

## **Reproductive performance evaluation of different prostaglandins for repeated synchronization program in postpartum dairy cows: preliminary results**

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### **Abstract**

This trial evaluates reproductive performance in a early-routine estrus synchronization program using two different PGF2?. Cows were administered D(+)-cloprostenol sodium (n=88; Group A) or dinoprost (n=78; Group B) between 35-42d postpartum. Pedometers were used to detect estrus. Evaluation of secondary signs of estrus and evaluation of vaginal mucus quality was made prior to AI. When estrus was not detected by day14 following PGF2?, the treatment was repeated, up to a maximum of 3 time. Progesterone were analysed by RIA in blood samples collected on the day of treatment. There was no difference in the estrus detection to both PGF2? treatments (A=79.7 vs B=75.6%). No treatment-related variation was recorded in respect of estrus signs (A=90.2 vs B=94.9%) nor good mucus quality (A=95.08 vs B=88.13%). First-service conception rate and conception rate at 200d were 45.9 and 65.2% in group A, and 22.0 and 67.9% in group B, respectively. There was no difference for the interval from parturition to first-AI; however, group A showed a significantly shorter interval from parturition to conception and services than group B (101.5 vs 122.6; 1.9 vs 2.6). Progesterone levels were lower in cows that needed 2 or 3 repeated treatment. In those individuals estrous response and conception rates were also lower. D(+)-cloprostenol proved to be as efficacious for estrus response as dinoprost, but better fertility results were reported with D(+)-cloprostenol.

### **Introduction**

The use of postpartum estrus induction and synchronization programs to shorten the calving interval and thus increase the economic profitability of the herd has been widely studied. In order to optimise the calving interval, it is essential to restore postpartum reproductive status as soon as possible; this is dictated largely by the resumption of hormonal cycling and uterine involution, both of which are in turn governed by the negative energy balance characteristic of

this phase. The difficulties inherent in optimising postpartum fertility and thus reproductive efficiency are often aggravated by unacceptably low estrus detection rates. Prostaglandin treatments include single-dose administration (1), double-dose administration at 11 to 14 d intervals (2), and combinations with other active ingredients including progesterone (3) and GnRH (4).

The many prostaglandins currently available differ largely in terms of their molecular composition; the chief distinction is between the so-called natural prostaglandins (dinoprost tromethamine) and a wide range of synthetic prostaglandins (e.g. D(+)-cloprostenol, racemic cloprostenol, luprostirol etc.) The efficacy of commercial prostaglandins is a matter of some debate, and depends to a large degree on the speed at which they are metabolised and on their affinity for myometrial and CL cell-membrane receptors (5). Although both D(+)-cloprostenol and dinoprost tromethamine are currently marketed, no comparison has yet been made of their reproductive efficiency, particularly within a working program.

The aim of this prospective study was to compare the effects on reproductive efficiency of a luteolytic dose of a synthetic prostaglandin F2 alpha (D(+)-cloprostenol) versus a natural prostaglandin F2 alpha (dinoprost tromethamine), both of which were routinely administered at 35 to 42 d postpartum.

## **Material and Methods**

Cows from a herd of 850 lactating Holsteins on a commercial dairy farm in southern Spain (38°02'N-4°10'W) were housed in stalls with open-air and sheltered areas, and fed a balanced diet in accordance with NRC requirements. All cows were milked twice daily. Average annual milk yield was 7500 kg per animal.

A voluntary waiting period of 35 days was established by selecting all cows at between 35 and 42 d postpartum on the day the study commenced. Treatment was routinely administered every Monday; in cows not displaying estrus, treatment was repeated 14 d later, up to a maximum of 3 applications.

Cows were randomly assigned to two treatment groups: group A (n = 88) received 0.15 mg of the synthetic prostanoid D(+)-cloprostenol sodium intramuscularly (Dalmazin<sup>®</sup>, Fatro Uriach, Spain), and group B (n = 78) received 25 mg of the natural prostaglandin dinoprost tromethamine intramuscularly (Dinolytic<sup>®</sup>, Pharmacia, Spain). Mean age was very similar in the two groups: 3.61 ± 1.52 in group A, and 3.80 ± 1.88 in group B.

