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Artificial Induction of Lactation in Cattle by Use of Dexamethasone Trimethylacetate

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Abstract

Injections of dexamethasone trimethylacetate initiated lactation in nulliparous Ayrshire heifers previously given a series of injections of oestradiol benzoate plus progesterone to develop mammary glands. Essentially normal lactation occurred following injection of 20 mg/day dexamethasone for 3 days, whereas injection of 40 mg/day for 4 days initiated secretion of smaller volumes of milk-like fluid containing relatively high levels of lipid. Milking alone failed to initiate lactation.

Introduction

In the past, lactation has been induced in cows by injection of oestrogen plus progesterone over prolonged periods to develop mammary glands, followed by relatively high doses of oestrogen to initiate milk secretion (cf. Meites 1961; Cowie 1971). Generally, milk yields of cows induced to lactate in this manner have been low and a proportion of cows have failed to lactate. Results of recent experiments at this laboratory (Fulkerson and McDowell 1974) demonstrated that a series of injections of dexamethasone trimethylacetate induced essentially normal lactation in non-pregnant, nulliparous ewes which had been treated previously with oestrogen and progesterone to develop their mammary glands. The present experiments were carried out in an attempt to determine whether similar treatment of nulliparous heifers would successfully induce lactation.

Materials and Methods

Heifers

Twelve nulliparous Ayrshire heifers (*c.* 21 months of age and weighing *c.* 350 kg) were purchased from a local breeder. Rectal examinations confirmed that all were not pregnant. The heifers were kept with the milking herd at the Dairy Research Unit and grazed at pasture which was supplemented with good quality lucerne hay and concentrate pellets.

Hormones

Progesterone (Calbiochem, La Jolla, California) and oestradiol benzoate (Schering AG, Berlin) were dissolved in ethanol, then suspended in peanut oil. Dexamethasone trimethylacetate (Opticortenol, 0·5%) was obtained from Ciba Geigy Pty Ltd, Lane Cove, Sydney.

Experimental Procedure

The heifers were injected subcutaneously every third day for 6 weeks with 840 mg progesterone plus 3·36 mg oestradiol benzoate. At the end of the 6-week period they were treated as follows:

Group 1: no further hormone;

Group 2: subcutaneous injection of 20 mg/day dexamethasone on 3 consecutive days commencing 3 days after the last injection of oestrogen plus progesterone;

Group 3: subcutaneous injection of 40 mg/day dexamethasone on 4 consecutive days commencing 3 days after the last injection of oestrogen plus progesterone.

Three days after the last injection of oestrogen plus progesterone milking commenced. Initially each heifer was milked by hand once daily at 1600 h. After 6 days the heifers in groups 2 and 3 (those injected with dexamethasone) were milked by machine at 0630 and 1600 h, whereas group 1 heifers were milked by hand at these times.

Yields of mammary secretion, in kilograms per day, were recorded at intervals after milking commenced, and samples were retained for analysis.

Analysis of Mammary Secretion

Lactose was assayed by the glucose oxidase method of Huggett and Nixon (1957) as modified by Cowie *et al.* (1969). Casein and fat levels were measured by the methods outlined by Davis (1959), i.e. fat by the Babcock method and casein from the difference between total nitrogen and non-casein nitrogen as assessed by the Kjeldahl method.

Results

Development of Udders

Definite increases in udder size, assessed visually, occurred during the period when oestrogen and progesterone were injected. After 6 weeks udders resembled those of pregnant heifers during the early stages of the last trimester. The udders of heifers injected with dexamethasone (groups 2 and 3) continued to increase in size after milking commenced and finally resembled the udders of heifers lactating after normal pregnancy. In contrast, udders of heifers given no dexamethasone (group 1) regressed after cessation of injections of oestrogen plus progesterone.

Yields of Mammary Secretion

It may be seen from Fig. 1*a* that group 1 heifers produced only trivial volumes of secretion, even after 32 days when milking of these heifers was discontinued. On the other hand, copious volumes were obtained from the heifers in groups 2 (20 mg/day dexamethasone for 3 days) and 3 (40 mg/day dexamethasone for 4 days) during the experimental period, which lasted 90 days. Heifers in group 2 produced significantly more secretion ($P < 0{\cdot}01$) than those in group 3 during most of the study period (see Fig. 1). For heifers in the latter group the rate of increase in levels of secretion was arrested after the fourth injection of dexamethasone.

