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Artificial Induction of Lactation in Ewes: The Use of Prostaglandin

W. J. Fulkerson,[AB] *G. H. McDowell,*[A] *R. D. Hooley*[C] *and L. R. Fell*[D]

[A] Dairy Research Unit, Department of Animal Husbandry,
University of Sydney, Camden, N.S.W. 2570.
[B] Present address: Department of Animal Science and Production,
Institute of Agriculture, University of Western Australia, Nedlands, W.A. 6009.
[C] Reproduction Research Section, University of Melbourne,
S. S. Cameron Laboratory, Werribee, Vic. 3030.
[D] Dairy Research Centre, P.O. Box 217, Richmond, N.S.W. 2753.

Abstract

Injections of an analogue of prostaglandin $F_{2\alpha}$ (T.F.101) initiated secretion of copious amounts of fluid resembling normal ovine milk when given to non-pregnant ewes with developed mammary glands. Injections of T.F.101 elicited a substantial but transient increase in the levels of prolactin in plasma. Results for intact and ovariectomized ewes were similar.

Introduction

There is evidence that administration of prostaglandin $F_{2\alpha}$ at doses sufficient to terminate pregnancy initiates lactation in women (Smith *et al.* 1972) and rats (Deis 1971). Moreover, injections of prostaglandin substantially raise levels of prolactin in the peripheral blood of a number of species (Vermouth and Deis 1972; Anfinson and Davis 1974; Louis *et al.* 1974). Previous studies from this laboratory have shown that, in non-pregnant ewes with developed mammary glands, lactogenesis is associated with elevated levels of prolactin in blood (Fulkerson *et al.* 1975, 1976). The present study was carried out to determine whether prostaglandin $F_{2\alpha}$ would induce lactation in intact and ovariectomized ewes with developed mammary glands. In addition, measurements of prolactin levels in plasma of ewes were made to determine whether lactogenesis was associated with elevated levels of this hormone.

Materials and Methods

Sheep

Four intact and four ovariectomized (operated on 3 weeks before the experiment commenced) nulliparous, crossbred ewes (Border Leicester × Merino) with no apparent abnormalities of the mammary glands were used in the experiment. When the experiment commenced the intact ewes were in anoestrus and ewes from the same flock remained in anoestrus over the period of the experiment. The ewes were housed and fed as described previously (Fulkerson and McDowell 1974, 1975) and all were accustomed to handling and could be bled from the external jugular vein with a minimum of restraint.

Hormones

Progesterone (Calbiochem, La Jolla, California) and oestradiol benzoate (β-oestradiol-3-benzoate, Sigma Chemical Co., St Louis) were dissolved in ethanol and administered either in ethanol or in peanut oil. The preparation of prostaglandin $F_{2\alpha}$ (T.F.101), obtained from Troy Laboratories, Sydney, was dissolved in ethanol to give a solution containing 25 mg hormone/ml.

Experimental Procedure

The mammary glands of all ewes were developed over 30 days with injections of ovarian steroids as described previously (Fulkerson *et al.* 1975). On the third day after the last injection of ovarian steroids each ewe was given subcutaneous injections of 37·5 mg T.F.101 in absolute ethanol at 1000, 1300 and 1600 h.

The above dose and time course of injections were chosen in an attempt to mimic the sporadic release of prostaglandin $F_{2\alpha}$ which occurs at the end of pregnancy. Prostaglandin $F_{2\alpha}$ peak values of 18 ng/ml have been measured in blood from the utero–ovarian vein of the ewe at parturition (Thorburn *et al.* 1972) and it has been demonstrated that subcutaneous injection of 25 mg prostaglandin $F_{2\alpha}$ elevates the level of this hormone in blood from the utero–ovarian vein by 12 ng/ml (McCracken *et al.* 1973).

