Effectiveness of norgestomet implants in suppressing ovulation and estrus in heifers varies with stage of estrous cycle when implanted

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Yavas, Y., de Avila, D. M. and Reeves, J. J. 2000. Effectiveness of norgestomet implants in suppressing ovulation and estrus in heifers varies with stage of estrous cycle when implanted. Can. J. Anim. Sci. 80: 729–732. Suppression of ovulation and estrus for 63 d by a 24-mg norgestomet ear implant with a delivery rate of 160 µg d⁻¹ was evaluated in beef heifers. Ovulation was suppressed in 80% of heifers implanted on day 7 of the estrous cycle, 40% on day 10, 33% on day 13, 53% on day 16, and 67% on day 19 (P < 0.05 for day 7 vs. days 10, 13 and 16). The norgestomet implant was more effective in suppressing ovulation and estrus when inserted on day 7 of the estrous cycle rather than later in the cycle.

Key words: Norgestomet, progestogen, ovulation, estrus, heifer


Mots clés: Norgestomet, progestogène, ovulation, œstrus, génisse

In beef heifers destined for the feedlot, estrus and pregnancy are undesirable. Recurrent estrus is associated with stress, which adversely affects feed intake and performance of heifers. Pregnant heifers have decreased dressing percentage (Bennett et al. 1984). Ovariectomy or separation of heifers from bulls is impractical. Ovariection is costly, may fail to remove all ovarian tissue in some heifers, has a certain degree of death loss, and reduces performance of heifers unless they are implanted with an estrogenic or androgenic implant (Gaebel et al. 1990).

One approach to solving this problem is to suppress estrus and ovulation by a long-acting synthetic progestogen. The only synthetic progestogen product on the market for suppression of estrus and ovulation is the feed-additive melengestrol acetate (MGA; Lauderdale 1983). Daily feeding of MGA is convenient for feedlot heifers, but impractical for heifers run on rangeland. Although a single injection of MGA or medroxyprogesterone acetate (MAP; Mackintosh and Pratchett 1988) suppressed pregnancy for up to 8 mo, neither of these products has been marketed for commercial use as of this date.

Norgestomet, another synthetic progestogen, is commercially available in the form of a 6-mg ear implant with a delivery rate of 240 µg d⁻¹ for estrus synchronization as part of Syncro-Mate B treatment (Spitzer et al. 1978). Recently, Geary et al. (1997) have reported that 24-, 36- and 48-mg commercially unavailable norgestomet implants with delivery rates of 160, 240 and 320 µg d⁻¹, respectively, prevented pregnancy for up to 154 d in 64, 81 and 91%, respectively, of heifers on range. However, none of the studies reported has taken into consideration the effect of stage of the estrous cycle when the progestational implant was administered on the long-term suppression of estrus and ovulation. The hypothesis of this study was that a norgestomet ear implant would prevent ovulation and estrus in beef heifers differently if administered at different stages.

Abbreviations: CL, corpus luteum; MAP, medroxyprogesterone acetate; MGA, melengestrol acetate

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of the estrous cycle. The objective was to evaluate the sensitivity of beef heifers to long-term suppression of ovulation and estrus by a 24-mg norgestomet ear implant with a delivery rate of 160 μg d⁻¹ administered on different days of the estrous cycle.

One-hundred-forty crossbred beef heifers, 12 to 16 mo of age, with an average body weight of 372 ± 30.8 kg (mean ± SD), were fed a diet of alfalfa hay cubes (70%) and barley (30%) to meet or exceed National Research Council nutrient requirements (NRC 1996) for a target body weight gain of 0.7 to 0.9 kg d⁻¹. The heifers were housed in feedlot pens with concrete floors and with no cover. The study protocol was approved by Washington State University’s Animal Care and Use Committee. Heifers were cared for according to the Consortium for Developing a Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching (1988), which meets guidelines of the Canadian Council on Animal Care (1993). Heifers were observed for standing estrus twice daily (for 30 min immediately before sunrise and beginning at sunset). The first 75 heifers to display at least two consecutive estrous cycles of 17 to 24 d were randomly assigned to 1 of 5 treatments (n = 15/treatment) in which they received a biodegradable norgestomet ear implant (Hoffmann-La Roche, Nutley, NJ) on either days 7, 10, 13, 16, or 19 of the estrous cycle (day of estrus = day 0). The implants were 1.6 mm in diameter and 11 mm in length, contained 24 mg norgestomet (98% norgestomet, 2% cholesterol; wt/wt), and were formulated to deliver 160 μg d⁻¹ norgestomet into the circulation. This delivery rate of 160 μg d⁻¹ is lower than that (240 to 320 μg d⁻¹) used for long-term prevention of pregnancy (Geary et al. 1997) and than that of the conventional 6-mg norgestomet implant (240 μg d⁻¹) used for short-term suppression of ovulation in estrus synchronization (Spitzer et al. 1978). It was used to prevent the effect of stage of the estrous cycle when the norgestomet implant is administered on the suppression of ovulation and estrus from being masked by the large dose of norgestomet. Implants were placed s.c. on the caudal surface of the ear, approximately equidistant from the tip to the base of the ear. Heifers were weighed on the day of implant insertion. Ear implant sites were visually inspected once a week, and twice-daily observations for standing estrus were continued until day 63 post-implant, when the implants were removed by making an incision on the ear with a scalpel.

