The Failure of a Prostaglandin F\textsubscript{2\alpha} Analogue, Cloprostenol, to Initiate Lactation in Cattle

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Abstract
An experiment was designed to determine if the analogue of prostaglandin F\textsubscript{2\alpha}, cloprostenol, at a dose sufficient to cause luteolysis, was lactogenic in cattle.

The mammary glands of eight Friesian heifers were developed by treatment with progesterone plus oestrogen. Lactation was then initiated by administration of cloprostenol and subsequent milk production was compared to that of heifers lactating after a normal pregnancy.

Injection of cloprostenol failed to initiate lactation. The level of prolactin but not cortisol in blood was substantially elevated following treatment.

The results cast further doubt on the importance of prolactin in the lactogenic process but indicate the likely involvement of glucocorticoids.

Introduction
The administration of prostaglandin F\textsubscript{2\alpha} (PGF\textsubscript{2\alpha}) has recently been shown to initiate milk secretion in suitably primed ewes (Fulkerson et al. 1977). There is also evidence that PGF\textsubscript{2\alpha} can be lactogenic in women (Smith et al. 1972) and rats (Deis 1971) but it is not known if PGF\textsubscript{2\alpha} is lactogenic ‘directly’ or whether it stimulates the release of other endogenous hormone(s).

Lactogenesis initiated by PGF\textsubscript{2\alpha} in the ewe is associated with release of prolactin (Fulkerson et al. 1977), growth hormone (Field et al. 1977) and cortisol (Fulkerson, unpublished data) and the possibility exists that any one or all of these hormones may be responsible for the lactogenic response.

The aim of the experiment reported here was to determine if the analogue of PGF\textsubscript{2\alpha}, cloprostenol, could initiate lactation in cattle, and to study the secretion of prolactin and cortisol during cloprostenol treatment.

Materials and Methods

Animals
Sixteen Friesian heifers, 26–30 months of age at the commencement of milking, were grazed on irrigated pasture for the entire experimental period.

Hormones
Oestradiol benzoate (Schering A.G., Berlin) and progesterone (Calbiochem, La Jolla, California) were dissolved in ethanol and then suspended in peanut oil. The synthetic analogue of PGF\textsubscript{2\alpha}, cloprostenol (I.C.I., Melbourne), was injected as supplied by the manufacturer.
Experimental Procedure

The heifers were randomly allocated to two equal groups and treated as follows:

*Group 1.* Heifers received 11 subcutaneous injections, at 3-day intervals (0800 h), of 10 mg oestradiol benzoate plus 100 mg progesterone, then 3 days later one injection of cloprostenol (500 μg) at 0600 h.

*Group 2.* Heifers were mated to calve at the same time as heifers in group 1 commenced to milk.

Group 2 heifers were machine-milked twice daily while heifers in group 1 were milked once a day until daily production exceeded 2 kg, then twice daily. Any heifer which did not produce more than 1 kg milk/day after 3 weeks of milking was no longer milked.

Collection of Samples

Milk yields were recorded at weekly intervals for the first 4 weeks, then monthly for a further 9 months. Composite milk samples were analysed for fat, protein and lactose using the Infra-red Milk Analyser (Biggs 1972).

Blood samples were collected by jugular venipuncture at −2, 1, 3, 7 and 15 h from injection of cloprostenol, centrifuged and the resultant plasma stored at −14°C pending analysis.

Hormone Assays

Both prolactin and cortisol were assayed by solid-phase radioimmunoassay. For prolactin the method of Hooley *et al.* (1978) was used with values expressed in terms of the NIH-P-B₂ standards (sensitivity 8 ng/ml; coefficient of variation 19%; range 34–680 ng/ml). Cortisol in plasma was determined by the Endocrine Sciences method [(Chandler *et al.* 1972) sensitivity 2 ng/ml, coefficient of variation 9%].

Results

Milk Yield and Composition

Total milk yield over the 300 days of lactation for heifers in group 2 was 3553 ± 168 kg (mean ± s.e.). In contrast, only two of eight heifers in group 1 produced more than 1 kg/day with total production of 352 and 256 kg, both in 146 days. Of the remaining animals two did not lactate, while four failed to produce more than 1 kg/day.

Milk composition for the two heifers which lactated in group 1 reverted from a colostral-type secretion to ‘normal’ milk after 2–3 weeks of milking (fat 3·1%, protein 4·0%).

Prolactin and Cortisol Concentration

The level of prolactin in plasma rose to peak values of 384 ± 44 ng/mg (mean ± s.e.) 1 h after injection of cloprostenol, then fell to basal level (c. 40 ng/ml) 14 h later. In contrast, cortisol concentration in blood remained unchanged following injection (see Table 1).

Ovarian Function

Rectal palpation of the ovaries at the cessation of hormone treatment showed that these organs had regressed to a stage similar to that found in prepubertal heifers.

Discussion

The present results indicate that administration of cloprostenol at a dose sufficient to cause luteolysis does not initiate lactation in heifers with developed mammary glands. This appears to contrast with the situation in the sheep (Fulkerson *et al.* 1977), although relatively higher doses on a body weight basis were used in that species.
The failure of cloprostenol to initiate lactogenesis, despite an associated rise in prolactin level, suggests that prolactin may not be lactogenic in the cow. This is supported by the recent finding of Peel et al. (1978) that lactation can be hormonally induced in mature cows receiving concurrent treatment with the prolactin inhibitor CB154. Similarly, in the ewe it appears that prolactin is not required for PGF$_{2x}$-induced lactogenesis (Field et al. 1977). Thus, it is tempting to suggest that failure of an analogue of PGF$_{2x}$ to initiate milk secretion in this experiment was due to the absence of cortisol release, similar to that observed in successfully treated ewes (Fulkerson, unpublished data). This conforms with earlier findings that the synthetic glucocorticoid dexamethasone is an effective lactogenic trigger in heifers similarly primed with oestradiol benzoate and progesterone (Fulkerson and McDowell 1975; Fulkerson 1978). However, it is also possible that other hormones (e.g. growth hormone) were not released in sufficient quantities to initiate lactogenesis. It must be emphasized, however, that the present data are not strictly comparable with the work in the sheep as the form of prostaglandin administered and the dose were different.

Table 1. Concentration of prolactin and cortisol in plasma following injection of cloprostenol

<table>
<thead>
<tr>
<th>Time after injection of cloprostenol (h)</th>
<th>Prolactin concentration (ng/ml)</th>
<th>Cortisol concentration (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>−2</td>
<td>63 ± 10</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>+1</td>
<td>384 ± 44*</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>+3</td>
<td>334 ± 50*</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>+7</td>
<td>223 ± 42*</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>+15</td>
<td>49 ± 9</td>
<td>11 ± 1</td>
</tr>
</tbody>
</table>

* Value is significantly greater ($P < 0.001$) than before injection of cloprostenol.

The nymphomaniacal behaviour associated with injection of ovarian steroids was less evident after cloprostenol administration. If this is confirmed in later experiments it may be possible to overcome one of the main drawbacks to the commercial acceptance of artificial induction of lactation.

In conclusion, the results of this paper indicate that doses of cloprostenol of up to 500 µg are insufficient to initiate milk secretion in heifers previously primed with oestrogen plus progesterone.

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References


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