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Effects of label-dose permethrin administration in yearling beef cattle: I. Bull reproductive function and testicular histopathology

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ABSTRACT

Pyrethroid administration to a wide variety of laboratory animals has been shown to cause detrimental effects on male fertility, including sperm quality, by means of endocrine disruption. The objective of this experiment was to study the effects of a commercial, permethrin-containing pour-on product on reproductive variables and testicular histopathology of yearling beef bulls. Black Angus bulls ($n = 60$; aged 369 ± 17 days; 511 ± 33 kg; 6.2 ± 0.5 body condition scores) were assigned to either (1) saline control (CON) or (2) permethrin pour-on administered at label dose (PYR). Blood samples were collected, and industry standard breeding soundness examinations (BSE), via electroejaculation, were performed on all bulls at 5 days before and 14 days after treatment. Progressive sperm motility and eosin-nigrosin–stained sperm were analyzed using high-power phase-contrast microscopy. Plasma testosterone concentrations were analyzed via radioimmunoassay. Bulls were slaughtered at 34 days, and one testicle per bull was randomly collected for histologic examination. Change in sperm motility between BSEs was not different because of treatment; sperm morphology however improved across treatments, but PYR bulls had less improvement in percent of head ($P < 0.001$) sperm abnormalities compared to CON, resulting in less improvement of primary abnormalities ($P = 0.04$). Nonetheless, morphological differences did not change the overall outcome for satisfactory breeder status. Change in testosterone concentration did not differ because of treatment. Histopathologic examination identified that testicular degeneration and tubule diameter did not differ as a result of treatment. It should be noted, however, that degeneration score (higher score having more degeneration) was positively correlated with primary abnormalities ($P < 0.01$; $r = 0.35$) and negatively correlated with normal sperm cells ($P < 0.001$; $r = -0.43$). In summary, these data indicate that a single use of permethrin at label dose in yearling Angus bulls results in minimal detrimental effects on sperm morphology but not to a degree that impacts the ability of bulls to pass a standard BSE.

1. Introduction

For the past few decades, pyrethroids have become the leading global insecticide used in agriculture, including animal products, because of the phasing out of the more ecologic harmful products such as organophosphates and

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carbamates [1]. In the beef industry, many producers and veterinarians use pyrethroid-based insecticide products to improve productivity in cow-calf operations by eliminating potential insect-borne diseases and to control biting flies. According to the National Animal Health Monitoring System of the United States Department of Agriculture, over one-half of beef operations used some type of insecticide fly control, and over 70% of larger herds (greater than 50 head) used insecticides to control production losses due to disease transmitting pests [2]. However, a report in the popular press has identified a potential link between the use of pyrethroids and negative effects on beef bull reproductive health [3], and this claim has stimulated uncertainties and fears for producers and veterinarians using pyrethroids on beef bulls before or during the breeding season.

One report describes detrimental effects on bull sperm morphology and motility shortly after being exposed to pyrethroid compounds [3]. These observations are supported by similar findings in other clinical cases and laboratory studies using different pyrethroid chemicals applied by differing routes and dosages in a variety of species, including humans, rats, mice, and goats [4–11]. The literature also supports potential endocrine disruption and its deleterious effects on male reproduction due to pyrethroid exposure in *in vivo* and *in vitro* trials [5,7,8,11–14]. However, reports on the effect of pyrethroid administrations on bull fertility are unclear and inconsistent with the previous claims [3]. In a case-controlled study, purebred beef bulls treated with 150% of the label dose of topical 1% permethrin on 0 and 14 days did not result in any negative effects on normal sperm morphology throughout the 12-week study [15]. French et al. [16] also reported no difference in sperm motility, sperm morphology, or serum testosterone concentrations between beef bulls treated with β-cyfluthrin pour-on or bulls exposed to a combination of pyrethroid pour-on and β-cyfluthrin fly tags. Similarly, Stewart et al. [17] reported no consistent difference in overall and progressive sperm motility or serum testosterone concentrations during a 9-week trial using two treated groups exposed to cyfluthrin and pyrethrin spray products in combination with cyfluthrin pour-on and fly tags in crossbred beef bulls. Effects of pyrethroid exposure of bulls have been assessed with standard breeding soundness examination (BSE) and serum steroid (testosterone) concentrations; however, the effects of 5% permethrin applications to peripubertal bulls and their testicular histology have not been studied. The objective of this study was to measure reproductive effects in peripubertal bulls exposed to a commercially available pyrethroid-based pour-on product. Our hypothesis was that permethrin topical application at labeled dose to yearling bulls via commercial, pyrethroid-based pour-on product would have limited effects on bull reproductive variables and would not change BSE classification 2 weeks after the treatment and would elicit no effect on testicular histology 1 month after application.

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 (3-14-7759-B). The project was conducted at the Armstrong Memorial Research and Demonstration Farm in Lewis, IA, USA, in April 2014. The project used bulls from the McNay Beef Research herd, which are sourced from a single herd within the Iowa State University system. The products used in this study included the following: 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). The permethrin pour-on (Ultra Boss) was chosen and evaluated because of its popularity in the Midwest and because this product had the highest concentration of pyrethroid substance in commercially available products.

2.2. Animals and treatments

Purebred Black Angus yearling beef bulls ($n = 60$; aged 369 ± 17 days; 511 ± 33 kg; 6.2 ± 0.5 body condition scores [BCS]) were assigned to either (1) a saline control group (CON; $n = 30$) or (2) a permethrin pour-on group (PYR; $n = 30$). The saline or pour-on products were applied topically along the dorsum of the bull per label directions. All animals in the study had been in their designated pens at the research location in excess of 4 months before study initiation, during which period there was no exposure to pyrethroids. The PYR bulls received a label dose of permethrin (5% permethrin and 5% piperonyl butoxide; 3 mL per 45 kg body weight [BW] with maximum of 30 mL/animal) for lice and fly control. Because all bulls weighed more than 455 kg, they all received the maximum label dose of 30 mL. The CON bulls received the same 30 mL volume of saline. Bulls were housed by treatment (one pen for each group) to avoid cross-contamination and were exposed to the same environmental and nutritional influences before and after treatment.

The experimental design is illustrated in Figure 1. Five days before the treatment, initial BW and BCS were recorded. At that time, all bulls were subjected to an industry standard BSE following published guidelines established by the Society of Theriogenology [18]. The BSE consisted of a general physical examination, scrotal circumference (SC) measurement, external palpation of sex organs (scrotum, testes, and epididymides) and palpation of internal accessory sex glands, visual assessment of the penis and prepuce, and collection of semen sample for microscopic evaluation. After the initial BSE on 0 days, bulls were treated on 5 days and were subjected to final BSE on 19 days.

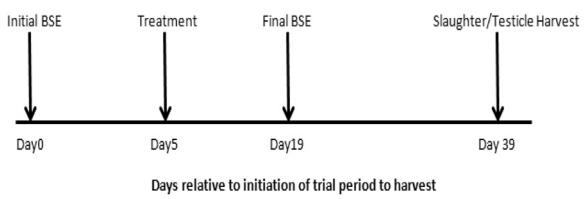

Fig. 1. Experimental design for the treatment of yearling Angus bulls with a pyrethroid pour-on. BSE, breeding soundness examination.