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Effects of oestradiol benzoate by injection at CIDR™ insertion for the treatment of postpartum anovulatory anoestrus in dairy cows

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ABSTRACT

The effect of an intramuscular (im) injection of oestradiol benzoate (ODB) at insertion of an intravaginal progesterone-releasing device (CIDR™, InterAg, NZ) during hormonal treatment for postpartum anoestrus in dairy cattle was investigated. Inclusion of injected ODB at CIDR™ insertion in synchronisation programmes for cycling cows can increase fertility, possibly by initiating an emergence of a new ovarian follicle wave with resultant improved oocyte competence.

A total of 882 cows, of mixed age and breed from 18 herds, were examined and diagnosed as anoestrous during the week preceding each herd's planned start of mating. Cows were allocated randomly as controls or to receive 0.5 or 1 mg ODB (Oestradiol Benzoate Inj., Intervet, Netherlands) by im injection at CIDR™ insertion. The device was removed after 7 days, and any cow which was not observed in spontaneous oestrus within 48 h received 1 mg ODB im (CIDROL™ Injection, InterAg, NZ). Cows with an observed heat within 12 days of CIDR™ removal were defined as responders, and returns to service in the subsequent 30 days were recorded.

There were no significant differences between the control, 0.5 and 1 mg ODB treatments for either the proportion responding (89.5%, 89.4% and 90.9%, respectively) or returning (52.3%, 50.3% and 55.4%, respectively); however the proportions of cows observed in spontaneous oestrus varied by treatment ($P < 0.01$; 28.5%, 22.9% and 17.2% for control, 0.5 and 1 mg ODB treatments, respectively). Conception rates were not significantly affected by treatment (35.9%, 42.5% and 43.2% for control, 0.5 and 1 mg ODB treatments, respectively). Of cows which did not become pregnant to the induced oestrus, 21.7%, 20.7% and 29.9% for control, 0.5 and 1 mg ODB treatments respectively, returned to service with an interval of more than 24 days.

These observations suggest that an injection of ODB at CIDR™ insertion may alter follicle wave patterns in cows with PPA, but that this may not result in increased conception rate, and might be detrimental to ovarian activity in a proportion of cows.

Keywords: postpartum anoestrus; oestradiol benzoate; progesterone; cattle.

INTRODUCTION

Postpartum anoestrus (PPA) is a major contributing factor to compromised reproductive performance in New Zealand dairy cows when it extends into the mating period. Despite the absence of oestrus and ovulation, waves of ovarian follicle development continue from about the 10th day *post partum* (McDougall, 1994). An established hormone replacement treatment for the condition (LIC Veterinary Products Manual, 1996) uses a progesterone-releasing intravaginal device (CIDR™, InterAg, Hamilton, NZ) for 5 days, with 1 mg oestradiol benzoate (ODB), by intramuscular (im) injection, 48 h after CIDR™ withdrawal if cows have not shown standing oestrous behaviour. This treatment mimics the pre-ovulatory surge of oestradiol, and ovulation occurs in about 75% of treated animals. Despite the majority of animals responding by coming into oestrus and/or ovulating, fertility is poor with subsequent pregnancy rates of about 40% (Macmillan *et al.*, 1995).

Results of field trials carried out on cycling cows indicated that fertility following oestrus synchrony treatments was improved by the inclusion of 2 mg ODB by im injection at the time that progesterone treatment is commenced (Day *et al.*, 1997). This improvement in fertility was attributed to the role of ODB in causing any dominant ovarian follicle present at the time of CIDR™ insertion to

regress, thus allowing a new follicle wave to emerge. A new dominant follicle, with a functional oocyte, will then develop during the period of progesterone treatment (Burke *et al.*, 1997).

It was hypothesised that ODB might play a similar role in cows with PPA, and that inclusion of an injection of ODB might improve fertility subsequent to treatment. Administration of ODB intra-vaginally by capsule at the time of CIDR™ insertion did not enhance response or pregnancy rates (Taufa *et al.*, 1997). We report here the results of a field trial, carried out on commercial herds in the central Waikato area, in which cows diagnosed with PPA during the week of planned start of mating (PSM) were treated with varying doses of ODB.