Estrus was detected by the use of pedometers (Westfalia, Germany) that registered physical activity twice daily during milking. Cows were bred by AI, by the same technician to

minimise any possible operator-related distortion. A record was made prior to AI of the following: a) whether cows showed typical estrus signs on the back and hindquarters caused by scratches from other animals' hooves during mounting; and b) whether vaginal mucus, evaluated by vaginal examination, was adequate; abundant, clear, watery, vaginal mucus was considered as good quality, and less abundant, thicker mucus was regarded as poor quality. Cows displaying purulent mucus consistent with endometritis were not inseminated and were withdrawn from the study group.

Pregnancy was diagnosed by rectal palpation between 45 and 60 d after insemination.

The following calculations were performed for both groups: estrus detection rate (number of treated cows displaying estrus); first-service conception rate (number of cows becoming pregnant divided by the number of treated cows); cumulative percent conception by 200 d; first-service pregnancy rate (number of cows diagnosed pregnant divided by the number of cows inseminated); percent of cows displaying estrus with abundant and clear vaginal mucus; percent of cows displaying estrus with characteristic estrus-related signs on back and hindquarters; interval from parturition to conception (days open); interval from parturition to first AI; services/gestation. The progesterone levels in samples obtained at the different sampling times were compared using Friedman Test. Chi-square test was used to compare proportions, while intervals were compared by ANOVA and when differences were significant ( $P \leq 0.05$ ), the Least Square Minimum was calculated. Results were expressed as mean  $\pm$  SD. The statistical software package SPSS 8.0 for Windows was used to perform statistical analyses (6).

## **Results**

Detected estrus rates following administration of synthetic or natural prostaglandin were 79.7% and 75.6% respectively; no significant difference was observed between groups.

Largely abundant, clear and watery mucus was observed in 95.08% of estrus cows treated with D(+)cloprostenol, compared with 88.13% in the dinoprost tromethamine group, although differences were not significant.

No treatment-related variation was recorded between groups with regard to the percentage of cows in which pedometer-detected estrus was accompanied by external signs (A = 90.4% vs B = 94.9%).

Overall first-service conception rate was calculated in synchronized cows; values were significantly higher in group A (45.9% vs 22.0%;  $P \leq 0.05$ ). The increase of first-service

pregnancy rates was steeper for group A, and this group needed 101.5  $\pm$  51.4 d. for 50% of inseminated cows to become pregnant, while group B needed 123.6  $\pm$  57.6 d. ( $p < 0.05$ ).

No statistically-significant intergroup difference was observed for the conception rate after 200 d (A = 65.2% vs B = 67.9%). There was no intergroup difference for the interval from parturition to first AI (A = 51.6  $\pm$  11.1; B = 51.49  $\pm$  12.1; N.S.). Cows became pregnant after significantly fewer services in group A (1.9 vs. 2.6;  $P < 0.01$ )

Progesterone result are presented in figure 1 and 2.

