

CLINICAL COMPARISON OF 3 PRODUCTS **AVAILABLE TO HASTEN OVULATION IN CYCLIC** **MARES**

C. J. Berezowski, DVM, K. L. Stitch, DVM, DACT, K. M. Wendt, DVM, DACT, and D. J. Vest, DVM

From the Department of Large Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, Texas.

Reprints requests: C.J. Berezowski, Department of Large Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4475. e-mail: cberezowski@cvm.tamu.edu

INTRODUCTION

Owing to the wide individual variation in estrus duration and ovulation interval in the mare, pharmacologic induction of ovulation is important for breeding situations. Since the 1970s, human chorionic gonadotropin (hCG) has been demonstrated consistently to induce ovulation and has been used routinely in broodmare practices.¹⁻³

Numerous studies have reported that a high percentage of mares with a follicle J 35 mm in diameter will ovulate within 48 hours of hCG treatment.^{1,4-9} Since hCG is a large glycoprotein, repeated doses over the course of a breeding season can result in high antibody levels against hCG.^{10,11} Some investigators have reported decreasing ovulatory response rates with repeated hCG administration, while others have failed to demonstrate an adverse effect.^{2,4,11}

One advantage of the use of a gonadotropin-releasing hormone (GnRH) agonist to hasten ovulation is that repeated use should not diminish efficacy.¹² The GnRH agonist deslorelin (Ovuplant, Fort Dodge Animal Health, Overland Park, KS) was approved for use in mares in the United States in 1999 in the form of a controlled-release subcutaneous implant. When administered to mares with an estral follicle J 30 mm diameter, Ovuplant induces ovulation within 48 hours on over 88% of cyclic mares.^{13,14}

Using frequent (ie, every 2 h) examinations, McKinnon et al¹⁵ reported hCG injection resulted in a shorter interval to ovulation than deslorelin, whereas Samper et al⁹ reported administration of deslorelin implants resulted in a shorter

interval to ovulation. One potential disadvantage to the use of deslorelin implants has been the need to remove implants at the time of ovulation in order to prevent follicular suppression and delayed return to estrus.^{15,16} Removal of deslorelin implants once ovulation is confirmed, while a relatively straightforward process, may be objectionable to some practitioners or mare owners.

Recent research demonstrated that deslorelin implants was effective for inducing ovulation when administered intramuscularly in a short-term biodegradable liquid.¹⁷ In 2003, a short-term-release (less than 24 hr) deslorelin (BioRelease Deslorelin injection, BET Pharm, Lexington, KY) product in a biocompatible liquid vehicle became available. This product is administered in a single dose by intramuscular injection.

The goal of this study was to compare the clinical efficacy in inducing ovulation among short-term-release deslorelin injection, deslorelin implants, and hCG in cyclic mares examined once daily.

Key words: mare; estrus; ovulation; GnRH; hCG

MATERIALS AND METHODS

Records of 112 estrous periods in 39 cycling Quarter Horse or Thoroughbred mares were analyzed retrospectively. No particular order of administration of products was followed. Mares were being bred in fertility trials (using hysteroscopic insemination techniques) with low numbers of sperm from subfertile stallions, so pregnancy rates were not evaluated as part of the current study. Mares in estrus were typically examined every other day by transrectal ultrasonography until a dominant follicle of 30 mm diameter was detected and thereafter were examined once daily. When the dominant follicle reached 34 mm diameter, an ovulation-inducing agent was administered (Group hCG 2500 units hCG intravenously [Chorulon, Intervet Inc., Milisboro, DE]; Group OVU 2.1 mg deslorelin implant [Ovuplant] injected beneath the vulvar mucosa and subsequently removed on the day ovulation was detected; and Group DES 1.5 mg deslorelin injection [BioRelease Deslorelin injection] intramuscularly).

Treated mares were examined once daily to confirm ovulation. Mares were then examined for pregnancy on day 14 post-ovulation, at which time 10 mg prostaglandin F2 J was administered intramuscularly to induce abortion or return to estrus. Each mare received a minimum of 2 weeks' sexual rest before being reassigned to another breeding trial.

Analysis of variance procedures were used to evaluate differences in interval to ovulation among treatments, and chi-square was used to evaluate proportional data.

RESULTS

Results were presented in Table 1. The interval to ovulation (*P* *R* .06) tended to be shorter for Group OVU than Group hCG mares but did not differ (*P* *J* .10) from Group DES mares (*P* *J* .10). Proportion of mares ovulation within 2 days of treatment did not differ among treatment groups (*P* *J* .10). All products used to induce ovulation resulted in acceptable response rates for use in clinical practice.

Table 1. Mean values (J SDs) for interval from treatment to ovulation and percentage of mares ovulating within 2 days in 112 estrous periods of 39 Quarter Horses or Thoroughbred mares treated on the first day that a J 347 mm diameter follicle was detected with either injection of 2500 units hCG (Group hCG), 1.5 mg short-release deslorelin (Group DES), or 21 mg deslorelin implant (Group OvtJ)

VARIABLE	hCG (n = 29)	DES (n = 17)	OVU (n = 66)
INTERVAL TO OVULATION^b	2.2 J 0.9 d ^a	2.0 J 0.4 d ^{a,b}	1.9 J 0.5 d
MEDIAN	2.0 d	2.0 d	2.0 d
OVULATIONS WITHIN 2 DAYS	83%	94%	92%

^{a,b}Means with different superscripts tended to differ.

