IMPROVED REPRODUCTIVE PERFORMANCE FROM DAIRY COWS TREATED WITH DINOPROST TROMETHAMINE SOON AFTER CALVING

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ABSTRACT

The first-service conception rate for 74 commercial dairy cows that were given a single injection of dinoprost tromethamine (prostaglandin $F_{2\alpha}$ THAM) between 14 and 28 d after calving was 56%. For 74 untreated control herdmates the rate was 47%. The average interval from calving to first oestrus was 57 d for treated cows and 70 d for the control group. The difference is significant at the P = 0.017 level. The advantage in the conception rate of treated over control group cows occurred mostly in cows with a blood progesterone concentration of less than 0.5 ng/ml at the time of treatment; this numbered about two-thirds of the cows in the trial. The results support the findings of a previous study.

Key words: dinoprost, post-partum, oestrus, conception rate

INTRODUCTION

Evidence has been produced to show that a single injection of dinoprost tromethamine ('Lutalyse', Trademark, Upjohn Ltd. Crawley, U.K.) administered routinely to apparently normal dairy cows between 14 and 28 d after calving can significantly improve conception from the first service and can shorten the interval from calving to conception. The response was thought to be associated with the smooth muscle effect of dinoprost tromethamine on the myometrium, because the improvement was demonstrated mostly when blood concentrations of progesterone were less than 0.5 ng/ml. This was assumed to infer that ovarian cyclicity had not been resumed after calving at the time of treatment and that luteolysis did not play a part in the response (1). Delay in the time taken for the uterus to involute after calving and return to a non-pregnant condition has been related to delay in the time needed to achieve the next pregnancy (2). In addition, and related to that, abnormal delay in uterine involution after calving has been associated with inadequate production of endogenous prostaglandin during the period shortly after calving (3). It was found that repeated administration of dinoprost twice daily from Day 3 to 13 after calving did in fact shorten the time needed for the recently pregnant uterus to involute (4).

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Repeated administration of prostaglandin over a period of time to compensate for suspected endogenous deficiency is logical because of the short half-life of prostaglandin. In the economics of veterinary practice, however, multiple administrations over a period of 10 d are quite impractical. It was for this reason, and in the knowledge of prolonged myometrial effect following a single administration of prostaglandin $F_{2\alpha}$ (5, 6, 7), that a single injection of dinoprost tromethamine was chosen in a previous study (1). In that study, the effect of dinoprost treatment on the occurrence of the first oestrus after calving was not recorded. The study reported here recorded an advance of oestrus in treated cows. The repeatability of increased first-service conception rate was confirmed in treated cows, and also the importance of low blood progesterone concentration at the time of treatment. The data suggest the possibility that dinoprost may be able to induce oestrus at a time when basal blood progesterone concentration indicates the absence of an active corpus luteum.

MATERIALS AND METHODS

In order to achieve comparable results, the conditions and protocol were deliberately kept the same as in our previous 1983 study(1), with the single addition of recording pre-service oestrus in all cows.

The three commercial dairy farms used in the 1983 study were again used. They were visited once every 14 d. Data were recorded on the microcomputer fertility programme at the University of Glasgow Veterinary Practice.

A total of 163 Friesian cows were available for the study. Fifteen cows were culled during the trial and were excluded from the data. One cow from the treatment group and four from the control group were culled for infertility; the remainder were culled for mastitis, lameness, hypomagnesaemia, and for management policy reasons. Of the remaining 148 cows, 74 cows each were placed into the treatment and control groups.

The cows, from each of the 3 farms, were allocated alternately to either the treatment or control group according to the chronological order of their calving dates. All cows that had calved during the first 3 months of 1984 in all 3 herds were included in the study. All cows had a blood sample taken for progesterone assay at the appropriate visit between 14 and 28 d after calving. At the same time, cows in the treatment group were injected with 25 mg of dinoprost tromethamine intramuscularly. Control cows were not injected.

Blood samples were centrifuged as soon as was possible, within about two hours of collection. The plasma samples were stored at -18°C until dispatch to the Milk Marketing Board Veterinary Laboratory, Worcester, for progesterone assay in one batch. The assay is a direct radio-immunoassay method described by Holdsworth (11), giving results closely correlated to, but somewhat higher than, the conventional extraction method. An identical standard internal control serum was used for the assay, so that results from different years are comparable.

Insemination of cows was started 56 d after calving on all three farms. The commercial inseminator service of the Scottish Milk Marketing Board, using frozen semen, was used for all cows, and the choice of semen was not specified. Oestrus detection was done by stockmen at least three times per day. Pregnancy diagnosis was made by rectal palpation about 7 to 8 weeks after insemination and confirmed by the calving date.

