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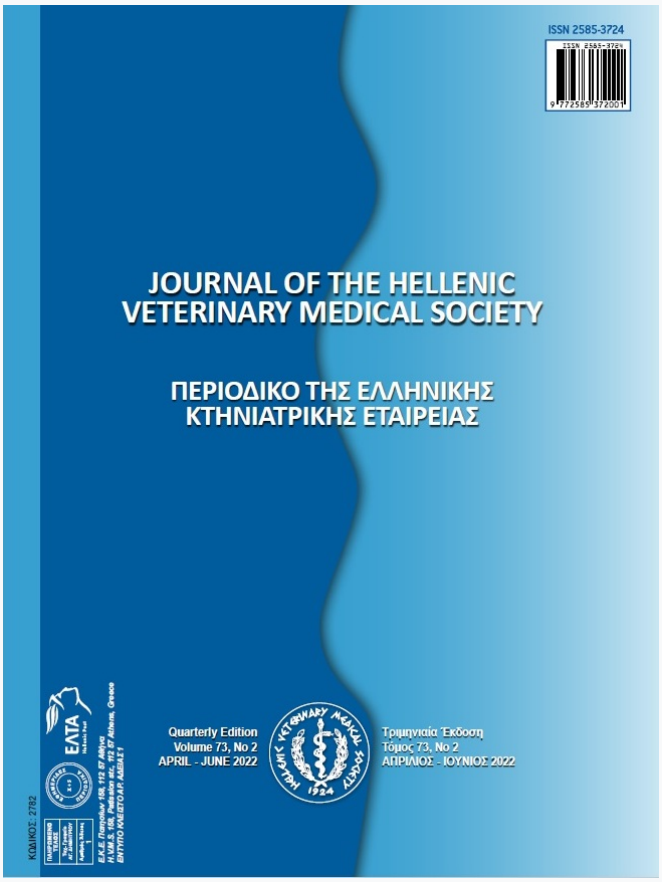

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Research article
Ερευνητικό άρθρο

Field observations on the use of Progestin device (PRID) for estrus and ovulation induction in anestrous Arab-Barbmares

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ABSTRACT: In the present study, we administered intravaginally a progesterone-releasing device (PRID) to acyclic Arab-Barb mares (n=39)in order to induce the first estrus with ovulation,for 11 days at different seasons: winter (n = 10), spring (n = 13), summer (n = 7) and autumn (n = 9). Twenty-seven of 39 mares responded to the PRID treatment with estrus and ovulation during the 42-day observation period; fewer mares were ovulated after treatment in winter (4/10, 40%),compared to thosein spring (9/13, 69%), summer (7/7, 100%) and autumn (7/9, 78%) ($P < 0.05$). At Day 2 of PRID treatment, mean progesterone concentrations were significantly increased in all mares in winter (7.20 ± 0.49 ng mL^{-1}), spring (7.30 ± 0.64 ng mL^{-1}), summer (7.5 ± 0.58 ng mL^{-1}) and autumn (7.60 ± 0.71 ng mL^{-1}) ($P < 0.05$) compared to Day 1. Total concentration of progesterone [area under curve (AUC)]during the treatment period revealed the highest values ($P < 0.05$)in spring (67.95 ± 2.40 ng $mL^{-1}h^{-1}$) and autumn (65.20 ± 1.37 ng mL^{-1} h^{-1}) compared with winter (54.19 ± 7.00 ng mL^{-1} h^{-1}) and summer (52.23 ± 3.32 ng mL^{-1} h^{-1}). In conclusion, administration of the PRID was able to induce estrus and ovulation in mares at different seasons of the year. However, the efficacy of the treatment was not satisfactory in all seasons (low response rate in winter) and the synchrony of intervals from removal of PRID to ovulation was not effective (especially in winter).

Keywords: Mare; estrus; ovulation; PRID; progesterone.

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INTRODUCTION

Mares are long-day seasonal breeders and start ovarian follicular activity during the spring. The ideal artificial breeding season for mares isfrom March to the first week of April. During this period, it is important to notice that there is a transition period characterized by delayed ovulation, andmares are not at their optimal reproductive potential (Handler et al., 2007). Moreover, mare breeders want foals born as soon as possible after the first of January (Mebarki et al., 2019), because, in the racing world, foals and yearlings are put into competition according to their year of birth. Moreover, anoestrus seasonality in the mare limits reproduction for a variable period. Mares have no sexual activity and their reproductive hormones are on basal levels during anoestrus. Thus, it is important to propose protocols for the induction of estrus during anestrous.

