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Combination treatments for synchronising oestrus in dairy heifers

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ABSTRACT

Progesterone (P4), oestradiol benzoate (ODB) and prostaglandin $F_{2\alpha}$ (PGF) have been used separately and in combination to synchronise oestrus in cattle by reducing the luteal phase of the cycle or delaying pro-oestrus after luteolysis. The latter mechanism can result in precise synchrony but with reduced fertility.

In the process of attempting to improve synchrony and fertility, a series of four trials was completed with dairy heifers. Each trial was based on the use of a CIDR-B device for 7 to 10 days with or without 10 mg ODB in a gelatin capsule and with an injection of PGF from 2 to 4 days before device removal or at device removal.

The results of these trials showed that injecting PGF before device removal could improve synchrony (in terms of animals inseminated at 48 h after device removal) but reduced pregnancy rates to first insemination by 5% to 10%. Incorporating ODB delayed the post-treatment interval to oestrus and insemination with a 7-day CIDR regime but improved synchrony with a 9 or 10-day CIDR regime. If the use of ODB was combined with an injection of PGF 4 days before CIDR device removal as part of a 10-day CIDR programme, the 48 h post-treatment synchrony rate was 93% and the pregnancy rate was 56%. Excluding the ODB from this programme reduced the 48 h synchrony rate to 87% and the pregnancy rate to 45%.

These results are additional evidence that combining ODB with P4 is altering ovarian follicle wave patterns with consequent effects on synchrony patterns and fertility.

Keywords: oestrous synchrony, progesterone, oestradiol benzoate, prostaglandin $F_{2\alpha}$, CIDR-B, dairy heifers.

INTRODUCTION

Systems for synchronising oestrus in cattle have been a focus for research during the 30 years since it was demonstrated that progesterone could be used to extend the inter-oestrous interval. They achieved a satisfactory precision of synchrony but were associated with low fertility (Lamond, 1964; Gordon, 1976). Potent synthetic progestagens were substituted and applied with oral, intravaginal or subcutaneous routes of administration but treatment periods of more than 14 days still produced precise synchrony with low fertility (Wishart, 1977). Treatment periods of shorter duration became possible when it was demonstrated by Lemon (1975), Mauleon (1974) and others that oestradiol administered concurrently at the commencement of a progestagen treatment produced a premature luteolysis in some animals. The benefits of combination treatments of progesterone and oestradiol benzoate or the synthetic progestagen Norgestomet with oestradiol valerate in terms of improved synchrony and fertility have been demonstrated repeatedly in breeding programmes in suckling beef cows in New Zealand (Smith, 1977; Smith and Tervit, 1980; Smith and McGowan, 1982; Smith and Kaltenbach, 1990). Their effectiveness may vary with the stage of the oestrous cycle at administration (Burns, *et al.*, 1992; Patterson *et al.*, 1989; Pratt, *et al.*, 1991; 1989; Sanchez *et al.*, 1992) and the increased incidence of oestrus may sometimes be associated with residual effects produced by oestradiol valerate (McGuire *et al.*, 1990).

The identification of prostaglandin $F_{2\alpha}$ as either the uterine luteolysin or an effective luteolytic agent was soon followed by the commercialisation of synthetic forms and potent agonists. Double injection regimes of these products were widely tested in dairy cattle (Macmillan and Curnow, 1976) but results with beef cattle in New Zealand have been variable (Smith, 1977; Smith and Kaltenbach, 1990). Two important reasons for this variability are: first, that the prostaglandins are ineffective in the absence of a corpus luteum as with anoestrous animals; and, secondly that there is a slower onset and wider spread in the post-treatment interval to oestrus (Smith and McGowan, 1982) because of the wave-like pattern of ovarian follicle development (Macmillan and Henderson, 1984). Shorter treatment periods with a progestagen or progesterone combined with injected prostaglandin $F_{2\alpha}$ have produced more precise synchrony (Odde, 1990), especially if the injection is up to 48 h before the end of the steroid treatment (Smith *et al.*, 1984).

Some exploratory studies were completed in the process of developing synchrony treatments with the CIDR-B device as a source of progesterone combined with a gelatin capsule containing 10 mg oestradiol benzoate. They showed that the reported luteolytic effect of the oestradiol occurred at least 7 days after oestradiol administration, but often after more than 12 days (Macmillan *et al.*, 1991). This suggested that some of the luteolytic properties may be associated with altered follicle wave patterns.

