RESEARCH FACTS

UNIVERSITY OF SASKATCHEWAN
Livestock and Forage Centre of Excellence
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COMPLETED

Improving reproductive efficiency in beef cattle

PROJECT TITLE

A new approach for improving reproductive efficiency in beef cattle

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RESEARCHERS

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Background:

Approximately 18 per cent of beef producers in western Canada utilize estrus synchronization protocols for artificial insemination or advanced reproduction. Among producers, the leading reason that estrus synchronization is not used is due to the difficulty of implementation. Currently used synchronization protocols can span a length of eight to more than 20 days in duration and require handling an animal upwards of five times.

We have recently investigated the use of the aromatase inhibitor, letrozole, for ovarian synchronization in cattle. Letrozole prevents the body from producing the steroid estradiol, which results in extended growth of the dominant follicle. This allows for implementation of a synchronization protocol that is effective yet short in duration. We hypothesized that a letrozole-based synchronization protocol will result in comparable pregnancy rates to commercially used protocols.

Objectives:

The objectives were to:

1. Develop a silicone intravaginal letrozole-releasing device (LRD) to provide sustained drug release throughout insertion (experiment 1),
2. Compare a four-day letrozole synchronization protocol to commercially used protocols for fixed-time artificial insemination (FTAI) (experiment 2), and
3. Compare a refined letrozole-based synchronization protocol to a progesterone-based protocol in a large field trial for FTAI (experiment 3).

What They Did:

Experiment 1

Beef heifers (n=6 per group) were assigned randomly and given one of the following six intravaginal devices for eight days:

1. A small surface area (SSA) silicone LRD containing 10 per cent letrozole (w/w),
2. A SSA silicone LRD containing 15 per cent letrozole,
3. A large surface area (LSA) silicone LRD containing 5per cent letrozole,
4. A LSA silicone LRD containing 15 per cent letrozole (see Figure 1),
5. A wax-based letrozole device (positive control), or
6. A blank device (control).

Frequent blood sampling was done during the first 24 h, followed by twice daily sampling until device removal.

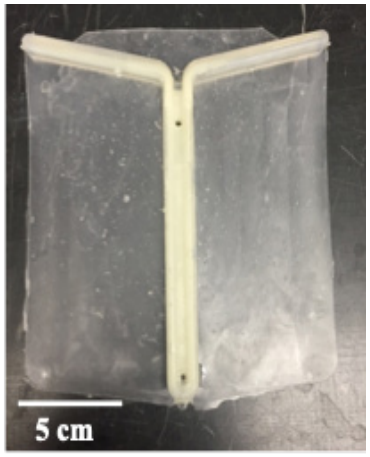

Figure 1. (right) A large-surface area silicone intravaginal letrozole-releasing device (LRD) containing 15 per cent letrozole. This intravaginal device provided sustained drug release of letrozole throughout the duration of insertion in cattle.

Experiment 2

Beef heifers (n=71) and lactating beef cows (n=126) were used during June and July (breeding season). At random stages of the estrous cycle, cattle were assigned randomly to one of the following three groups:

1. A four-day LRD, followed by prostaglandin F2a (PGF) given at device removal and gonadotropin-releasing hormone (GnRH) concurrent with FTAI 48 h after PGF,
2. 2.5 mg estradiol-17ß plus 50 mg of progesterone in oil and a progesterone intravaginal device for seven days, PGF at device removal and GnRH concurrent with FTAI at 60 hours after PGF, or
3. A five-day progesterone intravaginal device with PGF given at device removal and GnRH concurrent with FTAI 72 hours after PGF. Cattle were FTAI with frozen-thawed semen and pregnancy diagnosis by transrectal ultrasonography was done 28 days after FTAI.

