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INDUCTION OF ESTRUS AND OVULATION IN MARES: WHY SOME AND OTHERS DO NOT RESPOND?

Inducción de estro y ovulación en yeguas: ¿Porqué algunos y otros no responden?

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RESUMEN

Los dos procedimientos mas comunes en el manejo reproductivo de la yegua involucre la inducción de la luteólisis y ovulación. A pesar de estos dos efectos se logran con mucho éxito en la mayoría de los casos, hay una serie de condiciones fisiológicas que determinan el éxito o el fracaso en la respuesta de la yegua. Está bien documentado que el inicio del estro en una yegua que está siendo tratada con prostaglandína en el diestro es en promedio 3 a 4 días después, mientras que la ovulación ocurrirá a 8-10 días. Sin embargo, el diámetro folicular, así como el estado del folículo en el momento del tratamiento prostaglandína determina el intervalo entre tratamiento a la aparición del estro y el tratamiento a la ovulación que podría oscilar entre 48 horas a 12 días. La ovulación es rutinariamente inducida con gonadotrofina coriónica humana (hCG), LH recombinante (rLH), o Deslorelin análogo de GnRH. Existe reportes que afirman de que la ovulación ocurre alrededor de 36 horas (promedio) después del tratamiento, pero la eficacia puede ser determinada por día en estro, así como la madurez folicular con cualquiera de estas hormonas. El uso adecuado que de las hormonas para inducir ovulación es una herramienta invaluable para el manejo reproductivo y momento de cruzamiento.

INTRODUCTION

The use of ovulatory inducing agents is a key tool in the breeding management of mares. In order to maximize the efficiency of ovulatory inducing hormones it is imperative to have a clear understanding of the physiology and the dynamics of follicular growth during the mare's estrous cycle. The estrus period is characterized by receptivity to the stallion, cervical relaxation, presence of a large or dominant follicle and endometrial edema. The duration of behavioral heat is on the average 5 to 7 days but can vary widely between mares. The diestrus period is characterized by lack of stallion receptivity, presence of a corpus luteum, a tight cervix and lack of endometrial edema (circulating progesterone levels > 2 ng/ml). Although the normal mare diestrus lasts approximately 15 days, mares can, and often do, develop large preovulatory size follicles during diestrus.

MONITORING OF THE ESTROUS CYCLE

Ultrasonographic examination of the reproductive tract of the mare has become standard practice. Monitoring and determination of the stage of the estrous cycle, early pregnancy diagnosis, diagnosis of pathological reproductive conditions and monitoring responses to uterine therapies are some of the uses of ultrasonographic technology in equine reproduction. .

In order to implement therapies to hasten equine ovulation, the presence, detection and interpretation of endometrial edema is critical. Normal mares under the influence of estrogen will have edematous hyperplasia of the endometrial folds. The endometrial edema increases progressively during the first few days of estrus and decrease as the mare approaches ovulation (Samper *et al.*, 1997). Alterations of this normal pattern such as the presence of endometrial edema after ovulation or during diestrus could be an indication of endometrial inflammation or an underlying problem.

Maximal pregnancy rates are obtained when mares are bred within 48 hours prior to ovulation by natural mating, 12-24 hours prior with cooled shipped semen and less than 12 hours with frozen semen. In order to breed mares at these "ideal" times, it is imperative that estrus be detected and ovulation be predicted accurately.

INDUCTION OF ESTRUS

In the normal cycling mare, estrus is induced exclusively by terminating the luteal phase with an injection of prostaglandin. The author use an intramuscular injection of 5 mg of prostaglandin F 2 alpha or 250 ugs of cloprostenol for this purpose as early as 5 days post ovulation. Onset of estrus and ovulation after a prostaglandin treatment on the average occurs

in 3-4 and 8-10 days respectively. However, progesterone does not suppress FSH and therefore follicular development continues to occur during diestrus. Consequently often there are follicles of different sizes and different stages of growth during the progesterone dominated phase. When there is a large size follicle in the growing phase present on the ovaries at the time of treatment, ovulation is possible as early as 72 hours after treatment without overt signs of heat. On the other hand, if the follicle has reached its maximal diameter during the progesterone dominated phase this follicle will inevitably regress and a new cohort of follicles will have to be recruited and estrus and ovulation will take several days (Samper *et al.*, 1993).

