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Technical note

The effect of bromocryptine on plasma prolactin concentration and ovulation rate in ewe breeds with different fecundity rates

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Abstract

The objective of the study was to investigate the effect of bromocryptine on the neuro endocrine feedback mechanisms that control ovulation rate in two sheep breeds with different fecundity and ovulation rates (Scottish Black Face and Finnish Landrace). Bromocryptine was administered i.m. in doses of 1 mg at 12-h intervals for an entire estrous cycle (16.0 ± 0.5 days), to 12 Scottihs Black Face and 12 Finnish Landrace ewes. The aim was to record the blood prolactin levels and the effect of bromocryptine on ovulation rate. The experiment was carried out during the breeding season (November 1999) and repeated in January 2000. In the first study the ovulation rate was not affected by the low plasma prolactin (<0.5 ng/ml) levels induced by the drug. Ovulation rate in the Finnish Landrace was 2.85 ± 0.69 CLs/ewe for the control and 2.42 ± 0.53 CLs/ewe in the treated group. In the Scottish Black Face ewes, ovulation rate was 1.12 ± 0.35 and 1.37 ± 0.51 CLs/ewe for the control and treated ewes, respectively. When the experiment was repeated at the end of breeding season in January 2000, the ovulation rates were similar. It was concluded that the administration of bromocryptine during an entire estrous cycle at the beginning and the end of the mating season did not affect fecundity and ovulation rate in ewes with different prolificacies.
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Keywords: Bromocryptine; Prolactin; Ovulation rate; Sheep

1. Introduction

The important role played by catecholamines in the neuroendocrine control of sexual behavior have been reported in the rat (Clemens et al., 1977; Kendall and Tongue, 1977), sheep (Jackson, 1977; Riggs and Malven, 1974; Wheaton et al., 1975), birds (El Halawani and Burke, 1976), and monkeys (Gala et al., 1978).

Kordon and Glowinski (1969) first reported dopamine to induce the release of LH in the rat and the stimulation of dopamine receptors with bromoergocryptine to reduce prolactin secretion in ewe (Nisweder, 1974; Picazo et al., 2000) and human (Strauch and Bricaire,

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1977). The drug bromocryptine is clinically used in the treatment of hyperprolactinaemic amenorrhea in women to re-establish the menstrual cycle and ovulation (Katz and Adashi, 1990; Freeman et al., 2000).

In preliminary studies a difference was recorded in the prolactin blood levels between ewes of different fecundity and ovulation rates. Ewes with a high ovulation rate (2.6 CLs/ewe) recorded lower levels of prolactin while, the plasma concentration of prolactin was significantly higher in ewes with low ovulation rate (1.9 CLs/ewe) (Fuentes, 1986).

The number of ovulations per cycle varies in different animal species. The feedback mechanisms that underline the number of ova shed per cycle are an expression of the biological balance between ovarian secretions and the central neuro transmitters that modulate the release of hypothalamic releasing factors, which in turn promote or inhibit the release of the hypophyseal gonadotrophic hormones (Dominguez-Gonzalez and Genaro, 1994; Doney et al., 1976; Fluder and Tongue, 1977; Hokfelt and Fuxe, 1972; Strauch and Bricaire, 1977; Vijayan and McCaan, 1978; Freeman et al., 2000).

In view of the important role played by dopamine in prolactin secretion (Smythe, 1977) and the experimental evidence that favors prolactin as a modulator of ovarian function (McNatty et al., 1975; Freeman et al., 2000), this trial was initiated. The aim of this experiment was to study the effect of administering the dopamine agonist bromocryptine on the ovulation rate of two breeds of sheep with different fecundity and ovulation rates.

2. Materials and methods

For the purpose of this study, 12 adult Scottish blackface ewes, 2–3 years of age with a mean body weight of 32 ± 3 kg, and 12 Finnish Landrace ewes, 3–4 years old with a mean body weight of 35 ± 3.5 kg were used based on their difference in ovulation rate (1.96 and 2.6 CLs/ewe, respectively) (Fuentes, 1986). Ewes were housed in open paddocks exposed to the natural photoperiod (latitude 19°N), fed oat hay ad libitum and supplemented with 0.4 kg concentrate per animal per day. Water was available throughout the observation period.

To detect estrus, both groups of ewes were teased twice (at 8:00 and 16:00 h) daily with the aid of vasectomised rams. Ewes displaying at least two natural consecutive cycles were selected and used in the trial. In the control and treated groups, estrus was synchronized with intravaginal sponges (40 mg medroxi progesterone acetate MAP) for 14 days. Ewes in each breed were randomly divided in groups of six animals each. One group for each breed was injected (i.m.) twice daily with bromocryptine (1 mg at 8:00 h and 1 mg at 20:00 h) while the control groups were injected with 2 ml saline. Injections were initiated on termination of the synchronized estrus, and continued until the onset of the following estrus (16.0 ± 0.5 days).