The data used for comparison were the mean intervals in days from calving to first oestrus, calving to first service, calving to conception, and the calving rate resulting from the first service. These were the same parameters as those in the 1983 study, with the single addition that all prebreeding oestrus was also recorded. The influence of the concentration of the blood progesterone at the time of blood sampling on the conception rate to the first service was compared between dinoprost-treated cows and untreated controls.

For comparisons between calving to first oestrus, calving to first service and calving to conception intervals, the Wilcoxon Rank Sum Test, a non-paramatic equivalent of 't' tests, was used because the data was found to deviate from the normal distribution. Where statistical analysis of interaction and year effects were not significantly different, results of the 1983 and 1984 studies were also combined for comparison. Fisher's Exact Test was used for 1984 first-service conception rate data, and a linear model was used for the combined data for 1983 and 1984. We used a linear model for categorical responses in comparing the effect of blood progesterone concentrations at the time of treatment on the conception rate.

RESULTS

The average interval from calving to first observed oestrus was 57 d for dinoprost-injected cows and 70 d for the control group. The difference is significant at the level P = 0.017 (Table 1). The average calving-to-conception interval was 96 d for dinoprost-injected cows and 103 d for the control group. This 7-day advantage does not achieve statistical significance, but it is consistent with the 6-day advantage recorded in the 1983 study data.

Table 1. Calving to first oestrus interval, calving to first service interval, calving to conception interval and first service conception rate for dinoprost-treated and untreated control group cows, 1984

	Dinoprost injected	Control
Average calving to first oestrus interval (days ± SD)	57 ± 31.2[a]	[illegible] ± 33.5
Average calving to first service interval (days ± SD)	75 ± 22.9	78 ± 28.2
Average calving to conception interval (days ± SD)	96 ± 34.7	103 ± 37.3
First service conception rate (%)	56%	47%

[a] Difference significant at level P = 0.017.

The first-service conception rate for 74 dinoprost-injected cows was 56%; for 74 untreated control cows it was 47% (Table 1). This difference is not statistically significant. However, when the first-service conception rate data for 1983 and 1984 are combined, the conception rate is 62% for 138 dinoprost-injected cows and 45% for 138 control cows. This difference is highly significant at the P = 0.004 level (Table 2).

Table 2. Effect of dinoprost treatment on first-service conception. Combined results 1983 and 1984.

Year	Dinoprost injected: Number of cows in study	Dinoprost injected: Pregnant to first service	Control: Number of cows in study	Control: Pregnant to first service
1983	64	44 (68%)[a]	64	28 (43%)
1984	74	42 (56%)	74	35 (47%)
Total	138	86 (62%)[b]	138	63 (45%)

[a] Difference significant at level P = 0.007.
[b] Difference significant at level P = 0.004.

A plasma progesterone concentration of less than 0.5 ng/ml at the time of treatment was selected as an arbitrary measure of inactive ovaries in the context of this study. In this range, the first-service conception rate for 81 dinoprost-injected cows was 64% and for 79 control group cows was 44%. The difference is significant at the P = 0.010 level. Cows with a blood progesterone concentration of 0.5 ng/ml or greater at the time of treatment were considered as a group. The first-service conception rate of 48 dinoprost-injected cows was 56%, and it was 55% for 47 control cows. This difference is not statistically significant (Table 3).

Table 3. Effect of blood progesterone concentration at the time of treatment on first-service conception. Combined results 1983 and 1984.

		Dinoprost injected			Control		
Progesterone (ng/ml)	Study year	Number of cows	Pregnant	(%)	Number of cows	Pregnant	(%)
Less than 0.5 ng/ml	1983	30	21	(70)	38	17	(44)
	1984	51	31	(60)	41	18	(43)
	[a]Total	81	52	(64)[a]	79	35	(44)
0.5 ng/ml and more	1983	26	16	(61)	18	9	(50)
	1984	22	11	(50)	29	17	(58)
	Total	48	27	(56)	47	26	(55)
Not blood sampled	1983	8	7		8	2	
	1984	1	0		4	0	

[a] Difference significant at level P = 0.010.

Sixteen treated cows were seen in oestrus by 7 d after blood sampling and dinoprost injection, while only 5 of the control group cows were in oestrus by 7 d after blood sampling. Comparable numbers of both groups had basal progesterone concentrations at the time of treatment (Table 4).

