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Deslorelin acetate and human corionic gonadotropine and its ovulatory response in postpartum mares

Acetato de deslorelina y gonadotropina coriónica humana y su respuesta ovulatoria en yeguas postparto

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ABSTRACT

In order to evaluate the rate of follicular growth, the response time to ovulation and the percentage of ovulation in Quarter Mile postpartum mares, two treatments (T) were applied, the first with deslorelin acetate (DA) and the second with human chorionic gonadotropin (hCG). The study was conducted during January to June 2018, with sixteen 7-year-old mares, 450 kg of weight and 4.5 deliveries on average. Ovarian follicular diameter was evaluated by real-time transrectal ultrasonography in response to experimental treatments, in mares with ovarian follicles ≥ 35 mm in diameter: T1 (n= 8): Application of 1 mg of DA intramuscularly (IM), and T2 (n= 8): Application of 2500 IU of hCG via IM. There were no differences (P> 0.05) in the rate of follicular growth (AD: 0.48 ± 0.006 mm and hCG: 0.45 ± 0.035 mm), the time of response to ovulation (AD: 46.75 ± 0.48 h and hCG: 56.00 ± 8.00 h) and the percentage of ovulation (AD: 8/8, 100% and hCG: 7/8, 87.5%) in the postpartum mares evaluated. It is concluded that deslorelin acetate and human chorionic gonadotropin respond to ovarian activity in Quarter Mile postpartum mares with ovarian follicles ≥ 35 mm in diameter.

Keywords: GnRH analogue, hCG, equine reproduction, ovulation, folliculogenesis

RESUMEN

Con la finalidad de evaluar la tasa de crecimiento folicular, el tiempo de respuesta a la ovulación y el porcentaje de ovulación en yeguas postparto Cuarto de Milla se aplicaron dos tratamientos (T), el primero con acetato de deslorelina (AD) y el segundo con gonadotropina coriónica humana (hCG). El estudio se realizó durante enero a junio de 2018, con dieciséis yeguas de 7 años, 450 kg de peso y 4.5 partos en promedio. El diámetro folicular ovárico se evaluó mediante ultrasonografía transrectal a tiempo real en respuesta a los tratamientos experimentales, en yeguas con folículos ováricos ≥ 35 mm de diámetro: T1 (n= 8): Aplicación de 1 mg de AD vía intramuscular (IM), y T2 (n= 8): Aplicación de 2500 UI de hCG vía IM. No hubo diferencias (P > 0.05) en la tasa de crecimiento folicular (AD: 0.48±0.006 mm y hCG: 0.45±0.035 mm), el tiempo de respuesta a la ovulación (AD: 46.75±0.48 h y hCG: 56.00±8.00 h) y el porcentaje de ovulación (AD: 8/8, 100% y hCG: 7/8, 87.5%) en las yeguas postparto evaluadas. Se concluye que los tratamientos hormonales con acetato de deslorelina y la gonadotropina coriónica humana responden en la actividad ovárica en yeguas postparto Cuarto de Milla con folículos ováricos ≥ 35 mm de diámetro.

Palabras clave: Análogo de GnRH, hCG, reproducción en equinos, ovulación, foliculogénesis.

INTRODUCTION

Reproduction is considered one of the most important phases in the life of mares, mainly in those whose zootechnical purpose is to be reproductive (Cortés-Vidauri *et al*., 2018). Within the gonadotropic population, gonadotropin-producing cells located in the *o* pair and in the *tuberalis* pair of the pituitary and heterogeneity in the storage pattern of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are considered the basis for the differential regulation of gonadotropin secretion during the reproductive cycle (Aurich, 2011).

Increasing reproductive efficiency is the most important thing to have better use and intensification of the rate of genetic improvement of animals. Due to the photoperiod, the incidence of ovulations varies throughout the year, which limits the mare's reproduction; therefore, treating with hormone therapy plays a fundamental role (Ferris *et al*., 2012). Among the benefits of hormone therapy are an increase in the cycle period during the year, an increase in the number of ovulations, the possibility that the uterine environment favors embryonic development. Induction of labor, help in the treatment of uterine infections, and the contribution in the use of embryo freezing biotechnologies, *in vitro* fertilization and embryo vitrification (Faria and Gradela, 2010). also can be mentioned.