Blood samples were collected twice a week (every 3 to 4 d) from the coccygeal vein of heifers, from the day of estrus preceding implantation until implant removal. Blood was allowed to coagulate at 4°C; serum was separated by centrifugation and stored at -20°C until assayed for progesterone by a double-antibody radioimmunoassay (Grieger et al. 1990). Sensitivity of the assay was 0.45 ng mL⁻¹; the intra- and interassay coefficients of variation were 9.8 and 4.9%, respectively. Occurrence of ovulation during the implant period was determined from evaluation of serum progesterone profiles.

Suppression of ovulation and estrus for 63 d was analyzed by multiple covariate analysis, with body weight and serum progesterone concentration at implant insertion as covariates (Steel and Torrie 1980), using the General Linear Models Procedure of the SAS Institute, Inc. (1988). Body weights and serum progesterone concentrations at implant insertion were compared between heifers that ovulated and those that did not ovulate by analysis of variance (Steel and Torrie 1980), using the General Linear Models Procedure of the SAS Institute, Inc. (1988). Pearson coefficients of correlation were determined using SAS Institute, Inc. (1988) between proportions of heifers that did not ovulate during the implant period and day of estrus cycle at implant insertion, and between proportions of heifers that did not ovulate during the implant period and mean serum concentrations of progesterone at implant insertion.

The 24-mg norgestomet implant with a delivery rate of 160 μg d⁻¹ suppressed ovulation for 63 d in 55% of the heifers overall (Table 1). This finding is similar to that of Geary et al. (1997), who reported that the 24-mg norgestomet implant with the delivery rate of 160 μg d⁻¹ prevented pregnancy in 64% of heifers for up to 154 d. Treatment with the conventional 6-mg norgestomet implant with a delivery rate of 240 μg d⁻¹ (Spitzer et al. 1978) in the absence of a corpus luteum (CL) for 9 to 10 d has been shown to maintain the dominant follicle (Garcia-Winder et al. 1987). Thus, the 24-mg norgestomet implant with a delivery rate of 160 μg d⁻¹ in the present study may have maintained the dominant follicle until removal of the implant, resulting in the suppression of ovulation for 63 d in 55% of heifers.

Norgestomet implants suppressed ovulation in 80, 40, 33, 53, and 67% of the heifers implanted on days 7, 10, 13, 16,
and 19 of the estrous cycle, respectively ($P < 0.05$ for day 7 vs. days 10, 13 and 16; and day 13 vs. day 19; Table 1). Within treatments, body weights at implant insertion (372 ± 20.8 kg; mean ± SD) were not different between heifers that did not ovulate and those that ovulated during the implant period ($P > 0.08$). Norgestomet is a potent synthetic progestogen that binds to progesterone receptors (McFayd et al. 1993). The higher suppression rate (80%) of ovulation when a norgestomet implant was inserted on day 7 than between day 10 and 16 of the estrous cycle (33 to 53%) could be attributed to the longer time interval available for norgestomet to bind to progesterone receptors before the next ovulation. However, although a longer time interval was available for the action of the norgestomet inserted between days 7 and 16 of the estrous cycle than was available for the norgestomet inserted on day 19, ovulation suppression in heifers implanted on day 7, 10 or 16 was not different ($P > 0.10$) from those implanted on day 19, and was even lower ($P < 0.05$) in heifers implanted on day 13 than in those implanted on day 19. The proportion of heifers in treatment groups that did not ovulate during the implant period was also not correlated with day of estrous cycle at implant insertion ($r = -0.11, P = 0.86$). This suggests that the time interval available for norgestomet to act before the next ovulation is not critical for ovulation suppression.