A series of experiments was initiated to study the effects of varying the period of progesterone treatment using a CIDR-B device, with or without oestradiol administration at device insertion and with an injection of prostaglandin $F_{2\alpha}$ during or at the end of this period. Each of these studies was with dairy heifers and had the ultimate objective of producing a treatment regimen which could realistically allow the consideration of inseminating every treated animal at a pre-determined time after device removal.

MATERIALS AND METHODS

Each of the four trials involved from 370 to 511 heifers (Jersey, Holstein-Friesian or H-FxJ crossbreds) in from four to six herds. They were herd replacement animals which were being synchronised in October or November when they were about 15 months of age. Each animal was inseminated by a professional technician with semen from a progeny tested dairy sire after it had been detected in oestrus at 48, 72 or 96 h from the end of a synchrony treatment. The oestrous detection procedure relied on applications of tailpaint (at CIDR device insertion) and an aerosol raddle (at CIDR-device removal) (Macmillan *et al.*, 1988). The reproductive tract of each of those animals not presented for insemination was palpated to separate anatomically abnormal animals (eg. freemartins) from those which were anoestrus, still in pro-oestrus or had ovulated without being detected. This group also included those animals which had not retained the CIDR device for the whole of the treatment period. Conceptions to first insemination were confirmed initially by rectal palpation 5 weeks later and then by checking calving dates.

Each treatment involved the use of the intravaginal CIDR device containing 1.9 g progesterone (P4; 'Eazibreed' CIDR-B; Inter-Ag Ltd; Hamilton, New Zealand) which was inserted for 7 to 10 days. If oestradiol was included in the treatment, it was with a gelatin capsule containing 10 mg oestradiol benzoate (ODB; CIDIROL 10 MG; Douglas Pharmaceuticals Ltd; Auckland, New Zealand) placed in the grooved surface of a CIDR device before insertion. Prostaglandin $F_{2\alpha}$ (PGF) was administered as an intramuscular injection of 2.5 ml (0.5 PGF) or 5.0 ml (1.0 PGF) of a preparation containing 5 mg/ml of the tham salt of PGF (Lutalyse, The Upjohn Co.; Auckland, New Zealand).

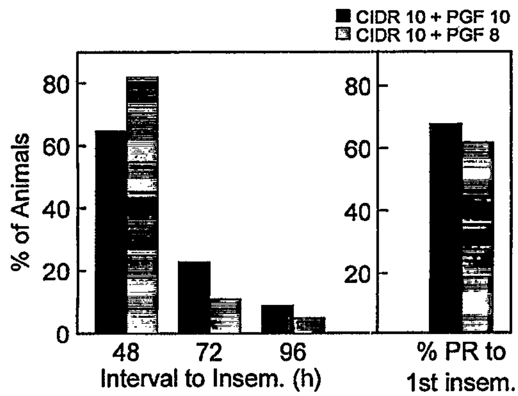
Trial 1 involved 370 animals (in 6 herds) divided randomly into 4 treatment sub-groups which each included a CIDR-treatment period of 10 days (CIDR 10) with 0.5 or 1.0 PGF injected either 2 days before device removal (Day 8 of CIDR treatment; 1.0 or 0.5 PGF 8) or at removal (1.0 or 0.5 PGF 10). **Trial 2** included 511 animals (in 5 herds) which were each treated with a CIDR device for 7 days (CIDR 7; 2 herds), 8 days (CIDR 8; 2 herds) or 9 days (CIDR 9; 1 herd) either with or without ODB and with either 0.5 or 1.0 PGF at device removal. **Trial 3** was with 491 animals in (4 herds) divided within each herd into three treatment sub-groups; namely, CIDR 10 + 0.5 PGF 10, CIDR 10 + ODB + 0.5 PGF 10, and CIDR 10 + 1.0 PGF 6. **Trial 4** used 483 heifers (in 6 herds) which each had CIDR 10, with or without ODB, but always with 1.0 PGF 6. In each of these trials, the previously used CIDR device was reinserted 18 days after its original removal for 5 days so that returns to service were re-synchronised and could be re-inseminated either 48 or 72 h after re-treatment. This re-synchrony had not altered pregnancy rates to first insemination in a previous trial.

Synchrony patterns were expressed as the percentage of heifers within a treatment sub-group within a herd which were first inseminated 48, 72 or 96 h after CIDR device removal. These response patterns were analysed using chi-square statistics. Pregnancy rates for treatment sub-groups included results for all inseminations from 48 to 96 h.