Ovulation induction has become a routine method in equine reproduction, since artificial insemination and embryo transfer require an accurate prediction of ovulation time, which supports the use of drugs (Cortés-Vidauri *et al*., 2018). Human chorionic gonadotropin (hCG) has been the first hormone used to induce ovulation in mares and is the most widely used; however, the frequent use of this hormone produces the formation of anti-hCG antibodies, with a subsequent loss of pharmacological efficacy (Figuereido *et al*., 2011).. Deslorelin Acetate (AD) is a drug created as an antagonist of the gonadotropin-releasing hormone (GnRH), and has the advantage that its repeated use does not decrease its effectiveness (Ferris *et al*., 2012).

Reproductive management protocols with GnRH in annestric mares to induce estrus and cyclicity provide evidence that there are multiple ovulations in some females with such treatment regimens. In this regard, applying deslorelin acetate with at least two follicles with diameters between 20 to 24 mm has been reported that could produce double ovulation in mares (Nagao *et al*., 2012).
Therefore, the objective of this study is to evaluate the response of hormonal treatments with deslorelin acetate and human chorionic gonadotropin in ovarian activity in postpartum Quarter Mile mares, with ovarian follicles ≥35 mm in diameter.

MATERIAL AND METHODS

Location of area of study. The study was from January to June 2018 carried ou,t at the Rancho "Mogotes", located in Aldama, Irapuato municipality, Guanajuato, Mexico. It is located at 20 ° 49' 23.77 " North Latitude and 101° 19' 33.80" West Longitude, at an altitude of 1700 meters above sea level, with a warm sub-humid climate, an average annual temperature of 20.5 °C and a rainfall of 692 mm (INAFED, 2018).

Experimental animals and management. Sixteen postpartum mares of the Quarter Mile breed, clinically healthy, 7 years old, weighing 450 kg and 4.5 calving on average, were used. The mares were kept in adequate feeding conditions and in good body condition, which is required for proper reproductive performance; represented in regular estrous cycles and good quality of the ovarian follicles. The present study was carried out in accordance with the standards for the use and care of research animals in accordance with the Official Mexican Standards NOM-024-ZOO-1995 and NOM-051-ZOO-1995 (NOM-024- ZOO-1995; NOM-051-ZOO-1995).

Experimental protocol and treatments. A complete design with randomized treatments was used. The mares were randomly assigned to one of two treatments (T, figure 1): T1 (n = 8) consisted on the application of 1 mg of deslorelin acetate (AD; Sincrorrelin®, Lab. Ourofino) per mare with follicular growth ≥ 35 mm in diameter. The T2 (n = 8): consisted on the application of 2500 IU of lyophilized human chorionic gonadotropin (hCG; CHORULON®, Lab. Merk Sharp & Dohme), for each mare with follicular growth ≥ 35 mm in diameter. Hormonal treatments were applied intramuscularly with 3 and 5 mL syringes (Terumo®) and a 21G (32 mm) hypodermic needle, after disinfecting the application area with cotton swabs moistened with alcohol.

