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Effects of label-dose permethrin administration in yearling beef cattle: I. Reproductive function and embryo quality of superovulated heifers

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ABSTRACT

The objective was to study the effects of a commercial pyrethroid-based pour-on product, permethrin, on reproductive performance in superovulated beef heifers by assessing steroid biosynthesis and embryo quality. Nonpregnant, yearling beef heifers (n = 10; 418 ± 33 kg; 5.5 ± 0.2 body conditioning scores) were assigned by body weight and breed to either (1) saline control or (2) permethrin pour-on administered at label dose (PYR). Superovulation was achieved on all heifers using a timed, 17-day, CIDR-based protocol with GnRH and PGF2α and decreasing total dosage of 240-mg FSH administered twice daily for 4 days. Heifers were artificially inseminated twice (at onset of estrus and 12 hours later) by same technician with frozen semen from single bull collection. To determine short- and long-term effects of permethrin on embryo quality and steroid biosynthesis, superovulation was initiated twice with collection of embryos occurring at 17 and 51 days after treatment. Embryos were recovered 6.5 days after first artificial insemination via nonsurgical flush and were evaluated by International Embryo Transfer Society standards. Blood was collected at standing estrus and day of embryo recovery. Estradiol (E2) and progesterone (P4) concentrations were analyzed via RIA. MIXED and GLIMMIX procedures of SAS were used to analyze continuous and categorical data, respectively. Heifer per flush was the experimental unit. Total embryos recovered did not differ because of treatment ($P = 0.30$), but did decrease in flush 2 compared with flush 1 ($P = 0.02$). Quality grade, total transferable quality embryos, and overall flush success did not differ because of treatment ($P \geq 0.16$). However, transferable quality embryos were decreased in flush 2 compared with flush 1 ($P = 0.05$). Total unfertilized oocytes were greater in saline control ($P = 0.04$). The PYR heifers tended to have less total P4 ($P = 0.15$) and P4 per CL ($P = 0.06$) at recovery. E2 per ovulated follicle and E2 per total ovarian structure was greater in flush 2 ($P \leq 0.03$) but did not differ because of treatment ($P \geq 0.23$). In summary, these data indicate that permethrin administration at label dose in superovulated beef heifers has a tendency to reduce P4, but embryo quality is not affected.

1. Introduction

Pyrethroid exposure has been implicated to disrupt male reproductive and endocrine functions [1–10]. In addition, endocrine disruption is speculated to influence the hypothalamic-pituitary-gonadal axis and impair the

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necessary feedback mechanisms of hormones that provide the required stability to regulate normal reproductive physiology. Previous observational findings have claimed that bulls exposed to pyrethroids have an increase in abnormal sperm morphology [11]. However, recent literature has refuted the claim by exposing bulls to multiple pyrethroid products and by different routes of administration [12–14], including recent data from our laboratory on peripubertal bulls exposed to label-dose pour-on permethrin [15].

Endocrine disruption is not believed to be sex specific, and thus likely affect female reproductive physiology by inhibiting normal reproductive cyclicity and the ability to maintain pregnancy [16]. Previous research has indicated pyrethroids may inhibit progesterone (P4) concentrations by downregulating expression of cP450scc and steroidogenic acute regulatory protein (StAR) [17,18]. In addition, Pine et al. [19] reported esfenvalerate, a type II pyrethroid, delayed vaginal opening, and decreased morning serum estrogen concentration after oral administration (1.0 and 5.0 mg/kg/day starting on postnatal Day 22) to prepubertal female rats. However, there are postulated thoughts that endocrine disruption chemicals could also stimulate changes in the reproductive tract that impede sperm migration, sperm adhesion, capacitation, zona binding, acrosomal reaction, or penetration into the oocyte or the competency for maturation of a developing embryos [20]. Preimplantation losses with reduction of implantation sites have been reported with rats receiving lambda cyalothrin orally in early gestation, which could imply that exposure to pyrethroids could develop a hostile environment or cause abnormal synchronization of implantation [16]. However, French et al. [13] did not find similar results when exposing mature cows with different applications of pyrethroids.