Blood samples were taken prior to injections to monitor the plasma prolactin levels, using a specific RIA assay as previously described by Fuentes (1986).

To record the effect of bromocryptine on the ovulation rate, ovaries were observed by laparoscopy 6–8 days following estrus.

The experiment was carried out in two phases, the first in November 1999 and the second repeated in January 2000. Analysis of plasma prolactin concentration and ovulation rate results was carried out using a 2×2 factorial analysis of variance (SAS).

3. Results

When the experiment was carried out during the breeding season in November 1999, it was observed that bromocryptine significantly ($p < 0.001$) decreased the blood plasma prolactin concentrations (<0.5 ng/ml) in both Scottish Black Face and Finnish Landrace ewes. Plasma prolactin levels increased in treated and control ewes on the 15th day of their cycle, reaching a peak on the 16th day, just prior to the onset of estrus. (Fig. 1).

When the corpora lutea were recorded by laparoscopy, the ovulation rate was recorded to be 2.4 ± 0.5 CLs/ewe for the treated and 2.9 ± 0.7 CLs/ewe for the control Finnish Landrace ewes. In the Black Face ewes the ovulation rate was 1.1 ± 0.4 and $1.4 \pm 0.$ 5 CLs/ewe for the control and treated ewes, respectively (Table 1). These differences were not significant.

To study the effect of season, the experiment was repeated in January 2000, and the ovulation rate in the bromocryptine-treated ewes was 3.0 ± 0.8 and

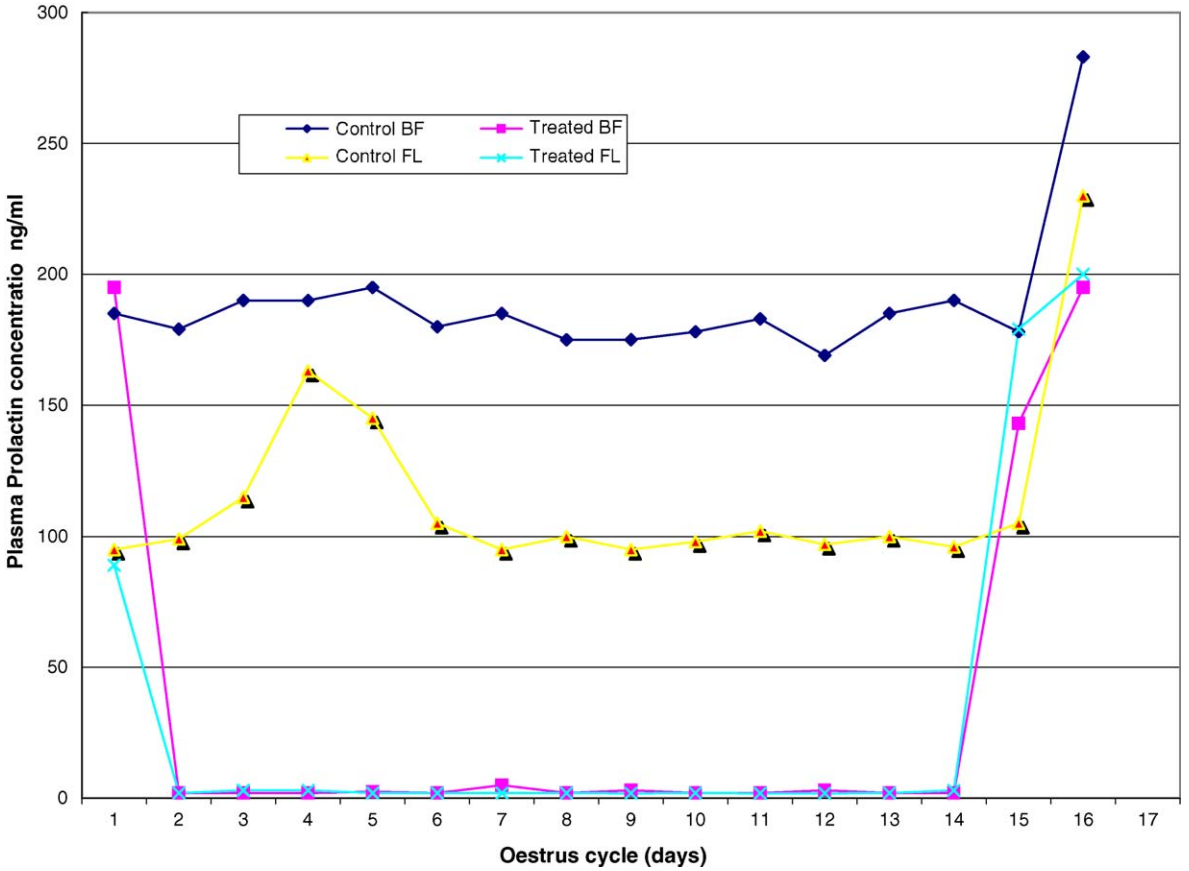


Fig. 1. The effect of bromocryptine on plasma prolactin levels of ewes of different ovulation rate. BT, Black Face treated; BC, Black Face control; FT, Finnish Landrace treated; and FC, Finnish Landrace control.

