

Clinical Effect of Buserelin on Pregnancy Rates in Cattle

Martin Sheldon, BVSc, DBR, CertCHP, MRCVS
Ark Veterinary Group, 5 Mansel Street,
Carmarthen, Dyfed, SA31 1QX, U.K.

Abstract

The trial used 2530 recorded services of 1619 animals on 19 dairy farms. Alternate cows were injected intramuscular with 10µg buserelin, a GnRH analogue (Receptal, Hoechst UK), 11 days after insemination. The pregnancy rate was calculated for control and treated cows, paired for calving to first service interval, parity and week of service. For 520 paired control and treated cows the pregnancy rate to first service was 50.6% and 60%, respectively ($p < 0.01$). For second and subsequent services each cow was grouped according to treatment or control status in the preceding dioestrus period, in addition to day 11 after service. This gave three treated groups: treated, treated (TT); treated, control (TC); and control, treated (CT) which could then be compared to the control, control (CC) group. For 136 paired CC and CT cows the pregnancy rate to second service was 41.2% and 54.4% respectively ($p < 0.05$). For 67 paired CC and CT cows the pregnancy rate to third service or more was 23.9% and 52.2% respectively ($p < 0.001$). For 40 paired CC and TT cows the pregnancy rate to third service or more was 15.0% and 45.0% respectively ($p < 0.01$). The increased pregnancy rate after treatment was associated with a reduction in the number of cows with interoestrus intervals of 11-17 days compared with control cows (2% vs. 7%, $p < 0.01$).

Introduction

Analysis of U.K. data revealed a first service pregnancy rate of 57% (Warren 1984). Fertilization losses for cows are estimated at 10% with embryo mortality losses about 30%. The greatest increment of embryo mortality is between day 15-18 after service (Sreenan & Diskin 1986). Embryo mortality may be the result of genetic or environmental factors.

Bishop (1964) advanced the suggestion that a considerable part of embryonic death was unavoidable and should be regarded as a normal way of eliminating unfit genotypes in each generation, at low biological cost. Examination of embryos for chromosomal abnormalities found about 9% were abnormal (Gayerie de Abreu & Lamming 1984).

A large number of environmental factors have been considered to cause embryo mortality including: age, climate, infectious organisms, nutrition, hormonal balance and the uterine environment (Ayalon 1978).

Attempts to improve pregnancy rates in dairy cattle have been the subject of many reviews that stress the importance of cow management and oestrus detection. In 10 herds over 5 years, using fertility control programs, Eddy (1984) reduced the calving to first service interval from 76 days to 64 days by increasing attention to first service and good oestrus detection. Pregnancy rates showed little change at 45.5% to 52% for all services.

A variety of hormonal treatments have been used to try to reduce embryo mortality and increase pregnancy rates, but often with equivocal results. However, in 1986 Macmillan and others reported that injection of 10µg of buserelin on day 11-13 after first service increased pregnancy rates of treated cows in New Zealand by 11.5% compared with control cows.

In practice the veterinarian was often presented with cows that had already received their first service. So, the aim of the trial was to confirm the efficacy of buserelin in the U.K. and investigate its use at second, third and subsequent services.

The Trial

The trial used 19 commercial dairy herds with a total of 2530 services of 1619 Holstein Friesian cows between July and December 1990. Clear instructions were given to the farmers and detailed record sheets were completed. Based on the order of service, alternate cows were injected i.m. with 10µg buserelin (2.5ml Receptal, Hoechst U.K.) 11 days after A.I. If a cow returned to oestrus and was served again, a new entry was made on the record card in the order of service. Pregnancy diagnosis was by palpation per rectum 6 - 12 weeks after the last insemination. Pregnancy rates were calculated for control and treated cows within each herd.

Analysis of results was performed so that within each herd for each treated cow there was a similar, but untreated, control cow and each "pair" were matched closely. Cows were not included if their interoestrus interval was less than 11 days because treatment was not

given until day 11. To reduce the effect of calving to first service interval on pregnancy rate, the treated and control cows were matched within the following periods: <40 days, 40-60 days, and >60 days calved. Each pair was also matched to avoid the effect of parity on pregnancy rate according to the following groups: maiden heifers, first calved heifers, second to fifth calvers and sixth lactation and above. Each pair was matched for service date within 7 days, to reduce effects of management factors on pregnancy rate, such as changes in nutrition and housing. Data for pregnancy rate were compared using the Chi-square method. Differences where $p < 0.05$ were considered statistically significant.

