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Observations on the reproductive effects of once or twice weekly injections for 6 weeks of the GnRH agonist deslorelin in the cow

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Abstract

This study investigated the reproductive effects in Holstein–Friesian cows of once or twice weekly intramuscular injection for 6 weeks of 100 μg of the GnRH agonist deslorelin at intervals. Oestrus was synchronized in non-lactating Holstein–Friesian cows before they were allocated randomly to receive either 100 μg deslorelin once weekly (D1; $N = 10$) or twice weekly (D2; $N = 8$) or acted as untreated controls (CON; $N = 8$). The first injection was given on day 6 post-oestrus and the last injection on day 48 post-oestrus. Blood samples were collected twice weekly from each cow until day 76 after the synchronized oestrus to profile plasma P4. A single injection of prostaglandin was administered to all cows on day 20 post-oestrus to ensure luteolysis occurred. Ovaries were examined twice weekly by transrectal ultrasonography and then subsequently at weekly intervals to monitor ovarian structures. Progesterone profiles observed over two complete cycles for CON cows were typical of those expected for cows displaying regular oestrous cycles. Injection of deslorelin on day 6 post-oestrus induced ovulation in 100% (18/18; D1 and D2) of deslorelin-treated cows. Three categories of responses based on plasma P4 profiles were defined amongst the deslorelin-treated cows. Complete anoestrus was observed in 20% (2/10) of D1 and 63% (5/8) of D2 cows. A partial response characterised by intermittently low concentrations of P4 was observed in 50% (5/10) of D1 and 25% (2/8) of D2. A complete lack of response to deslorelin, with P4 profiles indistinguishable from CON cows, was seen in 30% (3/10) of D1 and 13% (1/8) of D2 cows. When results from D1 and D2 were pooled, a greater proportion of deslorelin-treated cows had abnormal ovarian cycles during the treatment period (56% versus 0%; D1 and D2 versus CON, $P < 0.001$). In conclusion, the repeated injection of deslorelin either once or twice weekly for 6 weeks significantly altered the

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ovarian cycles of some cows; individual cow responses observed varied widely and ranged from complete anoestrus to a cycle indistinguishable from normal.

Keywords: GnRH agonist; Deslorelin; Cow; Anoestrus; Progesterone

1. Introduction

The bovine pituitary gland is considered highly sensitive to potent GnRH agonists. Downregulation of any further GnRH responsiveness and a state of anovulatory anoestrus readily result from continuous prolonged treatment (Gong et al., 1995). This downregulation response may provide a new experimental approach to the control of the bovine oestrous cycle and ultimately yield new therapeutic options. Induction of short-term anoestrus may have potential application in oestrous synchronization or precise control of the post-partum anoestrus period in dairy cattle. GnRH agonists are currently widely used in oestrous synchrony programs such as OvSynch^{TM}, where GnRH is given followed 7 days later by prostaglandin and then a further 8–24 h later with a second injection of GnRH (Stevenson et al., 1999). The potent GnRH agonist buserelin (Receptal®, Hoechst) is commonly used. The reproductive effects of continuous long-term treatment are well described but the effects of shorter and intermittent treatment with a potent GnRH agonist have not yet been described.

A number of studies have described the effects of varying regimes of repeated GnRH agonist administration on LH profiles. In a study designed to compare the relative potency of GnRH, buserelin and fertirelin through acute LH and FSH release (Chenault et al., 1990), it was noted that when higher doses (at least 10 μg buserelin, 500 μg GnRH or 50 μg fertirelin) were administered sequentially (every 48 h), there was a diminished LH and FSH output, suggestive of downregulation. In a separate study, injection of 5 or 10 μg buserelin i.m. in an aqueous solution (saline) twice daily for 21 days prevented follicle development beyond 9 mm in heifers when treatment was started on day 5 post-oestrus (Gong et al., 1995). Successive buserelin injections resulted in a diminished LH surge response and a complete suppression of pulsatile LH release (Gong et al., 1995). Likewise in the ewe, repeated injections of 50 μg GnRH into either OVX or anoestrous ewes initially stimulated LH release, but subsequent injections at intervals of less than 72 h could not reproduce the magnitude of the initial surge (Rippel et al., 1974).

The effects on ovarian function have been described following serial buserelin injections. The injection of 8 or 10 μg of buserelin at 3-day-intervals beginning 12 days after oestrus to Holstein dairy cows extended the life span of the corpus luteum and extended the interoestrous interval (Thatcher et al., 1989). Injection of 10 μg of buserelin s.c. four times daily between days 9 and 12 of the oestrous cycle in heifers extended the mean cycle length to 26.4 days compared to 20.3 days for untreated heifers (Milvae et al., 1984). Insertion of an absorbable low-dose deslorelin implant on day 5 of the cycle extended the mean interoestrous interval to more than 40 days (Rajamahendran et al., 1998).

The GnRH agonist deslorelin is one of the most potent agonists available, having a relative potency of approximately 144 times that of GnRH and seven times that of buserelin (Karten