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Prolonged Elevated Concentrations of Estradiol Do Not Affect Conception Rates in Beef Cattle

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Persistent ovarian follicles and associated elevated concentrations of estradiol which develop during progestin-based estrous synchrony programs are not detrimental to fertility if persistent ovarian follicles are not allowed to ovulate.

Summary

Following treatments causing either prolonged elevated concentrations of estradiol associated with development of persistent follicles or inhibited elevated concentrations of estradiol and development of persistent follicles, conception rates were compared. Beef females received either four norgestomet implants for 9 days (day 0 = treatment initiation; n=59) or one norgestomet implant for 7 days and three additional norgestomet implants for 2 days (n=60). All implants were removed on day 9 followed by estrous detection and AI for 7 days. Treatment and day interacted to affect estradiol concentrations from day 0 to day 9 with elevated estradiol in females treated with one norgestomet implant for 7 days. Conception rates to AI were similar across treatments. Prolonged elevated concentrations of estradiol associated with development of persistent ovarian follicles do not affect fertility when persistent ovarian follicles are not allowed to ovulate.

Introduction

Cattle treated with commercial doses of synthetic progestins, such as melengestrol acetate and norgestomet or small doses of progesterone in the absence of corpora lutea, often develop persistent ovarian follicles. These follicles develop because of greater LH pulse frequency than naturally occurs during the luteal phase which, in turn, promotes prolonged development of the dominant follicle and increased concentrations of estradiol.

Reduced fertility is associated with estrus and mating following development and ovulation of persistent ovarian follicles. This fertility reduction may be due to adverse effects of prolonged elevation of estradiol on the reproductive tract, compromised oocyte development in persistent ovarian follicles or a combination of these factors.

The objectives of this study were to compare conception rates and time to estrus in cattle following treatments designed to: 1) inhibit persistent ovarian follicle development and elevated concentrations of estradiol; or 2) cause development of persistent ovarian follicles and prolonged elevated concentrations of estradiol, but inhibit ovulation of the follicles.

Procedure

Heifers (n=80) and 2-year-old MARC III (1/4 Angus, 1/4 Red Poll, 1/4 Pinzgauer, 1/4 Hereford) cows (n=39) from the beef physiology herd were injected twice with $PGF_{2\alpha}$ (25 mg; Lutalyse® Sterile Solution, Upjohn, Kalamazoo, MI) 11 days apart. The last injection occurred on the day of treatment initiation to destroy the function of existing corpora lutea and synchronize the estrous cycle stage prior to experiment. All females exhibiting estrus were 6 to 8 days post-estrus at treatment initiation. Females were stratified by age, blocked by estrual status (previously exhibited estrus or anestrus) and assigned to receive either: 1) four norgestomet implants (4 Norg; n=59; hydron implant with 6 mg norgestomet; Sanofi Animal Health Inc., Overland Park, KS) for 9 days (day 0 = treatment initiation); or 2) one norgestomet implant from day 0 to day 7 and three additional norgestomet implants from day 7 to day 9 (1+3 Norg; n=60). All females received an injection of $PGF_{2\alpha}$ (25 mg) at treatment initiation and all implants were removed on day 9. Females were observed for signs of behavioral estrus every 6 hours from time of implant removal (day 9) until day 16 with the aid of K-Mar devices and epididymal ligated bulls. Females exhibiting estrus were bred by AI 6 to 12 hours following estrus detection.

Blood samples were collected daily from treatment initiation (day 0) until the end of estrous detection and AI (day 16) and twice weekly for an additional 30 days thereafter. While concentrations of progesterone were determined in all samples collected, concentrations of estradiol were determined only in samples collected from day 0 to day 16.

Females were considered pregnant when, following breeding, concentrations of progesterone increased to above 2 ng/ml of serum and remained at concentrations characteristic of normal luteal function until termination of the experiment. Uterine ultrasonography

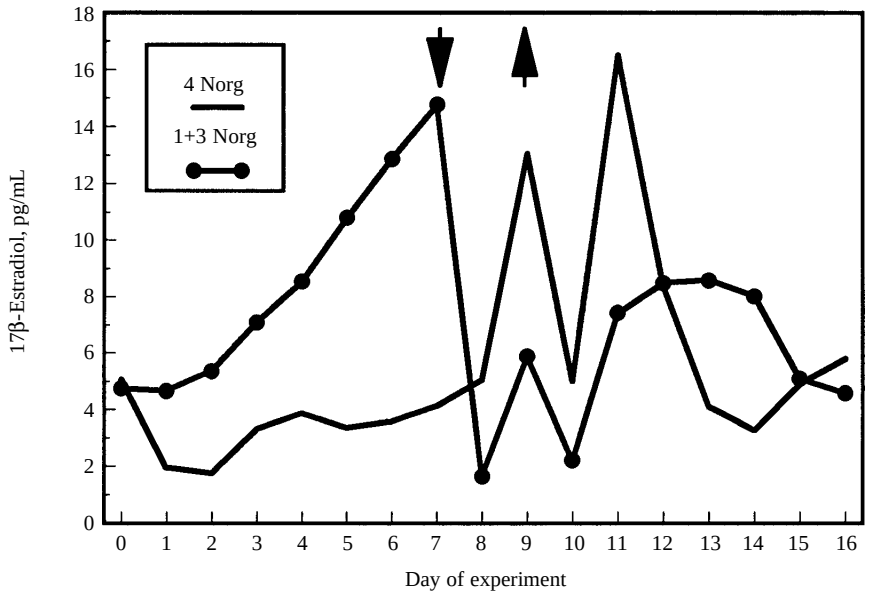

Figure 1. Concentrations of estradiol in circulation from day 0 to 16 of the experiment of females during treatment with either four norgestomet implants for 9 days (4 Norg) or one norgestomet for 7 days followed by an additional three implants for 2 days (1+3 Norg). Arrows indicate day of insertion of 3 norgestomet implants in 1+3 Norg treatment group and day of removal of all implants for both treatment groups. There is a treatment x day interaction ($P < .01$) from day 0 to 9 of the experiment.

approximately 35 days following AI was to confirm the progesterone profiles to determine if pregnancy occurred as a result of AI.