Secretion from heifers in groups 2 and 3 resembled normal bovine milk in appearance by 3–4 days after milking commenced. In contrast, the trivial volumes of secretion obtained from heifers in group 1 resembled pre-colostral secretion throughout the period of collection.

Production records were available for four additional heifers in the herd at the Dairy Research Unit, which calved at about the same time as lactation was induced in the experimental heifers. These 'normal' heifers were *c.* 28 months of age at calving and had been purchased from the same breeder as the nulliparous heifers. Their mean milk yields (obtained from herd records) were $6{\cdot}12 \pm 0{\cdot}62$, $6{\cdot}81 \pm 0{\cdot}80$, and $4{\cdot}77 \pm 0{\cdot}43$ kg/day (mean $\pm$ S.E.) at 40, 65, and 90 days after calving respectively.

Fat Content of Mammary Secretion

The concentrations of fat in mammary secretion from heifers in groups 2 and 3 are presented in Fig. 1*c*. Fat content of secretion from heifers in group 1 was not

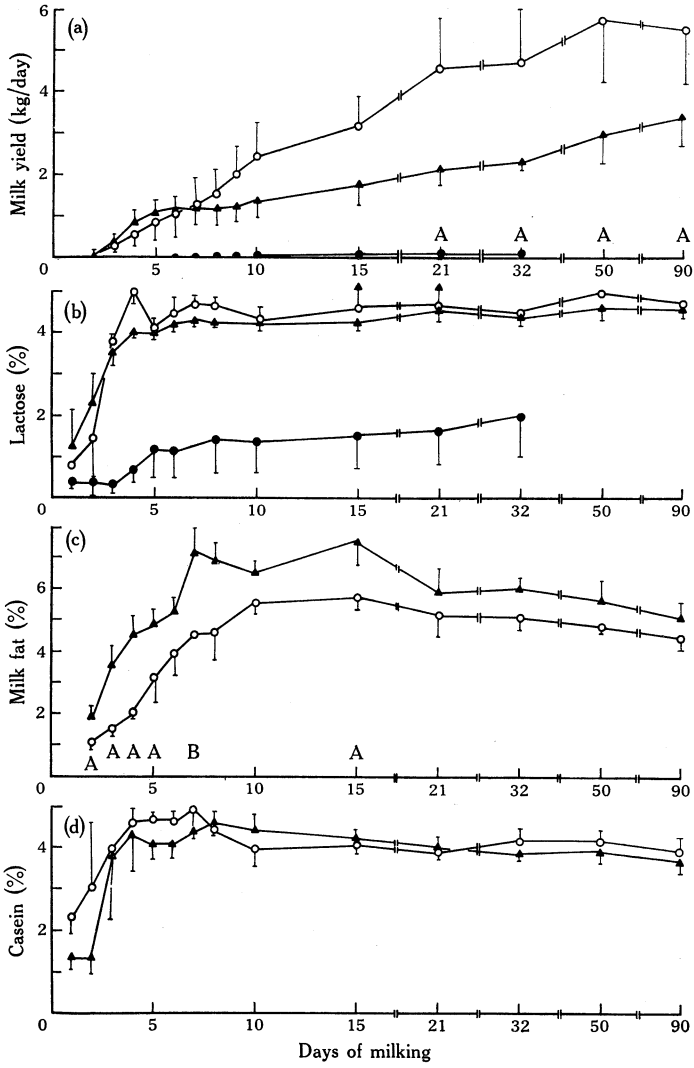

Fig. 1. Daily yields of mammary secretion (*a*) and concentrations in secretion of lactose (*b*), milk fat (*c*) and casein (*d*) for the three groups of heifers commencing on the first day of milking. Plotted points represent mean values; standard errors are shown as vertical bars. ● Group 1, no dexamethasone. ○ Group 2, 20 mg/day dexamethasone for 3 days commencing on day 0. ▲ Group 3, 40 mg/day dexamethasone for 4 days commencing on day 0. Significant differences, on any particular day, between groups 2 and 3 are indicated thus: A, $P < 0{\cdot}05$; B, $P < 0{\cdot}01$.