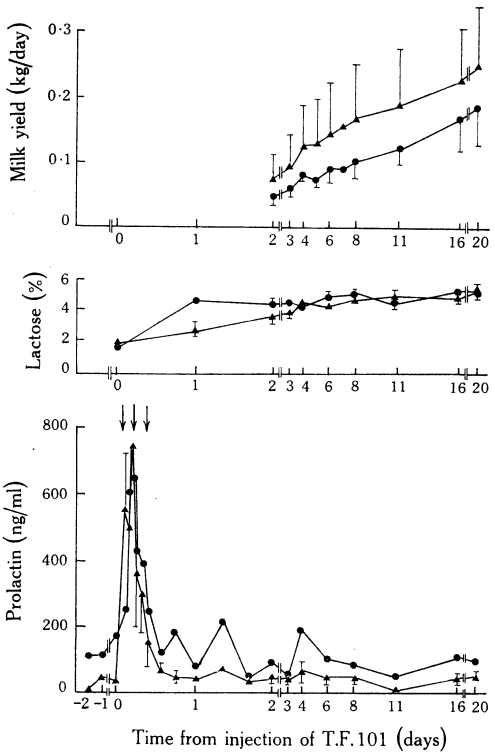

Fig. 1. Yields and lactose contents of mammary secretion, and levels of prolactin in plasma, for intact (▲) and ovariectomized (●) ewes. Injections of T.F.101 were given at the times indicated (↓). Values presented are means for four ewes except for the prolactin levels which are means for three intact ewes and for two ovariectomized ewes. Standard errors are shown as vertical bars.

Collection of Samples

All ewes were milked by hand from the day T.F.101 was injected. They were milked once daily at 0800 h for 6 days then twice daily at 0800 and 1600 h for a further 15 days. Milk yields were recorded daily and samples of milk were stored at −16°C pending analysis for lactose (Cowie *et al.* 1969).

Plasma samples, obtained at intervals before, during and after injections of T.F.101, were stored at −16°C until assayed for prolactin by solid-phase radioimmunoassay (Fell *et al.* 1972). Concentrations of prolactin were expressed in terms of the standard NIH-P-S8. Whenever appropriate, blood sampling occurred immediately before milking or injection of hormone.

Results

Yield and Lactose Content of Milk

The mean yields and lactose contents of milk from intact and ovariectomized ewes did not differ significantly ($P>0·05$) over the period of the experiment. By

21 days after milking commenced milk yields were *c.* 0·22 kg/day and the lactose content of the milk was *c.* 4·9% (Fig. 1).

Prolactin in Plasma

Prolactin levels in plasma are shown in Fig. 1. Injection of T.F.101 led to rapid and substantial increases in the levels of prolactin. Thus, levels increased from 20–80 ng/ml to *c.* 800 ng/ml by 1 h after the first injection of T.F.101 in both groups of ewes. Levels of prolactin then declined over the next 11–15 h despite further injections of T.F.101.

Discussion

Clearly, injections of T.F.101 initiated secretion, from the mammary glands of both intact and ovariectomized ewes, of copious amounts of fluid resembling normal ovine milk. Associated with this lactogenic response there was a marked increase in the level of prolactin in plasma of all ewes. Although no data for 'control' ewes have been presented, appropriate data are available from a study conducted concurrently with ewes from the same flock as those used in the present study (see Fulkerson *et al.* 1976). These 'control' ewes, which were simply milked after cessation of injections of ovarian steroids, produced only trivial amounts (<0·01 kg/day) of milk-like fluid containing low levels (*c.* 3·5%) of lactose (see also Fulkerson and McDowell 1974, 1975). Moreover, there was no appreciable change in the levels of prolactin in plasma from 'control' ewes when milking commenced. Thus it seems reasonable to conclude that T.F.101 was responsible for both lactogenesis and the release of prolactin in the intact and ovariectomized ewes used in the present study.

The pattern of prolactin release following injection of T.F.101 was similar to that reported by other workers for other prostaglandins. Thus, Anfinson and Davis (1974) recorded maximum levels of prolactin 30 min after injection of prostaglandin E_1 to sheep and they noted that prolactin levels rapidly declined thereafter. Similar observations also were reported by Louis *et al.* (1974) who injected cattle with prostaglandin $F_{2\alpha}$.

Although it is not possible to define the mechanism by which T.F.101 triggered lactation it is considered likely that the prolactin released shortly after injection of T.F.101 was a significant contributing factor. However, administration of prostaglandin has been found to stimulate release of growth hormone (Hertelendy *et al.* 1972; Anfinson and Davis 1974; Louis *et al.* 1974), ACTH (Hedge 1972), and glucocorticoids (Louis *et al.* 1974) all of which could be involved in the lactogenic response elicited by prostaglandin treatment.

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