Experiment 3

Following low pregnancy rates with the letrozole-based protocol in experiment 2, a small preliminary study revealed pregnancy rates were maximized in cattle initiating letrozole treatment during the metestrus period (i.e. shortly after estrus). Beef heifers and lactating cows (n=70 and 156, respectively) were assigned randomly to either a refined four-day letrozole-based or a conventional five-day progesterone intravaginal protocol. At random stages of the estrous cycle, cattle in the letrozole group were given PGF to induce luteolysis and five days later given a four-day intravaginal LRD. Cattle in the progesterone-based protocol were given GnRH at the time of insertion of a five-day progesterone device. In both groups, PGF was given at the time of device removal and 12 hour later to induce luteolysis; GnRH was given concurrently with FTAI with frozen-thawed semen 66 hours after the first PGF. Blood sampling was done seven-days post FTAI and ultrasonography was done 28-days post-FTAI for plasma progesterone concentrations and pregnancy diagnosis, respectively.

What They Learned:

Experiment 1

All intravaginal devices remained in place for the eight-day duration. Plasma concentrations of letrozole among groups are shown in Figure 2 (see below). The concentration of letrozole was sustained throughout the treatment period in the 15 per cent letrozole silicone LSA intravaginal device and this device was selected for further studies.

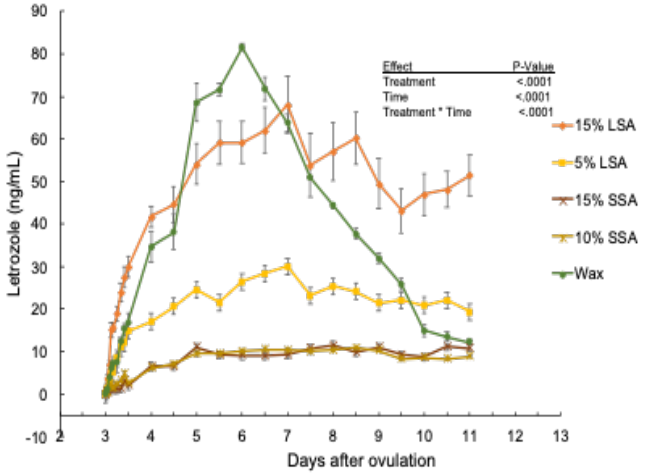

Figure 2. (right) Plasma concentrations of letrozole (mean ± SEM; n=6/group) following treatment with an intravaginal letrozole device for 8 days. LSA: large surface area; SSA: small surface area

Experiment 2

The pregnancy rate following FTAI was significantly lower in the letrozole-based protocol (20 per cent) than the estradiol- and intravaginal progesterone-based protocols (60 per cent and 44 per cent, respectively). In a follow-up study, we showed that estrus occurred ~60 hour after PGF was given during a letrozole-based protocol. We concluded that a letrozole-based protocol with a 48-hour interval from PGF to FTAI resulted in ovulation of a premature follicle. An unhealthy corpus luteum was formed that did not release enough progesterone to support a pregnancy.

Experiment 3

Following development of a refined letrozole-based synchronization protocol for FTAI, no difference was shown in the pregnancy rate between treatments in beef heifers and cows (overall average 54 per cent). However, heifers treated with a letrozole-based protocol had a significantly higher concentration of plasma progesterone seven-days post FTAI. This new approach may be useful to increase pregnancy rates following embryo transfer in cattle.

What It Means:

These studies have shown that a novel silicone intravaginal letrozole-releasing device can be used for ovarian synchronization in cattle. Through trial and error, we have developed a new protocol that can be used for ovarian synchronization and results in comparable pregnancy rates following FTAI to commercially used protocols. As patent-holders of this technology, it is our intention to license the letrozole device to a pharmaceutical company so that it may become commercially available, increase pregnancy rates, and help make reproductive technologies more user-friendly to cattle producers worldwide.

For more in-depth information, please refer the PhD thesis of Eric Zwiefelhofer located on the LFCE's website as well as the following published peer-reviewed article: Zwiefelhofer, E. M., Davis, B. M., Adams, G. P. (2020). Research and development of a silicone letrozole-releasing device to control reproduction in cattle. *Theriogenology, 146*, 104–10.

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