Available online at www.sciencedirect.com
ScienceDirect
Theriogenology 66 (2006) 1579–1582
Theriogenology
www.journals.elsevierhealth.com/periodicals/the

Progestin treatment for infertility in bitches with short interestrus interval

M.M. Wanke [a,*], M.E. Loza [a], M. Rebuelto [b]

[a] *Facultad de Ciencias Veterinarias, Área de Teriogenología, Chorroarín 280, 1427 Buenos Aires, Argentina*
[b] *Facultad de Ciencias Veterinarias, Área de Farmacología, Chorroarín 280, 1427 Buenos Aires, Argentina*

Abstract

The purpose of this study was to investigate if the suppression of estrus by the administration of a synthetic progestin, megestrol acetate or clormadinone acetate, could be an effective treatment to infertility in bitches with shortened interestrus periods and previous infertility. Ten bitches of different breeds and ages, with history of infertility and presenting repeated interestrus intervals of less than 4 months, were treated daily either with megestrol acetate (2 mg/kg, $n = 8$) or clormadinone acetate (0.5 mg/kg, $n = 2$) orally for 8 days. The treatments were begun within a maximum of 3 days after the onset of clinical signs of proestrus. Estrus was prevented in all animals and appearance of the following proestrus cycle was observed within 2.7 ± 0.6 months (mean ± S.D.) after the beginning of the treatment. When mated during the first post-treatment estrous cycle, bitches became pregnant and whelped normal healthy offspring. No negative side effects were clinically detected over the study period. Our results show that, in bitches with shortened interestrus intervals and previous infertility, suppression of one estrus with synthetic progestins administered at recommended doses, allows fertile breedings on the subsequent cycle, producing litter sizes within the normal range.

Keywords: Progestin; Bitch; Short interestrus interval; Treatment; Infertility

1. Introduction

In dogs, anestrus is an obligatory period of 2–10 months following diestrus and progesterone removal. Anestrus is characterized by an apparent quiescence of the reproductive tract without clinically relevant changes. It is associated with uterine regeneration and endocrine preparation of the following estrous cycle [1]. When anestrus is reduced below a few months, interestrus interval is significantly shortened and dogs are observed to come in estrus every 4 months or less. It has been observed that such a short interestrus, whether spontaneous or induced, may be the cause of breeding failures [1–4]. Recently, some breeds, as German Shepherds and Rottweilers, have been reported as presenting interestrus intervals shorter than in most other breeds and, often of less than 4 months, and associated with infertility [3,5]. Because about 3–4 months seems to be required for a complete endometrial involution after the influence of diestrus progesterone [3–7], it has been suggested that an incomplete endometrial repair may prevent implantation and the cause of infertility [1,3–5]. Mibolerone, a synthetic androgen, has been proposed for prolonging the interestrus period [1,3,6]. This application is, however, not supported by the manufacturer, particularly in breeding animals and not available in many regions, while synthetic progestins administered very early in the proestrus are approved and marketed in many countries

* Correspondence to: Facultad de Ciencias Veterinarias, Area de Teriogenología, Chorroarín 280, 1427 Buenos Aires, Argentina. Tel.: +54 11 4524 8425; fax: +54 11 4524 8480.
E-mail addresses: wanke@fvet.uba.ar, magdawanke@yahoo.com.ar (M.M. Wanke).

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doi:10.1016/j.theriogenology.2006.01.013

for the inhibition of estrus and prevention of ovulation when administered within 1–3 days after the beginning of proestrus.

The purpose of the present study was to investigate if early suppression of estrus by the administration of a synthetic progestin, megestrol acetate or clormadinone acetate, could be an effective treatment to infertility in bitches with short interestrus periods by increasing the interestrus-interval and thereby allowing for longer period for uterine regeneration.

2. Materials and methods

2.1. Animals

Ten bitches, presented for infertility at the Faculty of Veterinary Science, University of Buenos Aires ($n = 2$), and at one veterinary clinic ($n = 8$), during the years 1995–2001 were used in this study. The two conditions for inclusion in the present study were bitches having presented one or more short interestrus-intervals and having been non-pregnant at the previous cycle despite proper breeding management with a fertile male. They were of different breeds (seven German Shepherd, two Rottweiler, one Brussels Griffon) and ages (mean $\pm$ S.D. = 3.5 $\pm$ 1.2; range 2–6 years). No bitch had been treated previously with exogenous sex steroid hormones and all were nulliparous. All had a history of previous unfertile mating and of interestrus intervals less than 4 months (mean $\pm$ S.D. = 3.2 $\pm$ 0.5; range 2–4 months), calculated as the period between onsets of proestrus in successive cycles. To confirm that cycles were ovulatory, ovulation and corpus luteum function during the cycle preceding treatment were confirmed by determination of serum progesterone concentrations at 10 and 30 days of diestrus using a commercially available ELISA kit.[1] Each bitch constituted its own control. Each bitch was mated to a dog of confirmed fertility using proper timing and breeding management at the Veterinary clinic of the Veterinary College of the University of Buenos Aires during both the first non-treated cycle and the cycle following treatment.

2.2. Treatment

Treatment was administered within maximum 3 days of the proestrus onset (defined as the first day on which a sanguineous vaginal discharge was observed). Treatment as early as possible in proestrus was in agreement with approved usage of these progestins, and was done in this study to reduce or prevent any of the known side effects of progestin administration later during proestrus such as increased risk of pyometra, prolonged estrus, unwanted mating, or ovulation. Treatments consisted of daily oral administration of either megestrol acetate[2] (2 mg/kg, $n = 8$) or clormadinone acetate[3] (0.5 mg/kg, $n = 2$) for eight consecutive days. Clients were trained about the possibility of side effect occurrence and requested to present the animals at the observation of the first signs of proestrus following treatment.

2.3. Post-treatment fertility

Nine bitches were bred naturally to a proven fertile dog during the cycle immediately following treatment, according to the results of vaginal cytology and ELISA progesterone assay[1]. One bitch (# 8) was artificially inseminated using fresh semen. Two bitches (# 1 and 10) were treated twice, during two consecutive cycles before being allowed to reproduce. Pregnancy was determined by palpation of the uterus and/or ultrasonography realized around Days 25–30. Possible occurrence of fetal death and resorption during pregnancy was examined by ultrasonographic exam at Days 35–40 and 50–55. After whelping, litter size was recorded.

3. Results

Table 1 summarizes the results. All non-treated bitches included in this study accepted mating during the first cycle but none were diagnosed pregnant at Days 25–30. In all treated bitches, proestrus was stopped in a few days after the beginning of treatment, no ovulation was observed, progesterone remained basal and a normal estrus cycle was observed within 1.5–3.5 months of the end of treatment (mean $\pm$ S.D. = 2.7 $\pm$ 0.6).

All treated bitches accepted mating during the post-treatment estrous cycle, became pregnant and delivered healthy normal litters after a normal pregnancy. No fetal deaths or stillborn pups were recorded. No evidence of negative side effects such as pyometra was observed during the few months following the treatment period.

4. Discussion

Synthetic progestins (i.e. megestrol, clormadinone) have structural and biological activity similarities to

[1] TARGET, Serono, Buenos Aires, Argentina.

[2] Singestar, Konig, Buenos Aires, Argentina.

[3] Traslan, Gramon, Buenos Aires, Argentina.