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Effects of gonadotrophin releasing hormone (buserelin) on sheep fertility

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ABSTRACT

An agonist of gonadotrophin releasing hormone (GnRH) improves dairy cow pregnancy rates when injected at an appropriate stage after insemination. These studies were extended to ewes and hoggets in a series of trials to determine the effects of a single injection of GnRH made at varied intervals after mating. All sheep were mated at a synchronised oestrus (day of oestrus = day 0) with treated ewes being injected on a set date with 2 or 4 µg of the GnRH analogue buserelin. Among ewes injected on days 10, 11, 12, 13 or 14 post-mating, the increases in % ewes lambing were (number of ewes in brackets): 18(65), 1(204), 12(150), 4(131) and 8(20) respectively. Similarly, the increases for hoggets treated on days 12 and 13 were 23(98) and 5(86) respectively. Among ewes that did not conceive at the synchronised oestrus, GnRH did not affect return to service pregnancy rates, although return to service intervals were increased (17.5 v 16.9 days $P < 0.01$). These studies showed that a single injection of a small dose of a potent GnRH agonist had an effect on fertility and cycle length. The mechanism by which GnRH increased pregnancy rates probably involved corpus luteum function.

Keywords Gonadotrophin releasing hormone; GnRH; buserelin; sheep fertility; hoggets; oestrous cycles.

INTRODUCTION

A high pregnancy rate is a major component of high reproductive efficiency. Pregnancy rates following matings at one oestrus in ewes can be variable. High pregnancy rates have been reported in commercial South Island (Kelly, 1982) and North Island flocks (Quinlivan and Martin, 1971). Under North Island hill country conditions, pregnancy rates can be low (Knight and Hight, 1976).

Few hormonal procedures consistently improve ewe fertility. A recent series of trials in lactating dairy cattle demonstrated improved fertility following a single injection of synthetic GnRH (gonadotrophin releasing hormone) (Macmillan *et al.*, 1986); an effect that may have been associated with a modification of CL (corpus luteum) function and progesterone production (Macmillan *et al.*, 1985).

In this study, we evaluated synthetic GnRH effects on pregnancy and returns to service in ewes and hoggets.

MATERIALS AND METHODS

Five hundred and seventy adult Romney ewes and 286 Romney ewe hoggets that mated were used in 5 trials (Table 1). The ewes were mated over 3 days following oestrus synchronisation with sponges containing 70 mg MAP. The sponges were withdrawn on 12 April 1984, 7 February and 11 April 1985 in Trials 1 to 3

respectively. Return to service intervals were recorded over 4 weeks using entire rams in Trials 1 and 3 and vasectomised rams in Trial 2. The hoggets were mated over 2 days following oestrus synchronisation with sponges or CIDRs (McMillan, 1986). Return matings were determined 3 weeks after mating using vasectomised rams. Sponges were withdrawn on 20 May and 27 May, 1985 in Trials 4 and 5 respectively. About 10% of entire rams were used from sponge or CIDR withdrawal.

Within each trial, ewes were randomly allocated within date of mating to treatment with GnRH or untreated controls. GnRH was the synthetic analogue containing 4 µg/ml of the nonapeptide buserelin (DSer-tertiary-butyl⁶, des Gly-NH₂¹⁰ GnRH ethylamide), a potent GnRH agonist ("Receptal", Hoe 766; Hoechst NZ Ltd). Treated ewes in Trial 1 received 0.5 ml as an intramuscular injection. All other treated sheep received 1.0 ml. Sheep were treated once, on the same date in each trial (day of mating = day 0) (Table 1). The interval between sponge withdrawal and GnRH was different in each of Trials 1 to 3 to give different post-mating intervals at injection time. The number of ewes lambing was recorded.

Differences in proportions were tested by Chi-square contingency table analysis and cycle length differences by variance analysis.

TABLE 1 Percentage lambing to first mating and total number() in the group in ewes or hoggets either untreated or injected once with GnRH (buserelin) at a range of intervals after mating.

	Post-mating interval (d)				
	10	11	12	13	14
Trial 1 (ewes)					
GnRH	—	—	50(18)	55(37)	60(8)
Control	—	—	44(23)	41(44)	50(12)
Trial 2 (ewes)					
GnRH	—	53(15)	68(44)	48(27)	—
Control	—	63(19)	53(38)	61(23)	—
Trial 3 (ewes)					
GnRH	61(28)	56(70)	44(9)	—	—
Control	43(37)	52(100)	44(18)	—	—
Trials 1-3 (ewes)					
GnRH	61	55	60	52	60
GnRH-Control	+18	+1	+12	+4	+10
Trial 4 (hoggets)					
GnRH	—	—	55(22)	49(49)	—
Control	—	—	35(17)	53(49)	—
Trial 5 (hoggets)					
GnRH	—	—	52(27)	56(45)	—
Control	—	—	28(32)	42(45)	—

RESULTS

The mean joining live weights of ewes were 53, 51 and 50 kg in Trials 1 to 3 respectively. Hoggets weighed 35 kg (Trial 4) and 29 kg (Trial 5) at joining.