RESULTS AND DISCUSSION

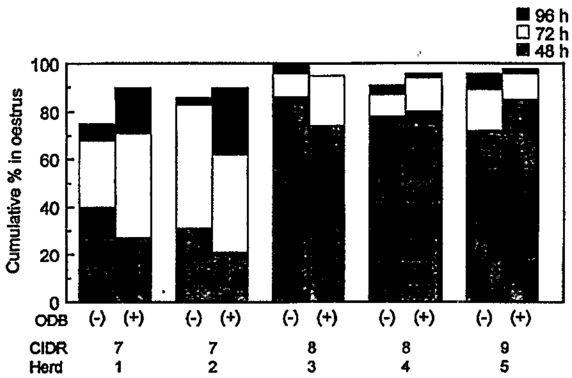
In Trial 1, injecting either 0.5 or 1.0 PGF was equally effective in terms of synchrony and fertility, irrespective of whether it was administered during (PGF 8) or at the time of device removal (PGF 10). However, the earlier injection (PGF 8) increased the 48 h synchrony rate from 65% (for PGF 10) to 82% ($p<0.01$; Fig. 1). This trend was observed in all herds and mainly involved a reduction in the percentage of heifers first inseminated at 72 h ($p<0.05$; Fig. 1). By 96 h post-treatment, 97% of the heifers in this trial had been inseminated. Although the pregnancy rate (%PR) to first insemination was not significantly different among PGF 8 sub-groups (61.0% vs 67.4%; Fig. 1), a lower result was observed in each of the 6 herds. This prompted the re-assessment of the use of ODB to avoid lower %PR's frequently occurring with improved precision in synchrony at 48 h.

FIGURE 1: The effects of injecting prostaglandin $F_{2\alpha}$ (PGF) either at the end of a 10-day CIDR treatment (CIDR 10 + PGF 10) or six days after device insertion PGF (CIDR 10 + PGF 6) on the average interval to oestrus and insemination and on the associated pregnancy rate (% PR)



Results in Trial 2 confirmed those obtained in Trial 1 for the use of 0.5 or 1.0 PGF. Synchrony patterns and fertility were not affected by the dose of PGF. The inclusion of ODB significantly altered synchrony patterns, ($p<0.01$), but the effect varied with the duration of CIDR treatment ($p<0.01$). When combined with CIDR 7 and PGF 7, the ODB delayed the post-treatment interval to oestrus in both herds (Herds 1 & 2) so that 20% (Herd 1) and 28% (Herd 2) of the heifers were not inseminated until 96 h. Without ODB, the comparable percentages were 7% and 3%, respectively (Fig. 2). The degree of delay until detection and insemination was less apparent when ODB use was combined with an 8-day CIDR treatment (CIDR 8 + PGF 8), although the percentage inseminated at 72 h was higher in the ODB sub-groups in both Herds 3 and 4 ($p<0.10$; Fig. 2). If the duration of CIDR treatment

FIGURE 2: The effects of varying the duration of treatment with a CIDR-B device from 7 to 9 days (CIDR 7 to CIDR 9) with (+) or without (-) the concurrent administration of oestradiol benzoate (ODB; 10 mg) at device insertion but always with an injection of prostaglandin $F_{2\alpha}$ (PGF) at device removal on the average intervals to oestrus and insemination in dairy heifers in five herds (Herds 1-5)



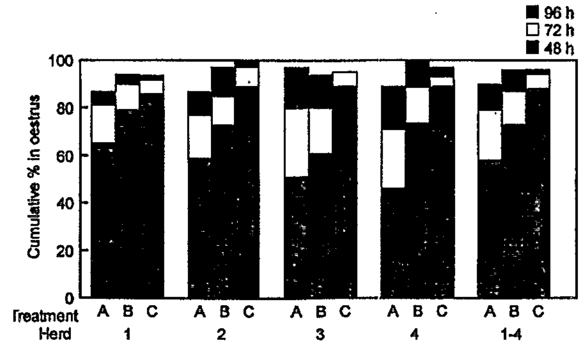
was increased to 9 days (Herd 5), then the use of ODB tended to increase the 48 h synchrony rate (72% vs 85%; Fig. 2) and was as effective as injecting PGF 2 days before device removal (Trial 1; Fig. 1). The average %PR was 61% and this was not affected by PG dose or the use of ODB.