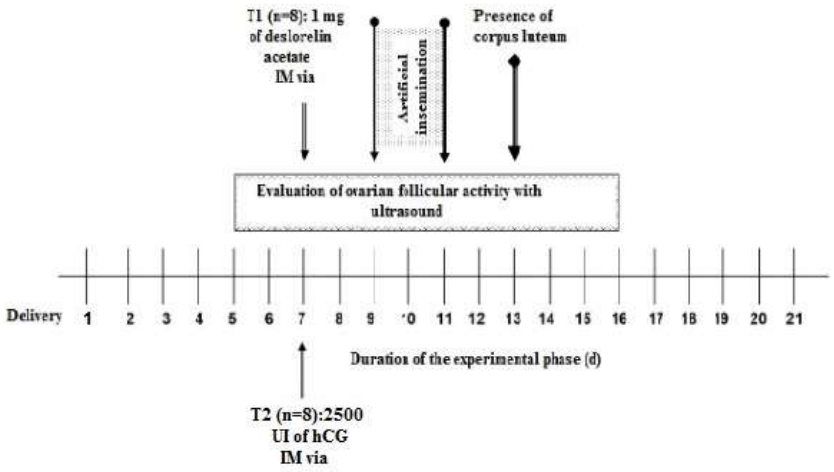

Figure 1. Reproductive management protocol in Quarter Mile mares

Evaluation of ovarian activity. All mares were explored by transrectal ultrasonography, in real time with a 7.5 Mhz transducer (CHISON ECO2, China); During the 9 and 11 days postpartum, known as "heat of the foal", to achieve pregnancy, a service was performed with semen refrigerated by artificial insemination (AI). Ovarian follicular diameter was evaluated every 24 h from the start of postpartum oestrus, until ovulation was detected by anechogenic imaging in the ovary due to the presence of the hemorrhagic body, after AI. The diameter of the dominant follicle was considered the measurement recorded on the day prior to the appearance of the corpus luteum. When observing ovarian follicles greater than or equal to 35 mm in diameter, the hormonal treatments T1: AD and hCG were applied. The ovarian follicular growth rate (mm), the response to ovulation (h) and the percentage of ovulation (%) were determined.

Statistical analysis. The data was analyzed with SAS (SAS Institute Inc, 2012). To analyze the ovarian activity data, an analysis of variance with repeated measures over time was performed; Tukey's test was used for multiple comparison of means ($P < 0.05$). To analyze the response time to ovulation, the log rank test was used with the LIFETEST procedure, using the survival curves, and the χ^2 test was used to assess the ovulation response (percentage).

RESULTS AND DISCUSSION

Ovarian follicular development. The Quarter Mile postpartum mares treated with AD and hCG presented similar ovarian follicular development ($P > 0.05$), evaluated during the experimental phase (Table 1). The ovarian follicular growth rate was similar ($P > 0.05$) between treatments (AD: 0.48 ± 0.006 and hCG: 0.45 ± 0.035). No differences were found ($P > 0.05$) in the response time to ovulation (Figure 2) and in the percentage of ovulation (Table 2).

Table 1. Ovarian follicular development in Quarter Mile postpartum mares treated with deslorelin acetate and human chorionic gonadotropin

TREATMENT (T)	Follicular diameter (cm)				
	Day 5	Day 6	Day 7	Day 8	Day 9
T1 (n=8) Deslorelin Acetate	2.55 a	3.05 a	3.53 a	4.00 a	4.48 a
T2 (n=8) Equine chorionic gonadotropin	2.70 a	3.10 a	3.5 a	4.05 a	4.5 a
E.E.M.	0.18	0.11	0.05	0.05	0.08
P-value	0.4358	0.6704	0.6202	0.3559	0.7502

a: Means with a similar literal in the same column are the same ($P > 0.05$)

The administration of 1 mg of deslorelin acetate via IM when identifying a dominant follicle of 38 to 40 mm in diameter, reduced the ovulation time between 24 and 48 h and; therefore, it favored the number of services per conception, compared to the response of treatment with human chorionic gonadotropin used in the present study. This can be

because the percentages of conception explained and ovulation are 55% and 60%, respectively, after 14 to 40 hours of applying the hormones (Figuereido *et al.*, 2011). Ovulation in Quarter Mile mares, on average, occurs with follicles 40 mm in diameter (Rodríguez *et al*., 2013). The optimal time for the application of hCG is when the mare has a dominant follicle greater than or equal to 35 mm in diameter, with a dose of 3000 IU. Ovulation occurs between 24 to 48 hours after application (Dolezel *et al*., 2012).