Overall, treatment with GnRH improved pregnancy rate to first mating (55 v 47%; $P < 0.05$). Treated ewes appeared to respond less than treated hoggets (57 v 50%; $\chi^2 = 2.5$ and 52 v 42%; $\chi^2 = 3.2$).

In Trial 1, GnRH tended to improve pregnancy rates to first mating (54 v 43%; $\chi^2 = 1.68$) (Table 1), but return to service pregnancy rates were not affected (79 v 81%). Although GnRH did not alter pregnancy rates in Trial 2 (59 v 58%), there was a suggestion that treatment on day 12 was effective ($\chi^2 = 2.1$; Table 1). The GnRH increase in Trial 3 was 7% (56 v 49%; $\chi^2 = 1.26$). Pregnancy rates of ewes returning to service were independent on GnRH (60 v 61%). The level of response to GnRH in ewes tended to vary with day of cycle when treated (Table 1).

Overall, hoggets treated with GnRH had similar pregnancy rates to controls in Trial 4 (51 v 48%), but improved pregnancy rates in Trial 5 (55 v 36%; $P < 0.05$). Treatment on day 12 (53 v 31%; $P < 0.05$), but not 13 (51 v 48%) improved hogget pregnancy rates.

The return to service interval was increased in treated ewes (17.5 v 16.9 d; $P < 0.01$). Treatment delayed returns in some ewes (Table 2).

GnRH reduced the proportion of hoggets returning within 3 weeks of mating in Trial 4 (10 v 22%; $P < 0.05$), but not in Trial 5 (22 v 27%).

DISCUSSION

These studies demonstrated that a single injection of a small dose of a potent GnRH agonist had effects on fertility and cycle length. Furthermore, hoggets tended to be more responsive than adult ewes. The fertility response appeared to vary with time of treatment. Ewes and hoggets treated on day 12 showed consistently large responses. Stage of cycle effects could not be

TABLE 2 Distribution of return to service intervals (% of total ewes in the group) in ewes either untreated or injected once with buserelin (Trials 1 to 3).

	Interval from 1st to 2nd mating (d)							
	15	16	17	18	19	20	21	21
GnRH (78 ewes)	0.4	3.9	9.8	9.0	3.9	1.2	0.4	2.0
Control (113 ewes)	3.5	9.9	11.8	6.1	1.9	1.6	0.6	0.6

separated from day of mating effects since GnRH was injected on the same date in each trial. Nonetheless, these results are consistent with those in dairy cattle where fertility responses to GnRH were obtained with treatment after mid-cycle (Macmillan *et al.*, 1986).

The pregnancy rates in untreated ewes were low in all three trials, possibly as a result of mating at the first oestrus after sponge withdrawal and frequent yarding in early pregnancy. Although GnRH improved ewe pregnancy rates under these conditions, it has yet to be demonstrated that similar improvements occur in ewes with higher fertility. The improvements in dairy cattle have been above "normal" levels (Macmillan *et al.*, 1986). The GnRH response in hoggets treated on day 12 was due to the prevention of a slump in pregnancy rates since pregnancy rates in controls on day 12 were lower than day 13 controls which in turn were similar to treated hoggets (30 v 48 v 53%). Although the pregnancy rate of day 12 controls was low, it is consistent with the high level of post-fertilisation loss apparent in hoggets cycling naturally (McMillan and McDonald, 1985) or following hormonal synchronisation (Quirke, 1979). The apparently different reasons for the GnRH response in adult and immature ewes suggests that the mechanisms may differ.

The effects of GnRH were short-lived and did not carry through into the next cycle of mating. By contrast, mid-luteal phase treatment improved pregnancy rate at the next mating in dairy cattle (Humboldt and Thibier, 1981; Macmillan *et al.*, 1986).

The change in cycle length distribution was consistent with reports in dairy cattle (Macmillan *et al.*, 1985). However, the GnRH pregnancy response in ewes appeared to be due to a lower return to service rate rather than a difference in ewes that did not return but failed to lamb. Thus, the proportion of ewes returning 15 to 17 days after mating fell by 11%, but those returning 18 and 19 days later rose by only 5%. The outcome of this was an increase in pregnancy rates and return to service intervals. Most of the non-returning barren ewes were from Trial 2. These ewes may have returned to anoestrus soon after the induced matings or returned at extended intervals.

The mechanism by which GnRH improves lambing rates in sheep may involve direct or indirect effects on CL function. Mechanisms controlling embryo survival rather than ovum fertilisation must be involved since treatments were after the expected time to fertilisation. Evidence from dairy cattle suggests that GnRH may act indirectly through enhanced progesterone production (Macmillan *et al.*, 1985). Similar effects occur in ewes where pregnancy rates have been improved following midcycle progesterone supplementation (Peterson *et al.*, 1984). Alternatively, GnRH may induce, via LH, a luteoprotective effect. The response on day 12 is consistent with a luteoprotective effect since the presence of an embryo on day 12 or 13 is necessary for normal CL function (Moor and Rowson, 1966).

In summary, a single injection of a GnRH agonist improves ewe and hogget fertility. This improvement is associated with fewer ewes returning to service and probably involves effects on CL function.

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