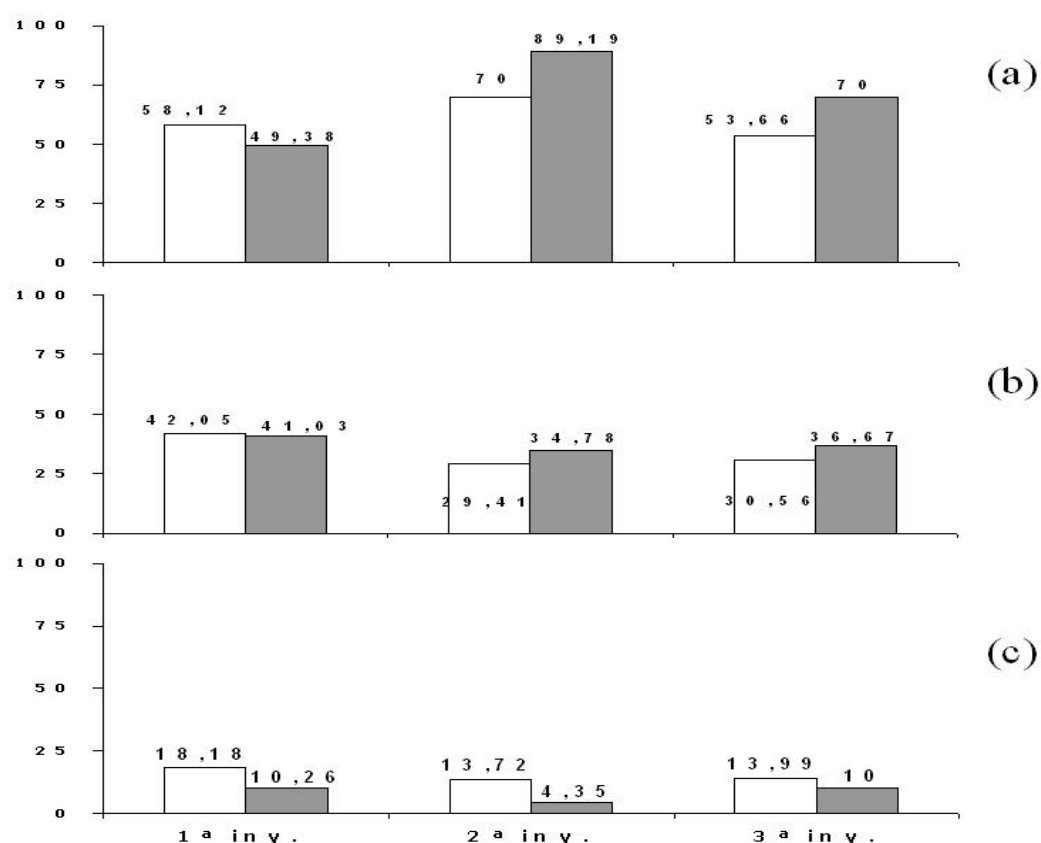


Figure 1. This figure represents the percentage of cows that showed progesterone levels higher than 1 ng/ml (a), percentage of cows that showed estrus (b) and percentage of cows that got pregnant (white bar= D-cloprostenol group; grey bar= dinoprost group).

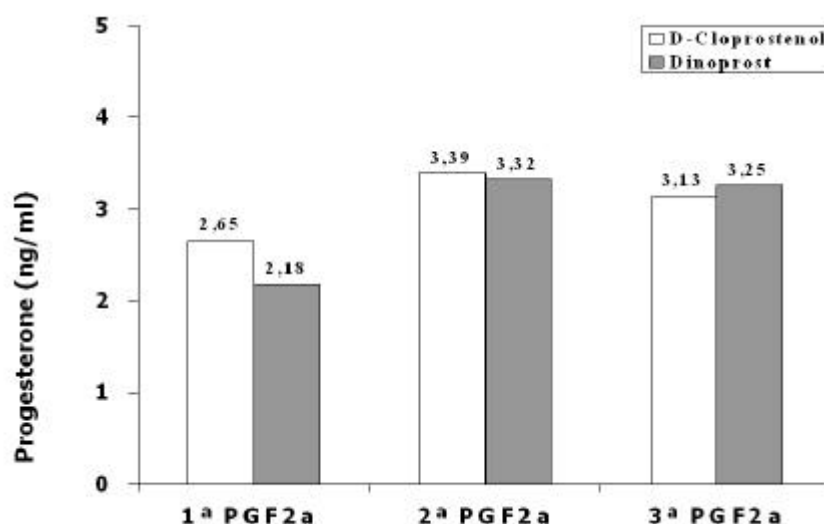


Figure 2. Average progesterone levels in cows obtained at the beginning of each treatment. This results shows that progesterone concentrations were homogeneous in both groups.

## Discussion

When selecting routine postpartum treatment schedules, priority must be given to ease of use or administration, scheduling convenience, clinical efficacy and cost effectiveness of the product; the final selection will depend on the particular characteristics and purposes of the farm.