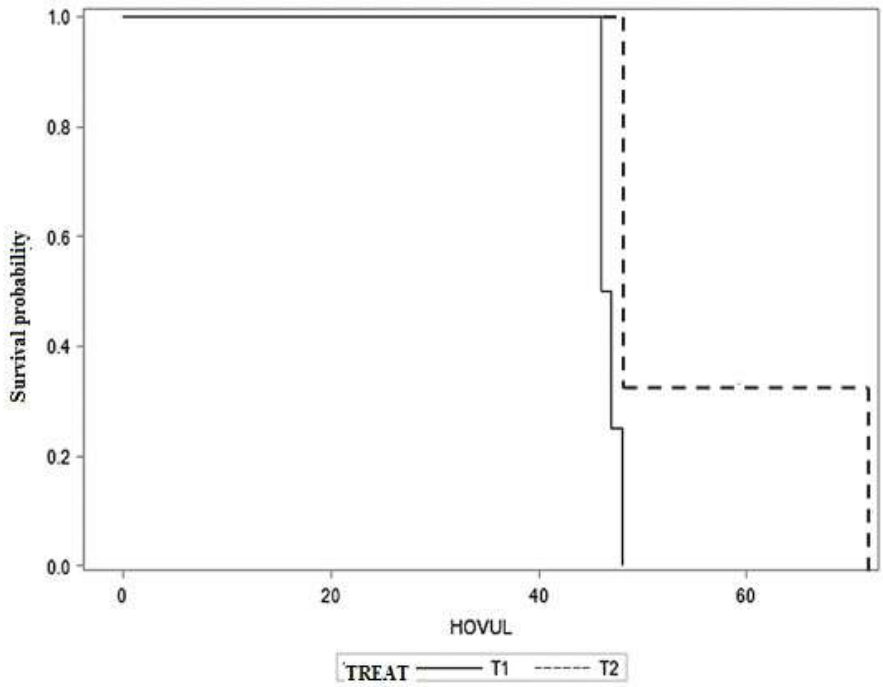

Figure 2. Survival curve for ovulation response time (h) in Quarter Mile mares, treated with deslorelin acetate (T1) and human chorionic gonadotropin (T2), HOVUL: Hours to ovulation

Response to ovulation. No differences were found (P> 0.05) in the response time to ovulation and in the percentage of ovulation (Table 2).

Table 2. Response to ovulation in Quarter mile mares treated with deslorelin acetate and human chorionic gonadotropin

Treatment (T)	Ovulation response time (h)	Ovulation (%)	Ovulation by right ovary (%)
(T1, n=8) Deslorelin acetate	46.75 ± 0.48 a	8/8 (100%) a	75.0 a
(T2, n=8) Human Chorionic Gonadotropin	56.00 ± 8.00 a	6/8 (87.5%) a	75.0 a

a: Means with a similar literal in the same column are the same (P> 0.05).

The results of the present study coincide with those reported by Dolezel *et al*. (2012), who administered intravenously 3000 IU hCG during estrus in mares with a dominant follicle ≥ 35 mm in diameter, and observed that ovulations occurred between 12 and 48 h after treatment. In this regard, it is possible that the growth of the dominant follicle after applying the hCG dose was influenced by the size of the follicles at the time of treatment. Finan *et al*. (2016) found that 93.75% of the mares ovulated within 48 h after treatment with deslorelin via IM; unlike Chávez *et al*. (2018), who reported that the ovulation time was 43.13 ± 4.48 h and 69.00 ± 8.41 h for the mares treated with deslorelin acetate and the control treatment, respectively. 87.5% (7/8) of the mares treated with deslorelin acetate ovulated within 48 h; while only 37.5% (3/8) for those of the control treatment.

The differences observed between the studies could be due to the experimental sample size, or to an environmental, nutritional or race factor (Boeta *et al*., 2006). The ability to induce ovulation at a predictable time has increased the efficiency of equine breeding programs, where benefits include a decrease in the number of servings per cycle for studs; which allows for greater mare registries annually (Finan *et al*., 2016).

Equine reproductive management protocols stimulate ovulation induction to provide programmed ovulation in mares for optimal management of reproduction. In this regard, numerous studies have been reported on the efficacy of prostaglandins, GnRH, GnRH analogs and hCG in inducing ovulation in the mare (Yoon, 2012). Diameter, fluctuating shape of the dominant follicle, and endometrial folding have been reported to be considered in estimating ovulation prediction; however, they are not precise or standard enough (Ramírez *et al.*, 2010). Therefore, hormonal induction or synchronization of ovulation is important, which favors the determination of the optimal moment for insemination. The administration of human chorionic gonadotropin (hCG) represents the most frequent treatment method for this purpose (Dolezel *et al*., 2012). Conversely, anovulation is a normal physiological activity in the mare during the transition from spring to autumn; however, anovulatory follicular development occasionally occurs in the reproductive season. This can be explained because the follicles grow between 5 and 15 cm in diameter and persist for up to two months. These follicles produce abnormal estrous behavior and prolong the inter-ovulatory period (Ángel and Bran, 2010).

CONCLUSION

Hormonal treatments with deslorelin acetate and human chorionic gonadotropin respond to ovarian activity in postpartum Quarter mile mares with ovarian follicles ≥ 35 mm in diameter; therefore, the two hormonal treatments are viable options to control ovarian follicular development, and induce ovulation in postpartum quarter mile mares in reproductive management protocols.

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