Clinically mares with a large follicle that is in the growing phase will display a significant degree of endometrial edema within 24 hrs post-treatment. Mares with large atretic follicles will not display edema for 3-5 days after treatment.

INDUCTION OF OVULATION

The main advantages of having ovulation at a predictable time include:

1) Breeding of mares to a highly booked stallions only one service per cycle; 2) Facilitating appointment servicing for mares transported to stallions; 3) Insuring a single insemination in attempt to reduce uterine contamination (particularly in mares with delayed uterine clearance or susceptibility to uterine infections); 4) Increasing the likelihood of inseminating close to ovulation when using cooled transported or frozen semen or stallions with low fertility; 5) Aiding spacing the time between natural breedings in mares, presented in estrus at the same time for the same stallion; 6) Helping ovulation synchronization between donor and recipient mares in embryo transfer programs and 7) Reducing labor and veterinary costs.

Due to the advantages of having ovulations at a predictable time as well as the increase in pregnancy rates when mares are bred close to ovulation, many veterinarians are relying on pharmacological agents to induce ovulation. Maximal effectiveness of these agents occur in mares with obvious endometrial edema, a relaxed cervix and a follicle of at least 35 mm diameter. Presently there are three available products to induce ovulation in mares: A) Human Chorionic Gonadotrophin (hCG) and B) The GnRH analogue, Deslorelin. and C) Recombinant equine LH (rLH).

A) hCG (Chorulon®) is a large protein hormone with LH-activity. The recommended dose of hCG varies among practitioners but ranges between 1,500 and 3,300 international units (IU) given intravenously or intramuscularly. In a recent report by Barbaccini *et. al.* (2000) 75% of hCG-induced ovulations occurred between 24 and 48 hours after treatment. However a significant number of mares ovulated within 12 hours of treatment while others ovulated more than 48 hours post-treatment. In the authors experience hCG effectiveness is reduced when used multiple times over the breeding season in the same mare. The author's recommended dose is 2,500 IU administered intravenously given 12-24 hours prior to the breeding when mares are going to be bred by artificial insemination. In natural breeding situations mares can be treated at the time of breeding.

B) Deslorelin (Ovuplant™) is a biodegradable short-term implant containing 2.2 mgs of the GnRH analogue Deslorelin (McKinnon et al. 1993). The implant comes as a preloaded syringe with an attached needle to facilitate placing the inert matrix subcutaneously. Recent studies indicate that OvuplantTM induces ovulation predictably between 38 and 42 hours after treatment (Samper *et al.*, 2002). Some mares, if not pregnant, may have a day delay in returning to the next natural estrus (McCue *et al.,* 2002). A small percentage of mares induced to ovulate with OvuplantTM have a delay of several days or weeks in returning to estrus, seemingly exacerbated when prostaglandin is used on day 5 or 6.(McCue et al 2002) There is no way to predict which mares will experience this delay but it may be avoided by removing the implant shortly after ovulation. Easy access for OvuplantTM removal is facilitated by submucosal placement in the vulva instead of the neck, which is the manufacturer's recommended site. The removal of the pellet results in no deleterious effect on the subsequent cycle when compared to control mares or those treated with hCG (McCue *et al.*, 2002).

Compounded Deslorelin is also available from multiple pharmacies in a liquid form. The injection of 1.5 mgs IM induces ovulation reliably 40-46 hrs after injection. There is no evidence of a delay in return to estrus in mares treated with injectable deslorelin.

Although hCG and OvuplantTM are the only approved products for induction of ovulation in horses, anecdotal evidence by practitioners would suggest that gonadotropin releasing hormone (GnRH) is effective. GnRH has to mimic the natural pulsatile secretion from the hypothalamus and thus must be administered at doses of 20 to 25 micrograms IM or SQ two or three times daily for 2 to 3 days. This regime makes GnRH impractical for induction of ovulation in mares. Mare's ovulating after a single injection of GnRH were committed to ovulating regardless of the therapy. However GnRH can be useful in inducing heat and ovulation in mares with unexplained ovarian inactivity during the normal ovulatory season. In most cases twice a day injections for 2 to 3 weeks will be necessary to stimulate follicular development.

Prostaglandin analogues have been used to induce ovulation. Further studies have not been able to reproduce the results of those preliminary studies and therefore prostaglandin F 2 alpha or any of its analogues are not recommended for ovulation induction. However veterinarians must be cautious about the fast ovulations in response to prostaglandin when mares have a mature corpus luteum and a large diestral follicle.

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