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Original Research

Effect of Cloprostenol Administration on Interval to Subsequent Ovulation and Anovulatory Follicle Formation in Quarter Horse Mares

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ABSTRACT

Prostaglandin F2α (PGF) treatment is routinely used in the reproductive management of mares to induce luteolysis and allow a subsequent return to estrus. The objective of this retrospective study was to assess the effect of follicle size at the time of administration of cloprostenol on interval to subsequent ovulation. A secondary objective was to determine the incidence of hemorrhagic anovulatory follicle (HAF) formation after PGF administration. Reproductive records of 275 mares monitored over a total of 520 estrous cycles were evaluated. All mares received a single intramuscular dose of 250 μg of the synthetic PGF analog cloprostenol sodium between days 5 and 12 after ovulation. The average interval from PGF to ovulation was 8.4 ± 2.5 days. The interval from PGF administration to subsequent ovulation was inversely proportional to the diameter of the largest follicle at the time of treatment. Administration of cloprostenol to mares with a large (≥35 mm in diameter) diestrous follicle resulted in one of three outcomes—ovulation within 48 hours (13.4%) with variable uterine edema, ovulation after 48 hours usually accompanied by the presence of uterine edema (73.1%), or regression without ovulation followed by emergence and eventual ovulation of a new dominant follicle (13.4%). There was no effect of mare age or season on interval from PGF to ovulation. The overall incidence of HAF development after PGF administration in this study was low (2.5%).

1. Introduction

Prostaglandins (PGFs) are commonly used in the reproductive management of mares as either a luteolytic or ecbolic agent [1–5]. Prostaglandins may be effective at inducing complete luteolysis if administered at least 4 days after ovulation [1], but the general convention in equine clinical practice is that PGFs are not routinely administered until the corpus luteum is at least 5 days old [2,6,7]. The intervals from PGF administration to initial return to estrus and subsequent ovulation are 3–4 days and 6–12 days, respectively [1,8,9]. The size of the dominant follicle at the time of PGF administration has been reported to be inversely correlated with the interval to subsequent ovulation [2,7,10]. For example, mares with small follicles at the time of PGF administration take longer to ovulate after PGF administration than mares with moderately sized follicles. It is important to note that mares with a large diestrous follicle (i.e. greater than 35–40 mm in diameter) may ovulate within 24–72 hours after PGF treatment without coming into behavioral estrus or developing endometrial edema [2,11–13]. In addition, Newcombe et al [7] reported that the interval from PGF to ovulation is shorter when larger doses of PGFs are administered in mid-diestrus, an effect that was observed at all follicle sizes. The dose of

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PGFs and follicle diameter at treatment also influenced the percentage of follicles that regressed after PGF administration, with lower doses and larger follicles more likely to be associated with follicular regression and replacement by another follicle.

Reports by Ginther and Al-Mamun [14] and Cuervo-Arango and Newcombe [15] indicate that the number of large dominant follicles and the subsequent ovulation rates are both higher after PGF administration than after non-treated or spontaneous cycles. In contrast, Samper et al [13] did not detect an increase in ovulation rate in the subsequent estrus after PGF administration. Similar discrepancies have also been reported for pregnancy rates after PGF administration, with some studies noting a decrease in pregnancy rates [10,16], whereas others report no change in pregnancy rate in the estrus after PGF administration [17].

Conflicting reports have also suggested either no association between administration of PGFs and development of a hemorrhagic anovulatory follicle (HAF) [7] or that administration of PGFs in diestrus is associated with an increased risk of development of a HAF [14,18,19]. Development of a HAF was not reported in earlier studies on the effects of PGF administration on subsequent follicular development and ovulation and is not a common observation in our clinical equine reproduction practice.

The primary objectives of the current retrospective study were to reassess the effect of follicle size at the time of administration of cloprostenol on interval to subsequent ovulation. A second objective was to determine incidence of HAF formation after PGF administration.

2. Materials and Methods

2.1. Mares

Reproductive records of American Quarter Horse mares housed and managed at the Equine Reproduction Laboratory, Colorado State University, between 2006 and 2013 were evaluated retrospectively. Mares and individual cycles were included in the study only if (1) the diameter of the largest follicle on each ovary was measured at the time of PGF administration; (2) serial reproductive evaluations were subsequently performed to monitor follicular development and determine whether the mare ovulated, the number of ovulations, and the day of ovulation; and (3) no hormones, such as human chorionic gonadotropin (hCG) or deslorelin acetate, were administered in the subsequent estrous period to induce an early ovulation.

2.2. Cloprostenol Treatment

A single intramuscular dose of 250 μg (1.0 mL) of the synthetic prostaglandin F2α analog cloprostenol sodium (Estrumate; Merck Animal Health, Summit, NJ) was administered between days 5 and 12 after ovulation. All mares were treated with cloprostenol; there was no untreated control group in this retrospective evaluation of privately owned mares in our clinical practice.

2.3. Reproductive Evaluations

An ultrasound examination (7.5 mHz; EXAGO; Echo Control Medical, Angoulême, France) was performed immediately before PGF administration, and the diameters of the two largest follicles on each ovary were recorded. Mares with follicle(s) less than 30 mm in diameter were initially evaluated 4 days after PGF administration. Mares with follicles 30–34 mm in diameter were examined 2 days after PGF treatment, and mares with a diestrous follicle of ≥35 mm in diameter were examined the day after PGF treatment. Ultrasound examinations were performed daily on all mares once the dominant follicle was at least 30 mm in diameter and continued until ovulation, follicle regression, or formation of a HAF was detected. Follicle regression was defined as a decrease in diameter of the dominant follicle without ovulation (i.e., atresia) and replacement by development of a new dominant follicle. A HAF was defined as a dominant follicle that initially developed echogenic particles in the follicular lumen, followed by echogenic strands and eventually complete infiltration with echogenic tissue in the absence of a discernible ovulation.

2.4. Statistical Analysis

Diameter of the largest follicle at the time of PGF administration was divided into subcategories for statistical analysis (<10, 10–14, 15–19, 20–24, 25–29, 30–34, and ≥35 mm). Continuous data were compared using a one-way analysis of variance with post hoc analysis by Student *t* test using the statistical software (Graphpad). Significance was set at $P < .05$. Categorical data were analyzed by chi-square analysis. All data presented are expressed as mean ± standard error of the mean.

3. Results

Reproductive records of 275 mares monitored over a total of 520 estrous cycles were evaluated. Mares ranged in age from 4 to 14 years.

Overall, the average interval to ovulation after cloprostenol administration to diestrous mares was 8.4 ± 2.5 days. The interval from PGF administration to subsequent spontaneous ovulation was inversely proportional to the diameter of the largest follicle at the time of treatment, if the follicle was <35 mm in diameter and went on to ovulate (Table 1).

Table 1
Interval to ovulation after administration of cloprostenol sodium to diestrous mares with a dominant follicle less than 35 mm in diameter.

Follicle Size (mm)	Number of Cycles	Interval to Ovulation (d)
<10	6	11.8 ± 1.1[a]
10–14	74	10.2 ± 0.2[b]
15–19	83	9.1 ± 0.2[c]
20–24	118	9.1 ± 0.2[c]
25–29	122	8.0 ± 0.2[d]
30–34	37	7.8 ± 0.5[d]

[a,b,c,d]Data within column with different superscript letters are significantly different ($P < .05$).