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Varying the form of oestradiol administration in anoestrous cows previously treated with progesterone

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ABSTRACT

The hypothesis tested in this field trial was that 1 mg oestradiol benzoate (ODB) could be equally effective where administered to anoestrous animals either by intramuscular injection or in a gelatin capsule per vaginum. The ODB treatment was administered to 412 cows in 8 dairy herds 24 h after the end of a 6-day priming treatment with progesterone, also administered per vaginum.

By 48 h after ODB administration, 87% of injected animals had been detected in oestrus and inseminated compared to only 44% of herdmates receiving the gelatin capsule (P<0.01). Re-examination of those animals not detected in oestrus by 13 days after ODB treatment showed that 30% of capsule-treated animals were still anoestrous and another 10% had ovulated without being detected in oestrus. Comparable percentages for the injected animals were 3% and 2% respectively (P<0.01). The vaginal treatment was also associated with a reduced pregnancy rate to first insemination (31.7% vs 47.7%; P<0.05).

The reduced efficacy associated with the vaginal administration of ODB to anoestrous animals most probably involved a prolonged rate of absorption which did not stimulate behavioural oestrus or an ovulatory surge of LH but did reduce fertility in those animals which were inseminated.

Keywords: Anoestrus; oestradiol; injection; vaginal administration.

INTRODUCTION

Postpartum anovulatory anoestrus is a major form of infertility among cows in dairy herds in New Zealand. It is characterised by a series of ovarian follicle waves which produce dominant follicles which fail to ovulate because pulsatile concentrations of luteinising hormone (LH) in plasma are insufficient to stimulate oestradiol production by follicular granulosa cells (McDougall et al., 1995). During the pro-oestrous phase of a normal oestrous cycle, oestradiol production is increased as a dominant follicle matures and finally stimulates the onset of the ovulatory surge of LH at about the same time as behavioural symptoms of oestrus are manifest. The pro-oestrous phase is preceded by the dioestrous phase which is characterised by a corpus luteum (CL) producing progesterone (P4) for about 2 weeks of a normal 3 week cycle.

Innovative studies in New Zealand demonstrated that administering P4 per vaginum to anoestrous cows for 5 days increased their sensitivity to oestradiol injected intramuscularly as oestradiol benzoate (ODB) 48 h later (McDougall et al., 1992). It also caused 85% of them to ovulate and recommence having normal oestrous cycles. This observation has subsequently been developed as an effective form of treatment for anoestrus and is based on using a CIDRTM device to administer the P4 per vaginum for at least 5 days followed by an injection of 0.75 or 1.0 mg ODB from 24 to 48 h later (Macmillan et al., 1995).

Synchrony treatments in cycling cows and heifers have also been based on the administration of P4 per vaginum for 7 or more days combined with the vaginal administration of 10 mg ODB concurrent with device insertion. Since this means that ODB can be administered per vaginum as well as by injection, the following experiment was designed to test the hypothesis that the injection of 1 mg ODB used in the course of routinely treating anoestrous dairy cows could be replaced by administering the same dose of ODB and at the same time as by injection but in a gelatin capsule inserted into the vagina. The latter route of administration would cause less discomfort and reduce some of the risks associated with intramuscular injections. However, the pattern of uptake and the maximum concentrations of oestradiol in the plasma may differ and consequently alter efficacy (Burke et al., 1996).

MATERIALS AND METHODS

A total of 412 cows comprising from 24 to 124 cows in each of 8 dairy herds were initially diagnosed as anoestrous 7 days before the planned date of commencement of each herd's seasonal breeding programme. The minimum postpartum interval to examination was 15 days after an uncomplicated calving not involving induced parturition and associated with a normally involuting uterus with no evidence of pathology or ovarian or uterine adhesions. None of these cows had been observed in oestrus. Any animal which had evidence of being mounted or had a CL on an ovary was also excluded.

A CIDRTM device (InterAg, Hamilton) with a gelatin capsule containing 10 mg ODB (CIDIROL™; InterAg, Hamilton) was inserted into the vagina of each selected animal following diagnosis to be removed 6 days later. The 6 animals which lost the device during this period were excluded from the study.