A systematic reproductive manipulation of the estrous cycle using exogenous compounds such as hormonal treatments and artificial light programs are used to induce the beginning of the breeding season in mares, allowing earlier ovulation in the year (Mateu-Sánchez et al., 2016). Several protocols have been utilized for estrus induction and ovulation in mare with ovarian inactivity such as: a) GnRH and GnRH agonist (Evans and Irvine, 1977; McKinnon et al., 1997); b) oral progestagens; (Webel and Squires 1982; Wiepz et al., 1988); c) progesterone administered parenterally (Alexander and Irvine 1991); d) progesterone releasing intravaginal device (Wittkowski et al., 1982; Ataman et al., 2000); e) FSH administration (Raz et al., 2009; Niswender et al,. 2004) and f) dopamine antagonists (Besognet et al., 1997; Panzani et al., 2011). In this study, the efficacy of progesterone (progesterone intravaginal device - PRID) was investigatedas a means of induction of the estrus and synchronization of ovulation in anestrous Arab-Barb-mares.

MATERIALS AND METHODS

Animals

A total of 42non-cycling and non-lactating Arab-Barb marescoming from breeding farms in the northeast of Algeria, aged from 5 to 23years, were included in this study. All mares spenta daily average of 8 hours on natural pastures. In addition, barley, hay or strawand a mineral vitamin complex were provided;water was freely available. Deworming was also performed at regular intervals. No artificiallight program was provided.

Treatments

Ultrasound and vaginal examinations were performed before treatment. Blood samples were also collected for determination of plasma concentrations of progesteronebefore each treatment; only mares with a true anestrus (no ovarian activityand progesterone concentration < 1ng mL^{-1}) and without infectious genital problems wereused in this study. A total of 42 mares received PRID, (PRID® Delta 1.55g progesterone, CEVASanté Animale, France) for 11 days (Day 1: day of device insertion;Day12: day of device removal).The insertion of the PRID was performed after a good washing and disinfection of the perineal region without the use of local antibiotics.

Three mares were excluded from the study (two mares lost their PRID and in one mare PRID provoked severe colics).The remaining 39mares were divided into four groups according to the season of experimentation, 10 mares in winter, 13 in spring, 7 in summer and finally9 in autumn.Uterus and ovaries were examined rectally before the insertion of PRID and every other day thereafter by palpation and ultrasonography (5-7.5MHz convex transducer; Mini Focus1402, BK Medical, Denmark). The mares were checked daily since the day of PRID removal until the detection of ovulating estrus. Examination for the onset of estrus was stopped after the detection of the first ovulatory estrus. If the mares did not have an ovulatory estrus (anovulatory estrus or anestrus) during 42 daysafter PRID removal, the treatment was considered as inefficient.

Blood sampling and hormone assays

Blood samples were collected daily by jugular venepuncture from Day 1 to Day 13 to determine serum progesteroneconcentrations. Blood samples were centrifuged immediately after collection over 10 min at 3000 g and serum wasstored at - 25 ± 6°C until assayed.Concentrations of progesterone were measured by enzyme-linked fluorescent assay (ELFA) using automated benchtop immunoanalyzer (Vidas®, bio Mérieux, France).

Cytological examination

On the day of PRID removal, mares were examined by vaginal inspection and vaginal smears were taken by using a cytobrush to assess the inflammatory reactions of the vaginal lining. Clinical signs of vaginitis were hyperemia, increased vascularization

and a mucopurulent discharge. Mares with neutrophilic granulocytes ≥ 5% among 200 cells counted on a smear, were classified as having an inflammatory reaction (vaginal inflammation).

Statistical analyses

As progesterone concentration in serumwas not normally distributed, non-parametric-tests were used throughout. We investigated the relationships between estrous manifestation and progesterone concentration with Wilcoxon signed rank test for comparisons between two groups and Friedman test among more than two groups of matched data, respectively. Results were considered to be significant at $P < 0.05$. A software program SAS mixed procedure (9.2version; SAS Institute, Inc., Cary, NC, USA)was used for all calculations., e.g. descriptive analyses (mean ± S.E.M.), area under curve (AUC), Wilcoxon signed rank test and Friedman testData arepresented as means ± S.E.M.

