BIBLIOGRAPHIC STUDY: PROTOCOLS FOR THE INDUCTION OF OVULATION IN THE MARE

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Abstract Although various regimes are available, some are specific to cycling mares during the ovulatory season and noncycling mares during anovulatory or transitional season and early postpartum. In this regard this paper discusses and summarizes the basis for the use of some regimens for controlling ovulation in the mare.

For controlling the estrous cycle of the cycling mare there are some conventional regimens and novel methods. Before beginning any regimen with the help of ultrasonography or transrectal palpation the reproductive tract should be assessed and then a decision about when to use one regimen over another can be taken. The most common hormonal treatments used in the regimens are presented below.

The natural form of PgF2α and some of its analogues have been used in mares to induce luteal regression and hasten estrous and ovulation. Treatment with native PgF2α (dinoprost, 5-10 mg/dose36) may induce some undesirable side effects, that’s why analogues (cloprostenol ,100-250µg/dose36; luprostiol 7,5 mg/dose3 ) that produce less side effects but with a potent luteolytic action are sometimes preferred . Treatment with PgF2α can be done by any parentheral routes, but the most common used is the intramuscular injection. A recent study involved administration of PgF2α at one-tenth the conventional dose (dinoprost .0.5 mg) into the sacral-lumbar space at mid-diestrus1. Results indicated a significant and sustained decrease in systemic levels of progesterone 24 hours after the sacral-lumbar injection, which was similar to the changes obtained in mares that received the conventional dose intramuscular.

A regimen for the induction of ovulation consists in a PgF2α injection (day1) followed by an hCG treatment (day 7-8) and another PgF2α administration (day 15) followed by hCG treatment (day 21-22). The interval between the end of the treatment and the ovulation time is of 2-4 days17.

The concept of using progestogen treatment during the estrous cycle is to prolong or extend the cycle by inducing an artificial progestational phase after spontaneous or induced regression of the corpus luteum. Progesterone has a negative feed-back effect on luteinizing hormone (LH) secretion from the anterior pituitary gland. Progestogen suppresses LH to levels that are inadequate to cause ovulation.

A regimen available consist in giving progesterone ( 150 mg/dose3) or altenogest daily for 8 to 12 days and to give PgF2α at the end of progesterone treatment to ensure the regression of primary or secondary corpus luteum. PRID-Spirals or CIDR-B-Sponge can also be used intravaginal for 8 days5. Estrus may be expected within 2 to 5 days, or hCG can be used to reduce the interval to ovulation. Since this regimen does not control the follicular development estrogen can be used as a potent inhibitor to control follicular development to
further ovulation synchrony. Common regimen involves the combined intramuscular injection of progesterone (150 mg) and estradiol (10 mg) for 10 days, beginning at random stages of the estrous cycle. Treatment with \( \text{PgF}_2 \alpha \) is given on the last day of steroid treatment. The results attested that a high degree of ovulation synchrony (81%) occurred between 10 to 12 days after \( \text{PgF}_2 \alpha \) treatment. This regimen has also been used with hCG when the diameter of the largest follicle reached >35 mm to ensure a more predictable ovulation.

Follicle ablation combined with \( \text{PgF}_2 \alpha \) and hCG treatments can be used as an alternative approach. Four days after ablation and aspiration of all follicles greater than 10 mm in diameter luteal regression can be induced with \( \text{PgF}_2 \alpha \) (cloprostenol 250 \( \mu \)g/dose) given twice, 12 hours apart. The 4 days interval is necessary for the luteinisation of the corpus luteum and the remaining tissue after ablation. Finnaly hCG (1500 UI) is given when the largest follicle is greater than 30 mm. The results indicated development of a new group of follicles in 1-3 days after ablation. 96% of the mares ovulated within 48 hours after hCG treatments. The interval from the start of the regimen (the follicular ablation) to the ovulation was of 10-14 days with 50% shorter than with conventional regimen of using progesterone or progesterone plus estradiol.

