–8 years with body condition scores (ECC) of 3.0–3.5 (where 1 = thin and 5 = obese; Edmonson et al., 1989) were used (n = 43). The animals were fed with *Avena sativa,* *Lolium multiflorum,* corn silage, minerals, and water *ad libitum.* The cows were randomly divided into 2 groups (G), G1 (treated, n = 25) and G2 (placebo, n = 18). Both groups received the same hormonal treatment from day (D) 0 to D8: D0 = placement of an intravaginal progesterone (P4) device (CIDR=1.9 g; Pfizer Animal Health, São Paulo, Brazil) + 2 mg of estradiol benzoate (EB = Cronibest®, Biogenesis-Bagó Animal Health, Curitiba, Brazil) intramuscularly (IM) and D8 = removal of the P4 + 500 µg IM cloprostenol (Ciosin - MSD Animal Health) + 400 IU of equine chorionic gonadotropin (eCG)(Novohormon, Coopers, São Paulo, Brazil) (IM) + ovarian ultrasound (US). On D9 (24 h later), the ovaries were scanned by ultrasonography (Aloka model 500, 5 MHz linear transducer, Japan) to examine the follicles and/or check for ovulation.

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that of the non-treated group (33.6 ± 5.3 h, p < 0.05). This result agrees with that obtained by Ambrose et al. (1998) in dairy cows but disagrees with Rajamahendran et al. (1998), who reported a 28.0 ± 1.2 h interval between administration and ovulation. Some factors could be mentioned for the difference in values (genetics, feed, way of application of deslorelin, milk production etc). The standard deviation in the present study (7.6 h in G1) was higher than the ±3.0 h observed by Ambrose et al. (1998); this discrepancy may be due to the genetics of the cows used in this study (crossbred Bos Taurus × Bos indicus vs. the Holstein-Friesian dairy cows used by Ambrose et al. (1998)) or the route of administration of deslorelin (Ambrose et al. (1998) implanted the deslorelin subcutaneously), among other potential causes.

Finally, Ambrose et al. (1998) administered the deslorelin 48 h after treatment with prostaglandin F2 alpha in order to use deslorelin for synchronization of ovulation as part of a TAI protocol. While the present study did not proceed to TAI, and the data strongly indicated that deslorelin could be used to induce ovulation as part of a 3-treatment protocol for TAI, as deslorelin administration and insemination would be performed on the same day, as well as in the Cosynch protocol (GnRH administered on the day of TAI). The mean interval of 22.3 h between deslorelin administration and ovulation could improve the pregnancy rate produced by TAI by supporting better viability of the sperm and oocyte in the female genital tract (Hafez and Hafez, 2004). The inclusion of deslorelin for synchronization of ovulation will thus improve pregnancy rates from TAI in commercial herds with the added advantage of requiring fewer animal-handling steps than traditional protocols (4 managements).

This is a subject of great interest for Brazilian researchers. The next steps in our studies are to examine the effects of deslorelin specifically on the success of TAI and determine whether changing the route of deslorelin administration to intravaginal will induce ovulation even sooner.

In conclusion, deslorelin significantly increased the ovulation rate and reduced the time interval between administration and ovulation.

REFERENCES


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