RESULTS

Clinical data (efficacy of treatment, vaginitis and vaginal cytology)

Failure to respond to treatment was defined by failure to ovulate within 42 days of PRID removal. Failure to respond occurred in 12/39 mares. No signs of estrus were detected in 9/12 mares (6/9 mares in winter, 1/9 mare in spring and 2/9 mares in autumn). In spring season, 3/12 mares manifested just one anovulatory estrus followed by a prolonged anestrus again. Twenty-seven mares responded to the PRID treatment with ovulating estrus. Significantly fewer anestrous mares ovulated after treatment in winter (4/10, 40%) when compared to mares in spring (9/13, 69%), summer (7/7, 100%) and autumn (7/9, 78%) ($P < 0.05$). Furthermore, intervals from removal of PRID to successive estrus did not differ among treatment groups (winter: 3.9 ± 0.4 days, spring: 3.7 ± 0.2 days, summer: 3.2 ± 0.2 days and autumn: 3.4 ± 0.5 days). Intervals from PRID removal to successive ovulations were longer in winter (19.75 ± 3.41 days; min: 14, max: 23), followed by spring (13.75 ± 5.42 days; min: 5, max: 22), autumn (12.25 ± 5.97 days; min: 5, max: 21) and summer (9 ± 3.74 days; min: 5, max: 14; $P < 0.05$). Comparison of ovulating follicle diameters after PRID treatment revealed no significant difference between seasons (winter: 4.25 ± 0.30 cm, spring: 4.34 ± 0.25 cm, summer: 3.91 ± 0.23 cm and autumn: 4.14 ± 0.55 cm).

All mares presented moderate vaginitis at PRID removal. Furthermore, the cytological examination showed a percentage of neutrophilic granulocytes greater than 5% (Fig.1) in all mares,which can be classified as vaginal inflammation.

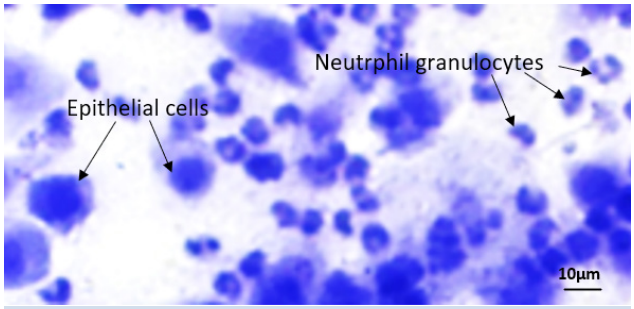

Figure 1. Inflammatory vaginal smear rich in neutrophils

Progesterone concentrations

Serum progesterone concentrations at PRID insertion (Day1) were less than 1.2 ng mL^{-1} in all mares.At Day 2 of PRID treatment, mean progesterone concentrations were significantly increased in all mares in winter, spring, summer and autumn, (7.20 ± 0.49, 7.30 ± 0.64, 7.5 ± 0.58 and 7.60 ± 0.71 ng mL^{-1}; $P < 0,05$; Fig. 2). Then, mean progesterone concentrations decreased steadily until removal of PRID, whereas all mares showed concentrations below 1 ng mL^{-1} at Day 13 (winter 0.22 ± 0.01; spring 0.28 ± 0.01; summer 0.27 ± 0.00 and autumn 0.47 ± 0.08 ng mL^{-1};$P > 0.05$). Total concentration of progesterone (AUC) during the treatment period (Fig. 3) revealed the highest values in spring (67.95± 2.40ng $mL^{-1}h^{-1}$) andautumn (65.20± 1.37ng $mL^{-1}h^{-1}$) compared to winter (54.19± 7.00 ng $mL^{-1}h^{-1}$) and summer (52.23 ± 3.32ng $mL^{-1}h^{-1}$; $P < 0.05$).

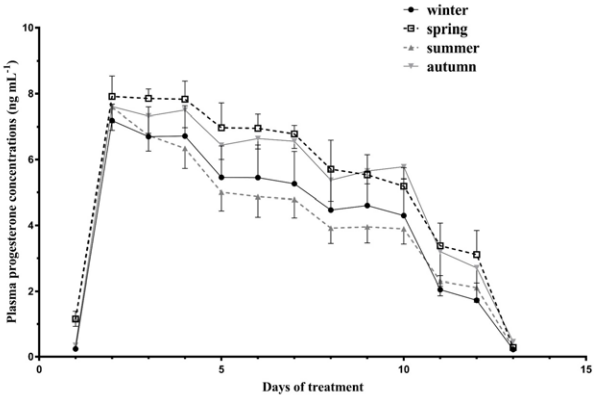

Figure 2. Daily serum progesterone concentrations in mares during PRID treatments at different seasons