Human chorionic gonadotropin (hCG) has been used for over 40 years for induction of ovulation in mares and is one of the most commonly administrated hormones for equine reproduction management. hCG can be used to shorten the interval from estrus to ovulation. There is no standard dose of hCG used to induce ovulation; a single dose can range from 1000 to more than 6000 UI (1500 to 5000 UI). Typically the treatment with hCG is done when the largest follicle reaches at least 35 mm in diameter during estrus. In 80% of mares ovulation occurs within 48 hours. Administration of 1500-330 UI of hCG to mares on or after their second day of estrus will cause > 80% to ovulate within 48 hours.

With hCG use there is always a potential of antibody production stimulation because hCG is a foreign protein to the mare. In one study mares continued to ovulate, maintain pregnancy and foal in the presence of high hCG antibodies. It was also noted that mares with high antibody titers still ovulated spontaneously because the antibodies did not react with equine luteinizing hormone (LH). Because of the potential decrease in efficacy with repeated use it is recommended to use hCG not more than once or twice during a breeding season. If a timed ovulation is required for additional estrous cycle it is recommended that an alternative ovulation-inducing agent such as deslorelin acetate be used.

A convenient and efficacious alternative agent to hCG with the advantages of avoiding hCG immunogenicity and hasten ovulation during estrus is represented by GnRH. Native GnRH (gonadorelin, 2-5 mg/dose) or analogues of GnRH (buserelin, 20-40 \( \mu \)g/dose) have been given to mare in estrus when the size of the largest follicle is greater as 30 mm. Buserelin 20 \( \mu \)g I.V every 12 hours induces the ovulation in 24-48 hours in 60-90% of the mares with at least a 35 mm follicle. Recently a biodegradable short-tern implant (Ovuplant) containing the GnRH analogue deslorelin 2.2 mg has become commercially available for use in mares (USA, Australia, Canada). Studies have indicated that when the implant is put in place (by a single injection, under the skin of the neck) when diameter of the largest follicle in greater than 30 mm a high percentage of mares (>80%) ovulate within 48 hours.

For inducing or hastening ovulation of the noncycling mare the most common regimens are presented below.

Hastening the first ovulation of the season is most practically accomplished by artificially controlling of the daylight period. A common lighting regimen is to provide 16 hours of light and 8 hours of dark; however shorter periods of light (14.5 hours) may also be
Light can be supplemented in the afternoon and evening to give a total of 16 hours light each day. A dark period should not interrupt the transition from daylight to supplemental light and the lighting program should be consistently followed each day. The light should be bright enough for you to read the small print of a newspaper throughout the mare’s housing area. The average time from the start of the typical lighting regimen (200 Watt /Box) to the first ovulation has been between 60 and 80 days. In this regard starting the light regimen between November 15 and December 1 results in the onset of the ovulatory season around 15 February. The same thing can be done in the end of the ovulatory season for the extension with 1-2 months of the ovulatory season into the fall by providing the same 16 hours of light regimen.

The efficacy of progestogen treatment alone for hastening the ovulatory season in transitional mares is equivocal. It has been suggested that prolonged progestogen treatment can inhibit pituitary release of LH so that at the end of the treatment an accumulation occurs and the systemic levels. This will be sufficient to stimulate follicle maturation and ovulation. It appears that progestogen treatment alone can synchronize the first ovulation of the year, especially when mares are in the transitional period with large ovarian follicles (>20 mm). Progesterone can be administered as an oily-based intramuscular injection, orally as a synthetic progestogen (Altrenogest-EquineRegumate) or by using a silastic progesterone-realizing intravaginal device. One regimen is to administer progestogen (progesterone 150 mg/day or altrenogest 0.44 mg/kg/day) for 10-15 days when the largest follicle is at least 20 mm. Ovulation may occur in about 12 days after cessation of treatment.