MATERIALS AND METHODS

A collaborative field trial involving herd owners and their respective veterinarians was carried out in 18 herds in the central Waikato region in spring 1997. Cows which had no record of oestrus in the previous 30 days were presented by the farmers for veterinary examination during the week of planned start of mating (PSM). Diagnosis of PPA was made on the basis that cows had calved at least 21 days before examination date, had no palpable luteal structures on either ovary and that uterine involution was proceeding

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normally with no palpable pathology present. A total of 882 cows of mixed age and breed were enrolled in the trial.

Following examination, a progesterone-containing CIDR™ device (InterAg, NZ) was inserted into the vagina of each animal. Cows were randomly assigned to treatments balancing for farm of origin, age and breed. Overall one third acted as untreated controls (CIDR™ only) while the remainder received an im injection of either 0.5 or 1 mg ODB (Oestradiol Benzoate Inj., 5 mg/ml, Intervet, Netherlands) at the time of CIDR™ insertion (control: n = 292; 0.5 mg ODB: n = 285; 1 mg ODB: n = 305). The device was removed after 7 days, and any cow which was not observed in spontaneous oestrus within 48 h was given an im injection of 1 mg ODB (CIDROL™ Injection, InterAg, NZ). Cows were bred by artificial insemination on observation of oestrus.

Cows inseminated within 12 days of CIDR™ removal were defined as responders, and returns to service in the subsequent 25 days were noted. All cows were palpated per rectum at 8-9 weeks following insemination to the induced oestrus to establish whether conception had occurred following the induced oestrus or the first subsequent oestrus.

Data were examined to determine proportions of cows responding spontaneously or following injection of 1 mg ODB post-CIDR™ removal, proportions of cows returning to oestrus following the induced heat, and conception rates (proportions of responding animals diagnosed pregnant) to the first and second inseminations following treatment. Treatment effects were tested statistically using Chi square analysis. Data for first lactation cows were compared with those for cows of two or more lactations, to determine whether their pattern of response was similar to that of the total group.

RESULTS

The 882 cows enrolled in the trial were from 18 herds - average herd size of 328 (range 135 - 750). The diagnosed PPA cows represented 20 ± 2% (range 10% - 40%)

of their respective herds. The average age of these cows was 4.9 ± 0.1 yr (range 2 - 13 yr) with 35% and 20% being in their first and second lactations, respectively. The mean postpartum interval for enrolled cows was 45.1 ± 0.8 days (range: 21 - 93 days), while for those cows in their first lactation as a sub-group, this interval was 60.5 ± 1.0 days (range: 21 - 93 days).

The overall response to treatment resulted in 89.8% of cows being inseminated at an induced oestrus within 12 days of CIDR™ removal. There was no effect of treatment on the proportion which responded (P = 0.8; Table 1); however there was a treatment effect (P < 0.001) on the proportion of cows which were observed in spontaneous oestrus (i.e. did not require 1 mg ODB at 48 h post-CIDR™ removal) with the proportion of the control group showing spontaneous oestrus being greater than for either 0.5 mg or 1 mg ODB groups (Table 1). A similar trend was observed with the first lactation cows, but this was not statistically significant (P > 0.3; Table 1).

Of all cows which responded to PPA treatment, 58.8% were not recorded in oestrus during the following 30 days, being similar for each treatment (59.0%, 56.3% and 61.0%, for control, 0.5 and 1 mg ODB, respectively). First lactation cows had a higher (P < 0.01) 30-day non-return rate of 66.1% overall which did not differ by treatment.

Conception rate to insemination at the induced oestrus (CR1) was 40.5% overall, being similar (P > 0.15) between treatment groups (Table 1). The CR1 for the subset of first lactation cows was higher than for the older cows (50.0% and 37.7%, respectively; P < 0.01), but did not differ between treatments (Table 1).