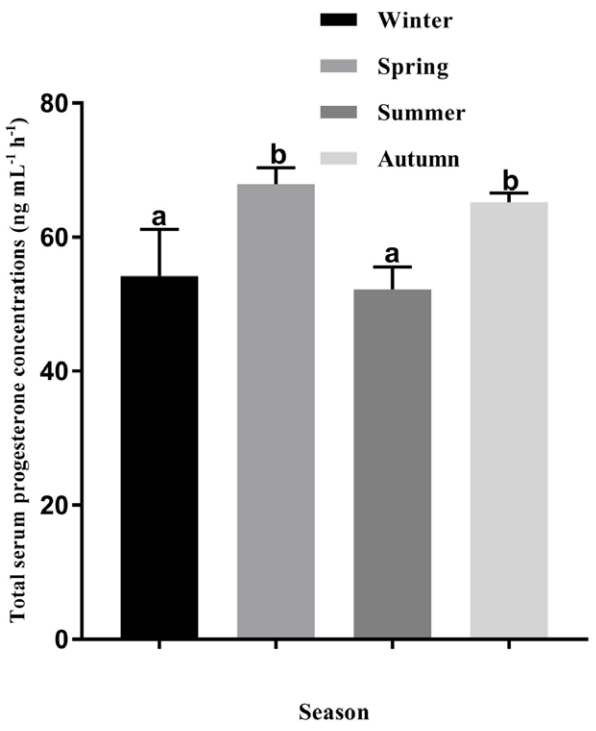

Figure 3. Total serum progesterone concentrations in mares during PRID treatments. Significant differences ($P < 0.05$) among seasons are marked by different superscripts (a and b)

DISCUSSION

In this study, the efficacy of PRID for estrous induction revealed acceptable results in anestrous mares. The manual placement of the devices in the vagina was easy to perform in this study as previously reported by Grimmett et al. (2002). Furthermore, the mares at pasture received the correct amount of drug every day, as it is demonstrated by plasma progesterone concentrations during PRID treatment.

A low rate of devices was lost. It is estimated that about 4% of mares expelled the coil, and the most PRIDs remained in place during the entire treatment period. PRID was originally developed for use in cattle (Broadbent et al., 1993; Uehlinger et al., 1995; Vanderwall et al., 2007). In cows, loss rates of 10 and 12% (Andresen et al., 1982; Newcombe, 2002) have been described. Among mares' losses rang from no losses (Arbeiter et al., 1994; Handler et al., 1999) for up to 5% (Taylor et al., 1982).

Although, most mares showed mild discomfort, 2.56% showed severe pain. The insertion of vaginal devices causes moderate vaginitis with clinical signs such as hyperemia and mucopurulent vaginal discharge, which disappeared within two to three days after the coil removal. However, the data from our study showed no signs of clinical endometritis or ascending cervicitis after PRID insertion without antibiotics. Local application of antibiotics to PRID insertion was recommended to reduce the incidence and severity of vaginitis (Rutten et al.,1986). Vaginal mucosa irritation (Arbeiter et al., 1994) and bacterial contamination by faeces and skin (Bulman et al., 1978) were supposed to contribute to the emergence of vaginitis caused by the intravaginal devices.

Treatment with the intra-vaginal device PRID for estrus induction revealed acceptable results in anestrous mares.Ovulation occurred in more than 69% of mares (except winter - 40%) which is similar to the resultsof Handler et al. (2006), who reported that more than half of the mares showed successful results of synchronization after PRID treatment. However, Alexander and Irvine (1991) reported thatthe ovulation rate had decreased to 37.5% in treated mares,which are consistent with the results ofother studies (Evans and Irvine, 1979; Palmer, 1979; Turner et al., 1981; Alexander and Irvine, 1991).Contrarily, Squires et al. (1999) concluded that the efficacy of PRID treatment for synchronization of ovulation was poor as demonstrated by low rates of suitably synchronized mares in all seasons.

In contrast, according to our data, the efficacy of the treatment was not satisfactory concerning ovulation synchronization, because intervals from PRID removal to ovulation varied within a wide range in all mares, especially those treated in winter.This may be due to the fact that the mares are in true period of seasonal anestrus (short days). During this period GnRH (Hart et al., 1984) and LH (Hart et al., 1984; Thompson et al., 1986) aremuch lowerregardless of the lack of progesterone.Similar observations werepreviouslyreported by Göhring et al. (1999). Handler et al. (2007) consider that their results are unsatisfactory in terms of the use of PRID for synchronization of mares during embryo transfer programs.

Our results share a number of similarities with Newcombe (2002) findings where the efficacy of PRID for estrus synchronization revealed acceptable results**.** However, Handler et al. (2007) reported low accuracy in ovulation synchronization. Newcombe and Wilson (1997) suggested the useof human chorionic-gonadotropin (hCG) for hastening ovulations during induced estrus. Arbeiter et al. (1994) obtained much better response after administration of extend-

ed-acting GnRH agonists.

In conclusion, administration of the intravaginal device releasing progesterone (PRID) was able to induce estrus and ovulation in mares indifferent seasons of the year. However, unlike the situation in cows, the efficacy of the treatment was not satisfactory in allseasons (low response rate in winter) and synchronization of ovulation was not effective (in all seasons andespecially in winter) in mares.

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CONFLICT OF INTEREST

There is no reported conflict of interest.

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