After systematic administration every 14 days, D(+)-cloprostenol and dinoprost tromethamine proved equally effective in achieving synchronized estrus induction in lactating dairy cows; results obtained with both products were higher than in previous trials (9). The higher percentages reported in other studies were attributable to stricter sample selection (2). The decrease obtained in estrus detection rates after each successive dose of PGF2alpha administration was to be expected, given the increased frequency of undetected estrus or other possible reproductive disorders. The results obtained here, like those reported by Tenhagen et al. (7) who measured progesterone levels following administration of luteolytic agents, suggest that the number of PGF2alpha applications should not exceed three; animals failing to display estrus after treatment should be further examined to ascertain the reason for absence of estrus.

Both prostaglandins produced abundant, clear vaginal mucus, perhaps due to improved PGF2alpha-mediated follicular growth (10) and estradiol and LH secretion (11). Pedometer-based estrus detection enabled evaluation of frequency of cows with estrus-related signs; results were equally high, suggesting that if this working protocol is adopted reproductive

efficiency can be improved even on farms in which visual observation is used to detect estrus. Although physical differences in vaginal mucus quality are not believed to directly affect fertility (11), the results obtained here suggest that abundant, clear mucus may serve as an indicator of estrus, thus indirectly improving pregnancy rates and enabling the timing of AI to be optimised. Similarly, PGF2alpha administration leads to improved estrus detection rates, since the number of mountings increases with the number of animals displaying estrus, due to behavioural and pheromonal interactions (12).

At onset of estrus, 5.73% of the cows displayed whitish speckled mucus consistent with genital infection; similar findings were reported by Drillich et al. (2). This suggests that the working method outlined here is not only an efficient tool for estrus induction and synchronization, but may also be useful on large farms with poor postpartum follow-up as a method of detecting mild endometritis (even if treatment is not required) and thus enhancing reproductive efficiency (13, 14).

A recurring doubt is whether or not the use of PGF2alpha has a negative effect on fertility, due to either incomplete luteolysis or interference of the protocol with follicular dynamics. Previous studies (2) deny the existence of any such negative effect. Minor improvements in reproductive performance are proof enough to justify the financial benefits of using PGF2alpha treatments (15).

First-service conception rates using D(+)cloprostenol were higher than those obtained using dinoprost tromethamine. Indeed, conception rates were twice those obtained using natural prostaglandins both here and reported in other studies (2, 9). This would suggest that certain complex and as yet unknown mechanisms affecting the molecular composition of the various prostaglandins may enhance breeding success in treated cows. Contrary to the findings of the present study, and perhaps due to differences in the working protocol adopted, Salverson et al. (3) report that following administration of PGF2alpha (dinoprost and racemic cloprostenol) combined with MGA, results for estrus synchronization and fertility were similar for the two prostaglandins.

A number of studies report that fertility rates obtained after routine administration of PGF2alpha with no prior animal examination are higher than those obtained following administration of a PGF2alpha after CL palpated per rectum or in association with the detection of high progesterone levels (8); this would justify use of the treatment as described in this study.

Although conception rates at 200 d did not differ significantly between the two experimental groups, other indices suggest a clear advantage in favour of D(+)cloprostenol. Treated cows

in group B required a further 21 d to gestation compared to those in group A; this represents a considerable financial drain for the breeder. Knutti et al. (13) observed that the interval between parturition and conception was shorter in non-cycling cows treated with PGF2alpha than in cycling herd mates. Although the authors were unable to account for this result, it would seem to further highlight the advantages of this type of breeding programme. No differences were observed in days to first insemination. The interval was relatively short in both groups, thus allowing conception to take place sooner, and enabling cows with reproductive disorders to be treated earlier.

Repeated administration of D(+)-cloprostenol reduced the number of services required for the cow to become pregnant, thus underlining again the positive effect of D(+)-cloprostenol on fertility.

The results obtained here demonstrate that routine postpartum administration of prostaglandins is a viable working protocol for some commercial dairy farms, enabling improved estrus detection, concentration of AI work and enhanced breeding efficiency.

Luteal function monitored using plasmatic progesterone previous PGF2a administration did not was reduced after three treatment. Although the precise mechanisms involved remain to be clarified, administration of D(+)-cloprostenol as opposed to dinoprost tromethamine offers clear advantages in terms of fertility, interval from parturition to conception and number of services per conception.

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