Results and Discussion

Out of a total of 1538 first services it was possible to pair 520 control and buserelin treated cows. The treated cows had a significantly higher first service pregnancy rate (60.0% vs. 50.6%; $p < 0.01$). This result agrees with Macmillan and others (1986) who reported an 11.5% increase in first service pregnancy rate for 225 treated cows, compared with 276 control cows (72.4% vs. 60.9%, $p < 0.01$). Lajili and others (1991) also reported a beneficial effect of 10 μ g buserelin on pregnancy rates when given to dairy cows 12-14 days after synchronized AI, but not after AI at observed oestrus. Peters and others (1992) found a 12% increase in first service pregnancy rate for 321 treated cows over the control pregnancy rate for 322 cows of 53.4%, using 10 μ g buserelin on day 12 after AI ($p < 0.01$). However, not all trials have shown a benefit of treatment: a double-blind trial in Australia by Jubb *et al.* (1990) revealed no benefit in first service pregnancy rate after 10 μ g buserelin on days 11-13 for 1028 treated cows compared with 1022 placebo cows.

The response to buserelin treatment varied between the 19 herds in the trial: 3 herds had a negative effect, 2 had no effect of treatment, and 9 herds had an increase of more than 10% in pregnancy rate (Sheldon and Dobson, 1993). A number of papers have also reported a variation in response between farms. The cause of this is not known. It may be a consequence of chance or there may be unknown factors involved.

Ryan and others (1991) in Saudi Arabia found no additive increase in first service pregnancy rate for 503 cows treated with 10 μ g buserelin on day 12 and at the time of AI (51.5%) compared to 514 cows treated only at AI (48.8%); although they both had a statistically greater pregnancy rate than the 516 control cows (42.4%).

Other trials have used different doses of buserelin and/or treated on days other than days 11-13 after AI. Coleman and others (1991) failed to detect an effect of 8 μ g buserelin given 14 days after synchronized AI in beef cattle. Peters and others (1992) found no effect of treatment with buserelin on days 8 or 10 after AI, which

agreed with the work of Macmillan and others in 1986. Thatcher and others (1993) treated 195 lactating dairy cows during summer heat stress with 8 μ g buserelin, 12 days after AI, with no effect on pregnancy rate compared to 191 control cows (33.3% vs. 37.2%). No beneficial effect was reported by the same workers, using heifers treated with 8 μ g buserelin 12 days after synchronized AI.

Humblot and Thibier (1981) used 20 μ g buserelin on day 12 after one heat and found an increase in the pregnancy rate to the subsequent service. Macmillan and others (1986) found the pregnancy rate after second insemination was increased by 15.6% for 47 cows treated with 10 μ g buserelin 11-13 days after first insemination, compared with 82 control cows (85.1% vs. 69.5%; $p < 0.05$). Peters and others (1992) reported a nonstatistical effect of 10 μ g buserelin treatment given after first service on the pregnancy rate to the second service. So, in the present trial when we looked at second service or more, each cow was considered for its "treatment" or "control" status in the dioestrus period before the service, as well as 11 days after the service. This resulted in three groups: control, treated (CT); treated, treated (TT); and treated, control (TC) to compare with control, control (CC) cows.

In contrast to the papers quoted above, in the present trial there was no effect on pregnancy rate at second service of a single buserelin treatment 11 days after first service (TC), compared with the CC cows. However, the CT group at second service had a 13.2% increase in pregnancy rate over 136 paired CC animals (54.4% vs. 41.2%, $p < 0.05$). At third or more service the increase in pregnancy rate by the CT group was 28.3% (52.2% vs. 23.9%, $p < 0.01$) in the 67 pairs analyzed. There was wide variation in the response between farms. A small number of farms showed a large increase and they had low pregnancy rates to first service for control cows. All 6 herds with a first service control pregnancy rate of <50% showed an increased pregnancy rate in the CT group. For 40 paired CC and TT cows the pregnancy rate to third service or more was 15.0% and 45.0%, respectively ($p < 0.01$).

There is little available information on the use of buserelin for second, third and more services for comparison with the present trial. Bentle and Humke (1987) used 20 μ g buserelin on days 9-13 after second and third service with no effect on pregnancy rate to the preceding or subsequent service. However, this was double the dose of buserelin used in the present trial and some cows were injected before day 11, which Macmillan and others (1986) found had no effect.

In the present trial analysis of interoestrus intervals of treated and control cows showed a statistically significant difference in the 11-17 day interval: only 2% of treated cows returned to oestrus at 11-17 days, compared with 7% for control cows ($p < 0.01$). We ignored

returns at 0-10 days as cows were not treated until day 11. This finding agrees with that of the majority of other workers. The increased pregnancy rate after treatment with buserelin was associated with a reduction in interoestrus intervals of less than 18 days.