The results of Trial 2 indicated that CIDR treatments incorporating ODB should be of at least 9 days duration. Consequently, Trial 3 was designed to compare the effectiveness of ODB and the administration of PGF during the period of CIDR treatment. The results showed that the use of ODB with 0.5 PGF at device removal (CIDR 10 + ODB + 0.5 PGF 10) increased the 48 h synchrony rate by an average of 15% ($p<0.05$) varying from 10% (Herd 3) to 28% (Herd 4; Fig. 3). This improvement was exceeded ($p<0.01$) by the earlier injection of PGF (CIDR 10 + 1.0 PGF 6; Fig. 3) increasing the 48 h synchrony rate to 88%, and only varying between herds from 86% to 89% (Fig. 3). However, this improved 48 h synchrony rate was associated with a lower %PR in 3 of the 4 herds. The exception was Herd 1 where the %PR was only 38% probably because the average liveweight of these Jersey heifers was only 178 kg at CIDR device insertion. Oestrus can be successfully synchronised in underweight heifers, but they may not conceive to first insemination. In the remaining 3 herds the average %PR for the ODB treatment (CIDR 10 + ODB + 0.5 PGF 10) was 62.3% compared to 52.5% for CIDR 10 + 1.0 PGF 6 ($p<0.10$).

The objective of Trial 4 was to combine the improved synchrony of an early PGF injection (1.0 PGF 6) within a 10-day CIDR treatment and with ODB to utilise its potentially beneficial effects on synchrony and %PR. The results showed that the inclusion of ODB increased the average 48 h synchrony rate from 87% to 93% and the average %PR from 45% to 56% ($p<0.05$). Only one herd had a lower 48 h synchrony rate with ODB (Herd 1) and every herd had a higher %PR even though the herd averages varied from 36% (Herd 2) to 63% (Herd 3).

Further studies are continuing to identify the ways in which the effects of P4 from the CIDR device and the ODB from the capsule combine to influence synchrony pattern and fertility. Sawyer *et al.*, (1992) have shown that changes in ovarian follicle wave patterns did occur when an ODB

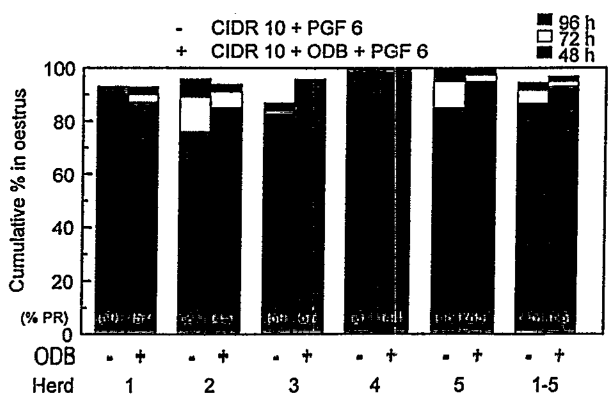
FIGURE 3: Intervals to oestrus in four herds (Herds 1-4) of dairy heifers which were all treated with a CIDR device for 10 days (CIDR 10) and: A. an injection of prostaglandin $F_{2\alpha}$ at device removal (PGF 10); B. 10 mg of oestradiol benzoate (ODB) at device insertion as well as PGF 10; or C. no ODB but PGF injected on Day 6 of CIDR treatment (PGF 6)



capsule was used with a PRID device. If the combined treatment produced atresia in some dominant follicles and this was followed by the emergence of a new follicle wave, then the effects on synchrony observed in Trial 2 may reflect substantial variation between animals in their follicle wave patterns 7 days after a P4 + ODB treatment. This variation may diminish as the exogenous P4 increasingly contributed to the maintenance of a dominant follicle (Sirois and Fortune, 1990). Providing this dominance was only maintained for a limited period, subsequent fertility may not be affected.

The results of these trials confirm the observations of Smith and McGowan (1982) in beef cattle that ODB can improve both synchrony and conception rates. The reasons for these improvements are still conjecture, but it does seem likely that synchronising ovarian follicle wave patterns as well as luteolysis and P4 withdrawal are necessary if the variation in the duration of pro-oestrus is to be minimised without sacrificing fertility. If we do confirm the ephemeral effects of vaginally administered P4 and ODB on follicle dominance and atresia, then the form, rate and duration of the ODB administration may need to be investigated to reliably obtain 48 h synchrony rates of around 95% with %PR of at least 65%.

FIGURE 4: Post-treatment synchrony patterns (48, 72 and 96 h) and pregnancy rates (% PR) among dairy heifers in five herds (Herds 1-5) treated with a CIDR device for 10 days (CIDR 10) and an injection of prostaglandin $F_{2\alpha}$ six days after device insertion (PGF 6) but with (+) or without (-) oestradiol benzoate (ODB) administration at device insertion



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