1.3 ± 0.5 CLs/ewe for Finnish Landrace and Scottish Black Face ewes, respectively, while the ovulation rate in the control ewes was 3.8 ± 0.6 and 1.0 ± 0 CLs/ewe for the Finnish Landrace and Scotish Black Face ewes, respectively. There was no significant difference between the time of the season administered and the ovulation rate in both breeds.

Table 1
The effect of bromocryptine, a dopamine receptor agonist on the ovulation rate of Finnish Landrace and Scottish Black Face ewes

	Finnish Landrace ovulation rate (CLs/ewe)	Scottish Black Face ovulation rate (CLs/ewe)
November 1999 trial		
Control group ($n=6$)	3.8 ± 0.6	1.1 ± 0.3
Treated group ($n=6$)	3.4 ± 0.5	1.3 ± 0.5
January 2000 trial		
Control group ($n=6$)	3.8 ± 0.6	1.0 ± 0
Treated group ($n=6$)	3.0 ± 0.8	1.3 ± 0.5

*No significant difference.

4. Discussion

The administration of bromocryptine was followed by a decrease in the plasma prolactin concentrations in all treated ewes. This is in agreement with other reports and previous findings (Wheaton et al., 1975; Fuentes, 1986). The effect following stimulation by dopamine receptors at the pituitary hypothalamic level showed that dopamine modulates the release of prolactin (DíChiara et al., 1977; Dominguez-Gonzalez and Genaro, 1994).

In this experiment, the length of the estrous cycle and the display of estrus in both breeds was not affected by the administration of bromocryptine. This latter observation is similar to that first reported by Nisweder (1974). If prolactin plays a luteotrophic role in the sexual cycle of the ewe, it would suggest that during the breeding season more prolactin is secreted in each cycle than needed, as bromocryptine did not completely inhibit the secretion of prolactin. In the bromocryptine-treated ewes, plasma prolactin was detected at concentrations of <1.5 ng/ml, and this concentration may be sufficient to activate the tuberoinfundibular neurons (Hokfelt and Fuxe, 1972; Andrews and Grattan, 2002), thus activating a short-loop feedback control of hypophyseal secretion. Furthermore, bromocryptine treatment does not appear to influence the basal or pulsatile release of LH in lactating ewes, even though the release of LH in response to exogenous GnRH may be elevated (Wright et al., 1981). It is worth mentioning the possibility of an interaction with androstenedione in the control of ovulation rate through a long loop feedback mechanism when taken up by the hypothalamus and aromatized into catechol estrogens, which in turn modulate the central catechol amine turnover (Paul and AxeIrod, 1977). In order to study the role of prolactin on ovulation rate, prolactin blood concentrations must be completely suppressed throughout the cycle and at the onset of estrus (Kann and Denamour, 1974).

In this trial it was observed that Scottish Black Face ewes with a low ovulation rate recorded higher blood prolactin concentrations, while the plasma prolactin concentration in Finnish Landrace ewes with a high ovulation rate was considerably lower, confirming previous findings (Fuentes, 1986). The latter observation gives support to the possibility that there is an increased turnover of the neuro transmitter 5-hydroxytryptamine (Kordon et al., 1977; Lawson and Gala, 1978), therefore limiting the basal concentrations of the gonadotrophins and consequently limiting ovulation rate in ewes with a low inherent ovulation rate or fecundity.

This explanation cannot be so simplistic as there is no doubt regarding the existence of an interaction of several factors that dictate the expression of ovulation and estrous behavior in the ewe. Peripheral hormone concentrations alone cannot explain the difference in fecundity and ovulation rate observed between sheep and other species. In recent observations it was reported that Suffolk ewes with a low ovulation rate and treated with low doses of naloxone increased the ovulation significantly. The latter shows that prolactin may be one of the factors that control ovulation rate. There may also be a cascade of hormonal interactions that dictate the number of ovulations for each species in accordance to their genetic potential (Fuentes et al., 2002).

It could be concluded that the administration of bromocryptine during and entire estrous cycle during the mating season to ewes with different fecundity rates did not alter estrous behavior and ovulation rate.

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