The overall reproductive effects of pyrethroid exposure to female cattle have not been studied in as much detail as the bull. The objective of this study was to elucidate the effects of a commercial pyrethroid-based pour-on product, permethrin, on reproductive performance in superovulated beef heifers by assessing steroid synthesis and embryo quality. It was hypothesized that exposure to pyrethroid pour-on at label dose would cause minimal effects on reproductive parameters in the female bovine.

2. Materials and methods

2.1. General

All protocols and procedures used were approved by the Iowa State University Institutional Animal Care and Use Committee (3–14–7760-B). The project was conducted at the Iowa State University Zumwalt Station in Ames, IA in May to July 2014. The project used single-sourced heifers from the Iowa State University Beef Teaching herd. Products used in this study included: a synthetic type I pyrethroid pour-on (permethrin; Ultra Boss; Intervet/Merck Animal Health, Summit, NJ, USA) and sterile saline (0.9% sodium chloride, Abbott Laboratories, North Chicago, IL, USA). We evaluated permethrin pour-on (Ultra Boss) at label dose because of its popular use on the basis of sales from local distribution companies in the Midwest and having the highest concentration of pyrethroid substance in commercially available products.

2.2. Animals and treatments

Nonpregnant, purebred Simmental and crossbred yearling beef heifers (n = 10; 418 ± 33 kg; 5.5 ± 0.2 body conditioning scores) were used in this study. Before treatment, all heifers were subjected to a trans-rectal reproductive ultrasound examination to confirm normal ovarian activity and cyclicity. At that time, initial body weight (BW) and body conditioning scores were recorded and heifers were blocked by breed and BW. Heifers were assigned to either (1) a saline control (CON; n = 5) or (2) a permethrin pour-on treatment group (PYR; n = 5). The PYR heifers received a one-time label dose of permethrin (Ultra Boss, 5% permethrin and 5% piperonyl butoxide, 3 mL per 45 kg BW up to a maximum of 30 mL) for lice and fly control. The CON group received the same volume of saline. Both products were administered on the topline of the heifers. Treatment groups were housed one pen per treatment to avoid cross-contamination. All heifers received the same environmental and nutritional treatment before and after treatment.

Treatments were initiated at the start of superovulation protocol. All heifers were subjected to superstimulation by using a timed, 17-d, CIDR (EAZI-BREED, Zoetis Inc., Kalamazoo, MI, USA)-based protocol with GnRH (Cystorelin, Merial LLC, Duluth, GA, USA), and PGF2α (Estrumate, Schering-Plough Animal Health Corp., Summit, NJ, USA) with decreasing total dosage of 240-mg FSH (Folltropin-V, Bioniche Animal Health Canada Inc., Belleville, ON, USA) administered twice daily for 4 days (experimental design, Fig. 1). Heifers were artificially inseminated (AI) twice either at the onset of estrus or by the timed-AI and additionally 12 hours later by same technician with one unit of frozen semen, at each insemination, from a single bull collection. A dose of GnRH (100 μg) was given at time of second breeding. At 6.5 days posttimed-AI, trans-rectal ultrasound was performed to assess number, number of unovulated follicles, and total ovarian structures (CL and unovulated follicles). Immediately after ultrasound, nonsurgical embryo recovery was performed by horn flushing, with utilization of a closed gravity-flow flush system with 2 liters of commercial grade flush media. All recovered embryos were evaluated according to International Embryo Transfer Society standards by blinded American Embryo Transfer Association certified personnel.

To determine potential long-term effects of permethrin on embryo quality and steroid biosynthesis, an identical superstimulation protocol, as previously described, was initiated again 34 days after treatment with embryo recovery performed 51 days after treatment. On the second flush, one heifer had abnormal oviduct pathology and embryo data were not used.

Blood was collected via coccygeal tail vein at insertion of CIDR, standing estrus, and day of embryo recovery to evaluate baseline (basal) estradiol-17β, peak estradiol-17β, and P4 concentrations, respectively. Blood was put on ice and was centrifuged (1750 × g for 25 minutes) and plasma was removed and frozen (−20 °C) for later analysis. Plasma samples collected on the day of CIDR insertion and at estrus