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On the seventh day following diagnosis (24 h after device removal), half of the animals in each herd were injected intramuscularly with 1 mg ODB in 2 ml of arachis oil (CIDIROL™; InterAg, Hamilton). Their anoestrous herdmates received the same dose of ODB dispersed in 1 g of pharmaceutical grade lactose encased in a gelatin capsule and deposited in the anterior vagina with a dedicated applicator.

Each animal had been tailpainted at the time of device insertion and those detected in oestrus were inseminated with other oestrous herdmates presented each morning to a technician who was employed by the Livestock Improvement Corporation (LIC) and who provided a standard Premier Sires Service™ using semen processed in Caprogen™. Those cows not inseminated within 13 days of ODB administration were presented for a second veterinary examination to determine whether: (i) an animal was still anoestrous and required re-treatment (Anoest.); or, (ii) there had been an ovulation without an observed oestrus (Ov.-Oest.) with the consequent probability of injecting a prostaglandin F₂α (PGF) to reduce the interval to the next device removal), half of the animals in each herd were

The experimental animals in each herd were pregnancy tested twice; first, to confirm a conception date coinciding with a first or second insemination, and then to confirm that pregnancy was proceeding normally. Comparisons using chi-square statistics included treatment-related post-treatment intervals to oestrus, proportions in the main response categories (inseminated, Anoest. and Ov.-Oest.) and pregnancy rates to first insemination.

RESULTS

A higher percentage of injected animals were detected in oestrus 1 and 2 days after ODB administration (54% vs 23%; P<0.01; and, 33% vs 21%; P<0.05) so that almost twice as many injected animals were inseminated on these two days (87% vs 44%; Table 1). The compensatory consequences were that more animals treated with the capsule per vaginum remained anoestrous (30% vs 3%; P<0.01) or ovulated without being detected in oestrus (10% vs 2%; P<0.05; Table 1).

The average pregnancy rate for 196 inseminations made within 13 days of the ODB injection was 47.7% compared to 31.7% for 123 inseminations in herdmates treated with the ODB capsule (P<0.05). Final empty rates were similar (9.4% vs 12.3%; injection vs capsule).

DISCUSSION

The results in Table 1 clearly demonstrate that an intramuscular injection is the preferred form of administering 1 mg ODB to increase the probability of oestrus and ovulation in anoestrous cows previously primed with P4 for 6 days. Whereas 95% of the injected animals were detected in oestrus and inseminated, only 60% of the capsule-treated herdmates were inseminated leaving 40% to be re-examined. Most of the re-examined animals (30%) had failed to ovulate. This suggests that the vaginal route of administration of ODB had not elevated plasma oestradiol concentrations sufficiently to induce an ovulatory surge of LH. This possible explanation is supported by Burke et al. (1996) who reported that plasma concentrations of oestradiol at 16 and 20 h after an intramuscular injection of 1 mg ODB were 20.9±1.9 pg/ml whereas a 10 mg ODB capsule inserted per vaginum produced an average peak concentration of 12.6±2.2 pg/ml. Since we used a 1 mg ODB capsule in the present comparison, plasma oestradiol concentrations would not have been expected to exceed 5 pg/ml. The study of Burke et al., (1996) also showed that concentrations of plasma oestradiol had returned to basal, pre-injection levels within 30 h of injecting 1 mg ODB, whereas the vaginal route of administration produced significant elevations in concentration for at least 70 h, with wide variation among individual animals. The occurrence of a similar pattern of absorption from a capsule containing 1 mg ODB could have produced a prolonged period of low but significantly elevated plasma oestriadiol concentrations and contributed to the lower pregnancy rate to first insemination.

Although the increased incidence of oestrus among the injected animals could have reflected a greater occurrence of oestrus without ovulation, this has not been the case in previous studies which reported similar response patterns to the same dose of ODB (Macmillian et al., 1995). These previous studies also included treatment groups which received no ODB and which had response patterns similar to those shown in Table 1 for anoestrous cows treated with a gelatin capsule of ODB.

Further attempts to administer ODB per vaginum instead of by injection will need to consider delivery systems which produce changes in plasma concentrations of oestradiol similar to those associated with an intramuscular injection of 1 mg ODB.

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REFERENCES