Norgestomet implants suppressed ovulation more in heifers implanted on day 7 of the estrous cycle than in those implanted between days 10 and 16 ($P < 0.05$). Conversely, serum progesterone concentration was lower on day 7 of the estrous cycle than between days 10 and 16 ($P < 0.05$; Fig. 1). Furthermore, in treatment groups, the proportion of heifers that did not ovulate during the implant period was negatively correlated with the mean serum concentration of progesterone at implant insertion ($r = -0.86, P = 0.06$; Fig. 1). Thus, the norgestomet implant suppressed ovulation more efficiently when inserted on day 7 of the estrous cycle, when circulating progesterone concentrations were at intermediate levels (3.8 ± 0.64 ng mL$^{-1}$) and before the development of a fully functional CL, than between days 10 and 16 of the estrous cycle, when circulating progesterone concentrations were at mid-luteal levels (between 5.7 ± 0.53 and 7.4 ± 0.55 ng mL$^{-1}$) and after the development of a fully functional CL. Brink and Kiracofe (1988) reported a higher conception rate (62.5% vs. 46%) in cows that were bred after receiving a conventional 6-mg norgestomet implant with a delivery rate of 240 µg d$^{-1}$ for 9 d in a Syncro-Mate B treatment earlier in the cycle, when serum progesterone was less than 1 ng mL$^{-1}$, than in cows that received the treatment later in the cycle, when serum progesterone was greater than 1 ng mL$^{-1}$. This suggests that norgestomet suppresses ovulation better if administered early in the estrous cycle.

In heifers implanted on day 7, 10, 13, or 16 of the estrous cycle, serum progesterone concentrations at implant insertion were not different within treatments between those that did not ovulate and those that ovulated during the implant period ($P > 0.12$). In heifers implanted on day 19 of the estrous cycle, serum progesterone concentrations at implant insertion were greater in those that did not ovulate than in those that ovulated during the implant period ($P = 0.05$; 4.3 ± 0.63 vs. 2.0 ± 0.89 ng mL$^{-1}$), but were similar to those at day 7 (3.8 ± 0.64 ng mL$^{-1}$). This suggests that the heifers with lower concentrations of circulating progesterone at implant insertion on day 19 were able to ovulate before norgestomet started to act.

Over all treatments, ovulation was suppressed in 55% (41/75) of heifers during the 63-d implant period, whereas estrus was suppressed in only 46% (19/41) of those heifers in which ovulation was suppressed and in 25% (19/75) of all heifers implanted. The highest estrus suppression rate was observed in heifers implanted on day 7 (Table 1). Geary et al. (1997) reported 91% ovulation suppression and 65% estrus suppression in heifers receiving the 48-mg norgestomet implant. This indicates that a given dose of norgestomet is less effective in suppressing estrus than in suppressing ovulation, and that a higher dose of norgestomet is required to prevent estrus than is required to prevent ovulation. It has been shown that treatment with the conventional 6-mg norgestomet implant in the absence of a CL maintained the largest follicle (Garcia-Winder et al. 1987) and increased circulating estradiol-17β concentrations (Garcia-Winder et al. 1987; Sanchez et al. 1995). Thus, estrus without ovulation in norgestomet-treated heifers may be a result of increased estradiol secretion from the norgestomet-maintained follicle. It may also be a direct effect of norgestomet which is independent of the ovaries because McGuire et al. (1990) reported that Syncro-Mate B treatment allowed estrus in approximately 53% of the ovariotomized heifers. Regardless of the mechanism, recurrent estrus in heifers receiving even the 48-mg norgestomet implant would still adversely affect feed intake and performance.

In conclusion, beef heifers were more sensitive to long-term suppression of ovulation by the 24-mg norgestomet implant with a delivery rate of 160 µg d$^{-1}$ when inserted on day 7 of the estrous cycle before development of a fully
functional CL than between days 10 and 16 of the estrous cycle after development of a fully functional CL. Even though the 48-mg norgestomet implant has been shown to suppress ovulation in 91% of heifers, recurrent estrus in 35% of heifers receiving this dose of norgestomet (Geary et al. 1997) would prevent further potential increase in performance of treated heifers. Thus, further research is needed to determine 1) whether the 48-mg norgestomet implant needs to be inserted on or before day 7 to maximize ovulation suppression as well as estrus suppression, and 2) whether a dose of norgestomet implant greater than 48 mg is needed to maximize ovulation suppression and especially estrus suppression regardless of implantation day.