Of cows which did not become pregnant to insemination at the induced oestrus, 7.0% were recorded in oestrus again within 17 days (short returns), and 23.9% returned at an interval greater than 24 days (long returns). For the cows in their first lactation, 2.3% had short returns and 28.5% had long returns. There were no significant treatment effects on the proportions of animals having short returns, while the proportion with long returns tended to be greater following the 1 mg ODB treatment (P = 0.12; Table 1).

TABLE 1: Response to treatment for postpartum anoestrus, conception rate to the induced oestrus (CR1), cows which showed a return pattern of greater than 24 days following induced oestrus (long returns) and conception rate to second insemination of those cows which returned to service within 18 to 24 days of induced oestrus (CR2), among cows injected im with oestradiol benzoate (0.5 or 1 mg at the time of CIDR™ insertion), or in a control group.

	Control (no ODB)	0.5 mg ODB	1 mg ODB
<i>All enrolled cows</i>			
n	305	292	285
% responding (n)	89.5% (273/305)	89.4% (261/292)	90.9% (259/285)
% spontaneous (n)	28.5% (87/273)	22.9% (67/261)	17.2% (49/259)
CR1 (n)	35.9% (98/273)	42.5% (111/261)	43.2% (112/259)
Long returns (%)	21.7% (38/175)	20.7% (31/150)	29.9% (44/147)
CR2 (n)	52.0% (66/127)	58.9% (66/112)	67.8% (59/87)
<i>First lactation cows</i>			
n	72	68	76
% responding (n)	84.7% (61/72)	89.7% (61/68)	84.2% (64/76)
% spontaneous (n)	26.4% (19/61)	23.5% (16/61)	17.1% (13/64)
CR1 (n)	47.5% (29/61)	50.8% (31/61)	50.0% (32/64)
CR2 (n)	50.0% (16/32)	75.0% (15/20)	89% (17/19)

For those cows which returned to service within 18-24 days of the induced oestrus, the conception rate to insemination (CR2) was 58.8% overall, and 68.2% for the subset of cows in their first lactation. There was a strong tendency for an improved PR2 in the 1 mg ODB treatment group ($P = 0.07$; Table 1).

DISCUSSION

The proportion of cows showing spontaneous oestrus was decreased by the use of oestradiol benzoate at the time of CIDR™ insertion, but there was no effect on conception rate to the induced oestrus. The altered occurrence of spontaneous oestrus could be due either to an absence of a preovulatory follicle at CIDR™ removal, the presence of a preovulatory follicle which is not sufficiently oestrogenic to initiate oestrus and ovulation, or a failure of the behavioral centres to respond to hormonal signals for the initiation of oestrous behaviour. The large proportion of cows which did not become pregnant and which failed to return to oestrus within 18-24 days, especially in the 1 mg treatment group, suggests that the treatment may have had a detrimental effect on the development of ovarian follicles. This may be due to an increased pituitary gland sensitivity to the suppressive effects of the oestradiol when activity is already reduced in the anoestrous state. This scenario would also explain the increased proportions of cows which did not have a spontaneous heat in the ODB treated groups, for which it is possible that the induced oestrus was a “false heat” from the exogenous oestradiol administered at a time of low plasma progesterone concentration following CIDR™ withdrawal. Despite these observations, there was a tendency for a greater conception rate in the cows which received ODB. Taken together this suggests that the treatment may have been beneficial in some cases but detrimental in others, and may have been a consequence of the varying depth of anoestrus in the enrolled cows at the time of treatment.

Overall first lactation animals had better conception rates which may be a consequence of their greater days postpartum (60 days vs. 45 days) which would improve their chances of remaining pregnant. If the variable response to treatment was due to an inhibitory effect of oestradiol on pituitary function, then one would expect

that this group of cows would be more sensitive to such an effect. This is in fact supported by the greater proportion of cows in their first lactation which had delayed return to oestrus following the induced heat.

CONCLUSION

These observations support the hypothesis that an injection of ODB at CIDR™ insertion will alter follicle wave patterns in cows with PPA, but suggest that the subsequent effect on fertility is variable. Some clinical means to identify the “depth of anoestrus”, such as ovarian size or ultrasound examination, may be a useful adjunct to determining whether ODB at the time of CIDR™ insertion would be beneficial in the treatment of PPA.

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