Macmillan and others (1989) used ultrasound to observe dry Holstein cows following 10µg buserelin on cycle day 12 and found altered patterns of follicle development: atresia or premature luteinisation especially in follicles of 6 to 9 mm diameter. Furthermore, Peters and others (1992) showed that mid-luteal buserelin reduced the mean plasma oestradiol concentration after treatment compared with control cows.

The mechanism of action is unknown but the following theory has been proposed. The interoestrus interval is controlled by the lifespan of the corpus luteum. Once luteolysis occurs, generally the cow will exhibit oestrus. The timing of luteolysis is variable and depends on the synthesis of prostaglandin in the endometrium, which is stimulated by oxytocin released from the corpus luteum acting on oxytocin receptors in the endometrium. In turn, the concentration of oxytocin receptors in the uterus rise with increasing oestradiol produced by the developing second or third follicular wave. Maternal recognition of pregnancy relies upon the embryo secreting a chemical messenger known as bTP-1 (bovine Trophoblast Protein 1) from about day 15, which blocks prostaglandin synthesis and therefore prevents luteolysis. The production of bTP-1 may vary with the size of the embryo. Injection of 10 µg buserelin on day 11-13 of the oestrus cycle causes partial luteinization or atresia of the developing follicular wave, probably through release of LH from the pituitary. It is proposed that this disruption in folliculogenesis, and subsequent reduction in oestradiol concentration, delays luteolysis. It is proposed that the delay in luteolysis gives the embryo more time to produce bTP-1 before prostaglandin is produced. In essence, the buserelin is

buying time for the embryo to signal its presence to the dam.

Injection of 10µg buserelin i.m. on day 11 after first, second, and third or more service significantly increased pregnancy rates in dairy cattle. A variety of strategies for use of buserelin are available and it is a matter for discussion between veterinary surgeon and client how the technique might be employed as part of a fertility control program.

The work also shows that not all embryo mortality is predetermined and mortality can be reduced. We can do better!

References

- Ayalon, N. (1978) *Journal of Reproduction and Fertility*, 54, 483-493. Bentle, von W. & Humke, R. (1987) *Tierärztliche Umschau*, 42, 388-394. Bishop, M.W.H. (1964) *Journal of Reproduction and Fertility*, 7, 383-396. Coleman, D.A., Bartol, F.F., Spencer, T.E., Floyd, J.G., Wolfe, D.F. & Brendemuehl, J.P. *Journal of Animal Science*, 69, Suppl. 1, 396 (abstract). Eddy, R.G. (1984) In "Dairy Cow Fertility", pp 89-98. Eds R.G. Eddy and M.J. Ducker. B.V.A., London. Gayerie De Abreu, F. & Lamming, G.E. (1984) *British Cattle Breeders Club Digest*, 39, 55-59. Humblot, P. & Thibier, M. (1981) *Theriogenology*, 16, 375-377. Judd, T.F., Abhayaratne, D., Malmo, O. J. & Anderson, G.A. (1990) *Australian Veterinary Journal*, 67, 359-361. Lajili, H., Humblot, P. & Thibier, M. (1991) *Theriogenology*, 36, 335-347. Macmillan, K.L., Taufa, V.K. & Day, A.M. (1986) *Animal Production Science*, 11, 1-10. Macmillan, K.L., Thatcher, W.W. & Drost, M. (1989) *Proceedings of the New Zealand Society of Animal Production* 49, 91-96. Peters, A.R., Drew, S.B., Mann, G.E., Lamming, G.E. & Beck, N.F.G. (1992) *Journal of Physiology and Pharmacology* 43, 4, (Suppl 1), 143-152. Ryan, D.P., Kopel, E., Boland, M.P. & Godke, R.A. (1991) *Theriogenology*, 36, 367-378. Sheldon, I.M. & Dobson, H. (1993) *Veterinary Record*, 133, 160-163. Sreenan, J.M. & Diskin, M.G. (1986) In "Embryonic Mortality in Farm Animals", pp 1-11. Eds. J.M. Sreenan and M.G. Diskin. Martinus Nijhoff for C.E.C. Thatcher, W.W., Drost, M., Savio, J.D., Macmillan, K.L., Entwistle, K.W., Schmitt, E.J., De la Sota, R.L. & Morris, G.R. (1993) *Animal Reproduction Science*, 33, 27-49. Warren, M.E. (1984) In "Dairy Cow Fertility", pp 1-14. Eds. R.G. Eddy and M.J. Ducker. *Proceedings of Joint B.V.A./B.S.A. Conference*. B.V.A., London.