DISCUSSION

Under the restrictions of this study (ie, once daily examinations), the percentage of mares ovulations within 2 days of treatment was similar among products. Ovulation rates within 2 days of treatment were also similar to those reported in previous studies using hCG^{1-9,18,19} or Ovuplant^{3,6-9,19-21}; therefore, injectable deslorelin was found to be suitable for routine use in broodmares.

Use of the short-term-release injectable deslorelin in prospective trial involving more frequent examinations will be required to more precisely determine variation in timed insemination protocols. In addition, a prospective study designed to confirm that there is no delayed return to estrus associated with the use of this product would be valuable. A recent study evaluating ovulation rates with the short-term-release injectable deslorelin in postpartum mares found no suppression of follicular development during subsequent cycles.

22

Acknowledgments

The authors wish to thank BET Laboratories and Fort Dodge Animal Health for graciously providing the deslorelin products used in this study.

REFERENCES

1. Loy RG, Hughes JP. The effects of human chorionic gonadotrophin on ovulation, length of estrus, and fertility in the mares. *Cornell Vet* 1966;56:41-50.
2. Sullivan JJ, Parker WG, Larson LL. Duration of estrus and ovulation time in nonlactating mares given human chorionic gonadotropin during three successive estrous periods. *JAVMA* 1973;162:895-8.
3. Voss IL, Pickett BW, Burwash LD, Daniels WH. Effect of human chorionic gonadotropin on duration of estrous cycle and fertility of normally cycling, nonlactating mares. *JAVMJ* 1974;165:704-6.
4. Ducharop G, Bour B, Combarous Y, Palmer E. Alternative solutions to hCG induction of ovulation in the mare. *J Reprod Fert* 1987;35(Suppl):221-8.
5. McKinnon AC, Nobelius AM, del Marmol Figueroa ST, Skidmore J, Vasey JR, Trigg TE. Predictable ovulation in mares treated with an implant of the GnRH analogue deslorelin. *Equine Vet J* 1993;25:321-3.

6. Barbacini S, Zavaglia G, Gulden P, Marchi V, Necchi D. Retrospective study on the efficacy of hCG in an equine artificial inemination program using frozen semen. *Equine Vet Ed* 2000;12:404-10.
7. Janderwall DK, Juergens TD, Woods GL. Reproductive performance of commercial broodmares after induction of ovulation with hCG or Ovuplant (deslorelin). *J Equine Vet Sci* 2001;21:539-42.
8. Blanchard TL, Brinsko SP, Rigby SL. Effects of deslorelin or hCG administration on reproductive performance in first postpartum estrus mares. *Theriogenology* 2002;58:165-9.
9. Samper JC, Jensen S, Sergeant J, Estrada A. Timing of induction of ovulation in mares treated with ovuplant or chorulon. *J Equine Vet Sci* 2002;22:320-3.
10. Roser JF, Kiefer BL, Evans JW, Neely DP, Pacheco DA. The development of antibodies to human chorionic gonadotropin following its repeated injection in the cyclic mare. *J Reprod Fert* 1979;27(Suppl):173-9.
11. Wilson CC, Craig ED, Hughes JP, and Roser JF. Effects of repeated hCG injections on reproductive efficiency in mares. *J Equine Vet Sci* 1990;110:301-8.
12. Mumford EL, Squires EL, Jochle E, Harrison L, Nett Tm, Trigg TE. Use of deslorelin short-term implants to induce ovulation in cycling mares during three consecutive estrous cycles. *An Repro Sd* 1995;39:129-40.
13. Jöchle W, Trigg TE. Control of ovulation in the mare with Ovuplant: a short-term-release implant (STI) containing the GnRH analogue deslorelin acetate: Studies from 1990 to 1994. *J Equine Vet Sci* 1994;14:632-44.
14. Jöchle W, Merkt H, Waberski D. Control of ovulation in the mare using a subcutaneous implant: effects on stallion use. *Equine Prac* 1997;19:10-12.
15. McCue PM, Farquhar Vj, Carnevale EM, Squires EL. Removal of deslorelin (Ovuplant) implant 48 h after administration results in normal interovulatory intervals in mares. *Theriogenology* 2002;58:865-70.
16. Wendt KM, Stich KL, Blanchard TL. Effects of deslorelin administration in vulvar mucosa, with removal in 2 days, in foal-heat mares. *Proc 48th Ann Mtg Am Assoc Equine Prac* 2002;:61-4.
17. Burns PJ, Thompson Jr O, Donahue F. (1997) Pharmacodynamic evaluation of the SABER delivery

system for the controlled release of deslorelin acetate for advancing ovulation in cyclic mares. Proc 24th Mt Symp Control Rel Bioact Mater, Stockholm, Sweden 24,737-738.

18. Voss IL, Sullivan JJ, Pickett SW, Parker WG, Burwash LD, Larson LL. The effect of hCG on duration of oestrus, ovulation time and fertility in mares. J Reprod Fert 1975;23(Suppl):297-301.
19. Palmer E, Jousset B, Synchronization of oestrus in mares with prostaglandin analogue and hCG. J Reprod Fert 1975;23(Suppl):269-274.
20. Meinert C, Silva JF, Kroetz I, Klug E, Trigg TE, Hoppen HO, et al. Advancing the time of ovulation in the mare with a short-term implant releasing the GnRH analogue deslorelin. Equine Vet J 1993;25:65-ES.
21. Farquhar VJ, McCue Pm, Vanderwall DK, Squires EL. Efficacy of the GnRH agonist deslorelin acetate for inducing ovulation in mares relative to age of mare and season. J. Equine Vet Sci 2000;20:722-4.
22. Stitch KL, Wendt KM, Blanchard TL. (in press). Effects of a new injectable short-term-release deslorelin in foal-heat mares.