Table 4. Days from dinoprost injection/blood sampling, to oestrus, and progesterone concentration in all cows exhibiting behavioural oestrus in less than 8 d

Dinoprost injected (n = 16)				Control (n = 5)	
Days	Progesterone ng/ml	Days	Progesterone ng/ml	Days	Progesterone ng/ml
1	0.0	4	0.0	2	0.6
3	0.0	4	0.3	4	0.0
3	0.0	4	1.3	5	1.0
3	0.1	4	4.3	5	1.1
3	0.9	5	0.8	6	1.6
3	0.9	5	2.3		
3	1.1	7	0.0		
3	2.1	7	0.0		

DISCUSSION

The ability to deduce blood concentrations of prostaglandin $F_{2\alpha}$ from assay of its less transient metabolite 15-keto-13,14-dihydro-prostaglandin $F_{2\alpha}$ (PGFM) has produced new information. It has been shown that high concentrations which arise early in the process of parturition do not quickly subside but are sustained for long periods of 1 to 4 wk (3, 8). Moreover, the longer that high concentrations of PGFM persist, the shorter is the time needed for uterine involution to be completed in cows with no detectable uterine or ovarian abnormality or pathology (3).

The studies cited here as well as others have drawn attention to the considerable variability in the time required for involution of the uterus of a cow after calving before it is again capable of a successful pregnancy. Physical uterine dimensions and characteristics have been used as a working measure of return to function, but there is also a hormonal dimension involved in restarting ovarian activity and regular fertile oestrus cycles. Longer periods of high concentrations of PGFM have been associated with both a faster rate of uterine involution and a stimulatory effect on follicular and luteal components of the ovary (9). The occurrence of the first ovulation followed by a normal luteal phase length after calving in 29 cows was positively correlated with the time needed for completion of uterine involution (8).

In addition to a significant shortening of the interval to first oestrus in treated cows in our study, more treated cows (n = 16) than control cows (n = 5) were in oestrus within 7 d of treatment/blood sampling (Table 4). If, as appears possible, oestrus was induced by dinoprost, then the basal concentrations of progesterone in many cows at the time of injection suggest that a mechanism other than luteolysis is involved.

Although involution of the uterus is an integral part of the process of return to ovarian cyclicity, subjective manual assessment may not be necessary to measure its progress in the context of these studies. It was notable in the present study that improved conception occurred mostly in dinoprost-treated cows with a blood progesterone concentration of less than 0.5 ng/ml at the time of treatment. Progesterone assay is now readily available and as an alternative to assessment of uterine involution by rectal palpation, it might be used to identify cows with a low progesterone concentration at an early stage after calving.

In deciding on a suitable time to administer exogenous prostaglandin, it was thought that a stimulus to natural synthesis would be most likely to be effective when endogenous concentrations were declining. The frequency of visits was planned to be compatible with routine herd fertility visits at two-week intervals, hence the choice of the two-week period 14 to 28 d after calving. About this time, PGFM concentrations can be expected to decline and progesterone concentrations start to rise, so basal concentrations of progesterone are compatible with the required hormone profile for effective treatment. The first-service conception rates in the study tend to support this concept that cows with low progesterone concentrations had a poor conception rate of 44%, which was improved to 64% by dinoprost treatment. Cows with higher progesterone concentrations, indicative of ovarian activity, had an acceptable conception rate of about 55% with or without dinoprost treatment; this is a further indication that luteolysis may not be important in this context.

It seems that ovarian cyclicity was achieved sooner in treated cows with low progesterone concentrations at the time of treatment, thus allowing them to reach optimum fertility sooner. The prevailing level of fertility in the herd then applied equally to treated and untreated cows. Increased fertility per se in treated cows would infer a hormone release function which has not as yet been attributed to dinoprost.

Trends similar to those reported here are recorded in a multifactorial trial that included a comparison between control cows and cows injected with a single dose of prostaglandin on Day 24 after calving. Prostaglandin treatment in that study reduced the interval from calving to first observed oestrus and from calving to conception. In the entire study, plasma progesterone concentrations on Day 24 after calving were less than 1 ng/ml in about two-thirds of the cows (10).

The results of these studies suggest that resumption of ovarian cyclicity after calving may be advanced by the administration of dinoprost tromethamine soon after calving. It may be possible to identify the cows most likely to respond to such treatment by milk progesterone assay about 2 to 4 wk after calving.

Such results occurred in about two-thirds of the cows in the two studies. The technique might be used to improve conception rate to first service earlier in a herd's breeding period and would be suitable to employ in routine herd fertility care systems.

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