Another regimen has been to expose anestrous mares to control lighting for 60 days before the start of the progestogen treatment and to administer hCG on the second day of estrus. A PRID-Spiral (Progesterone Releasing Intravaginal Device) or a CIDR-Sponge (Controlled Internal Drug Releasing Device) can be administered intravaginal for 12 to 14 days, followed by a Pgl&ta; treatment and than 3000 UI hCG, when the biggest follicle is >35 mm. The ovulation can occur in 20 days from the begining of the treatment.

hCG alone can be used to induce or to hasten the first ovulation. In one study, an intravenous injection of hCG (3300 UI) was given when the largest follicle attained 40 mm diameter and behavioral estrus was displayed for at least 3 days during the transitional period. Results indicated that 89% of the mares ovulated in 1 to 6 days after hCG treatment. It appears that hCG can be used alone to hasten or ensure ovulation in late-transitional mares when diameter of the largest follicle is greater than 30 mm and characteristic signs of estrus are displayed for several days. Administration of higher doses will normally produce a more rapid effect, although doses over 4500 UI are associated with ovulation but lower pregnancy rate.

GnRH has been use not only in cycling mares but also in noncycling mares to induce ovulation in “deep anestrous” mares and to hasten ovulation in transitional mares. There is a limited data available in witch the clinicians claim a success treatment with repeated implantation of GnRH superagonists such as deslorelin, or repeated administration of GnRH agonists such as buserelin. There have been some discussion of subsequent prolonged luteal phase in mare treated with deslorelin.

Numerous studies have indicated that administration of GnRH in a frequent (pulsatile) intermittent (once every 12 hours), or continues manner stimulated follicular growth, maturation and ovulation in anestrous mares. The duration of the treatment, the percentage of mares ovulating in a defined time, and subsequent maintenance of pregnancy are all related to the degree of follicular development at the start of the treatment. The most common method of delivering GnRH is by intramuscular or subcutaneous injections twice daily for
about 2 to 3 weeks or until the first ovulation of the year. With the use of a GnRH analogue (buserelin) to transitional mares in February, subcutaneous injections of 10-40 µg every 12 hours for 21-28 days or until ovulation have resulted in 47% to 78% of the mares ovulating within 3 weeks from the start of the treatment. 

Although artificial control of photoperiod is probably still the most efficient nonhormonal method for hastening the ovulatory season, other factors along the neural-hormonal pathway, apart GnRH, may provide alternative methods for controlling the length of seasonal anestrus. Dopamine antagonists can hasten the ovulatory season in mares through the inverse relationship between prolactin and dopamine in the mare. The systemic levels of prolactin are low during anovulatory season and cerebrospinal fluid levels of dopamine high. When a dopamine receptor blocker was given to mares during the anovulatory season, circulating concentrations of prolactin increased in association with increased follicular growth. The mechanism by which the dopamine-prolactin interaction exerts its effect at the level of the ovary is unknown. Investigators have examined the potential of using dopamine D-2 antagonists as an alternative hormonal method of hastening the ovulatory season.

Domperidone and sulpiride are two antagonists of dopamine with a low prevalence of side effects that have been recently evaluated (are not licensed for use in the mare). In separated studies, anestrous mares were treated daily with intramuscular injections of either domperidone (1.1 mg/kg) or sulpiride (200 mg/mare) beginning from middle January to the first days of February for 55-58 days, or until the first ovulation. The first ovulation in the season occurred in 27-41 days from the beginning of the treatment (12-24 days). Consequently the ovulatory season can be hastened by as much as 2.5 month with dopamine D-2 antagonists. Sulpiride can be administrated in a dose of 0.5 mg/kg.

A poor management of breeding can be one of the most important causes of reproductive inefficiency in the horse. Most of the problems result from a failure to appreciate either the seasonal nature of reproduction in the horse, or the fact that mares have a variable estrous cycle pattern even during the ovulatory season. A thorough understanding of the breeding management and careful attention to the specific treatments and regimes for a breeding program should maximize the chances of success.

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