determined. The secretion from the heifers in group 3 contained significantly higher levels of fat than secretion from group 2 heifers, particularly during the early stages of

the experimental period. Mean fat content of milk from the normal lactating heifers was $4 \cdot 9 \pm 0 \cdot 3$, $3 \cdot 6 \pm 0 \cdot 2$, and $3 \cdot 8 \pm 0 \cdot 2\%$ on days 40, 65, and 90 of lactation respectively.

Lactose and Casein in Mammary Secretion

It may be seen from Fig. 1 that the levels of lactose and casein in mammary secretion were not significantly different between heifers in groups 2 and 3, and were similar to those usually found in bovine milk. On the other hand, the secretion from heifers in group 1 contained very low levels of lactose even after 32 days of milking. Casein levels were not determined in mammary secretion from the group 1 heifers.

Discussion

It was reported recently that lactation could be initiated artificially in non-pregnant cows given daily injections for only 7 days of oestrogen plus progesterone at doses of 0·1 and 0·25 mg/kg body weight respectively (Smith *et al.* 1973; Smith and Schanbacher 1973, 1974). Although relatively high yields of milk were obtained from some cows a number failed to lactate following treatment. This suggests that previous development of mammary glands may be an essential prerequisite for successful artificial induction of lactation (see Meites 1961; Cowie 1971) and results of experiments conducted at this laboratory indicate that this is so, at least in sheep (Fulkerson, unpublished data).

An undesirable side-effect of large doses of oestrogen is that cows may exhibit abnormal oestrous behaviour. Indeed, Smith and Schanbacher (1973, 1974) observed that the cows in their experiments exhibited increased oestrous activity. Other workers using doses of oestrogen similar to those used by Smith and his co-workers have also observed intense oestrous activity for as long as 20–50 days after cessation of oestrogen injections (Paape and Guidry 1973; Narendran and Hacker 1974).

In the present study no evidence of abnormal oestrous behaviour was obtained. Moreover, all cows given dexamethasone as a lactogenic trigger came into lactation. In this respect the results are in conformity with those of earlier studies with sheep (Fulkerson and McDowell 1974). That dexamethasone, and not the stimulus of milking, was the trigger responsible for initiating lactation is confirmed by the results for group 1 heifers, in which milking alone failed to initiate secretion of substantial volumes of fluid.

Yields of secretion from heifers in group 2 approached yields from a group of heifers (of the same breed and subject to the same environment) which lactated after normal pregnancy. This finding, together with the resemblance of the secretion to normal bovine milk in appearance and contents of lactose, casein, and fat, suggests that this induced lactation was essentially normal.

On the other hand, heifers in group 3 produced significantly less secretion. In these heifers there was an appreciable decline in rate of increase in level of secretion 4–5 days after commencing injections of dexamethasone. It would seem, therefore, that there is an optimum dose beyond which lactation in inhibited.

Although yields of secretion were low in group 3 heifers, the secretion resembled normal milk in appearance and content of lactose and casein. However, the levels of fat were high relative to those in normal bovine milk and in secretion from group 2 heifers, particularly during the early stages of lactation.

In this connection, it has been found in rats that corticosteroids release free fatty acids from adipose tissue and triglyceride from the liver and also cause blood glucose levels to rise (Fain *et al.* 1963; Klausner and Heimberg 1967). Similarly, in sheep injections of dexamethasone result in increased levels of esterified fatty acid and glucose in plasma (Fulkerson, unpublished data). Thus the high levels of fat in secretion from group 3 heifers may have been due to increases in the blood levels of precursors of milk triglyceride.

The results of the present studies indicate that it may be possible to develop procedures which will be suitable for initiating lactation artificially in commercial situations. Clearly, the effect of hormone treatment on subsequent reproductive performance should be determined. Preliminary evidence from this laboratory indicates that sheep and cattle can become pregnant after hormone treatment (Fulkerson, unpublished data).

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