Results

There was a treatment x day interaction ($P < .01$) for concentrations of estradiol from day 0 to day 9 of the experiment, with elevated estradiol occurring in females receiving the 1+3 Norg treatment (Figure 1). The increase in concentration of estradiol from day 0 to day 7 in females treated with 1+3 Norg was indicative of persistent ovarian follicle development and the acute decline in estradiol observed after treatment with three additional norgestomet implants was indicative of induced atresia of persistent follicles. Concentration of progesterone in females of both treatment groups declined from day 0 to day 1 in response to $PGF_{2\alpha}$ injected on day 0 and remained low through day 9 of the experiment.

Estrous synchronization rate (number in estrus/number in treatment group) and pregnancy rate (number conceived to AI/number in treatment group) were affected ($P < .10$) by treatment x estrual status. Estrous synchronization rate of estrual females did not differ between treatment groups (Table 1). There was a greater percentage ($P < .10$) of previously anestrus females displaying signs of estrus within 7 days after removal of norgestomet implants in the 4 Norg group (97 %) as compared with the 1+3 Norg group (67 %). Age, estrual status, treatment x age and treatment x estrual status affected neither conception rates nor time to onset of behavioral estrus after removal of norgestomet implants. Conception rates (number conceived/number inseminated) to AI were not different among females treated with 1+3 Norg (72%) and those treated with 4 Norg (67%). Pregnancy rates of both estrual and anestrous females did not differ between treatment groups (Table 1). Mean time from norgestomet withdrawal to behavioral estrus was longer ($P < .001$) in females treated with 1+3 Norg (105 hours) than with females treated with 4 Norg (61 hours).

Table 1. Estrous synchrony rates, conception and pregnancy rates to AI and time to behavioral estrus of females treated with 1+3 Norg or 4 Norg implants

	Treatment	
	4 Norg	1+3 Norg
Estrous synchrony[a] (%)		
Estrual	97	100
Anestrous	97†	67
Conception Rate (%)	67	72
Pregnancy Rate[a] (%)		
Estrual	66	77
Anestrous	63	43
Time to estrus (hours)	61***	105

†P < .10
***P < .001
[a]There was a treatment x estrual status interaction ($P < .10$), therefore animals that were estrual and anestrous were analyzed separately.

Using two different protocols of synthetic progestin treatment, elevated concentrations of estradiol associated with development of persistent ovarian follicles were unable to affect conception rate to AI. Results indicate similar conception rates can be achieved in cattle in which progestin treatment allows a persistent ovarian follicle to develop and subsequently causes its regression, as compared with cattle in which larger doses of synthetic progestin treatment prohibit the development of persistent ovarian follicles. It appears that allowing persistent ovarian follicles and their associated elevated concentrations of estradiol to develop is not detrimental to fertility when the follicle is regressed before the ovulatory follicle associated with pregnancy ovulates. Conclusions drawn from this and other studies indicate decreased pregnancy rates observed in association with ovulation of a persistent ovarian follicle are likely due to abnormal maturation of the oocyte rather than effects of elevated concentrations of estradiol on oviductal or uterine function.

Because we induced regression of the persistent ovarian follicles by treatment with three additional norgestomet implants, we also shortened the duration of elevated concentrations of estradiol when compared with the duration in cattle ovulating persistent ovarian follicles. In cattle receiving the 1+3 Norg treatment, there was a 105 hour interval from time of removal of norgestomet implants until the onset of estrus; cows treated with 4 norgestomet implants had a 61 hour interval. It is possible lesser concentrations of

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circulating estradiol from the time of induced regression of the persistent ovarian follicle until preovulatory follicle development allowed for oviductal and uterine function to return to normal before the oocyte/embryo entered the reproductive tract. The extended interval from treatment withdrawal to onset of estrus may be due to an acute reduction in LH pulse frequency resulting from treatment with three norgestomet implants. It is likely treatment with the three additional norgestomet implants caused an immediate decrease in the frequency of LH pulses, induced atresia of the persistent ovarian follicle and delayed development of the next dominant follicle. Dominant persistent ovarian follicles suppress development of subordinate follicles; therefore, it is plausible that, in females treated with 1+3 Norg, subordinate follicles were smaller resulting from the presence of persistent ovarian follicles and thus required more time to develop to ovulation.

The present study provides evidence that estrous synchrony programs based on treatment with doses of commercially used synthetic progestins will not result in compromised fertility at the synchronized estrus if persistent ovarian follicles are regressed before the ovulatory follicle associated with pregnancy is allowed to ovulate. Development of future estrous synchrony programs using small doses of progestins should focus on allowing for ovulation of typically growing dominant follicles or using larger doses of progestins to inhibit development of persistent ovarian follicles.

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