

THERAPEUTIC EFFICACY OF MIFEPRISTONE, CABERGOLINE AND CLOPROSTENOL FOR TERMINATION OF PREGNANCY IN BITCHES

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ABSTRACT

A total of 24 cases of misalliance in bitches were utilized to study the efficacy of various therapeutic protocols for termination of pregnancy after early confirmation of pregnancy. These bitches were randomly allotted to three treatment and one control group with 6 bitches in each group. Pregnancy was terminated 100 per cent in all the three treatment groups. The incidence of abortion and resorption in mifepristone treated group was 15.38 and 84.62, in cabergoline plus cloprostenol group was 0 and 100, in cloprostenol group was 26.09 and 73.91 and in control group was 0 and 6.66 per cent respectively. Treatment groups had significantly shorter inter estrous cycle interval than control group. The average number of pups born in the next whelping was 3.5 ± 0.22 , 5.67 ± 0.33 , 3.34 ± 0.55 and 5.0 ± 0.58 in mifepristone, cabergoline plus cloprostenol, cloprostenol and control groups respectively. These three treatment protocols can be effectively used for the termination of pregnancy in bitches.

Key words: Bitches, Misalliance, Mifepristone, Cabergoline, Cloprostenol

INTRODUCTION

Pregnancy termination is one of the most common requests from the dog owners, when bitches are bred at too young age or old age and due to mismating. Pregnancy should be confirmed before treatment for pregnancy termination is initiated (Feldman *et al.*, 1993). Bowen *et al.* (1985) recorded the side-effects such as cystic endometrial hyperplasia, pyometra and bone marrow suppression with the estrogen treatment. Onclin and Verstegen (1996) terminated pregnancy during mid-gestation by using pharmacological agents which suppress prolactin release or interfere with the action or synthesis of progesterone. Fieni *et al.* (1997) reported that with repeated administration of PGF_{2α} and its analogues during mid-term pregnancy in the bitch resulted in luteolysis. The combined use of cabergoline and prostaglandins has also been suggested by the Onclin *et al.* (1995). When used in combination, they are generally effective at lower doses than with single

administration and result in minimum side-effects. Cabergoline has no side effects, longer half life (24 hours) and requires lesser dose when compared to other antiprolactin drugs. The present study was carried out to compare the therapeutic efficacy of mifepristone, cloprostenol and cabergoline plus cloprostenol for termination of pregnancy in misalliance bitches.

MATERIALS AND METHODS

Clinical cases presented to the Teaching Veterinary Hospital of Veterinary College, Rajendranagar, Hyderabad with the history of misalliance or unwillingness of the owners to continue pregnancy were used for the study. Out of a total 43 misalliance bitches presented with the above history only 24 were found pregnant. Pregnancy was tentatively confirmed by abdominal palpation (Johnston *et al.* 2001). Pregnancy was also confirmed using a B-mode ultrasound scanned with 5 MHz linear transducer between 20 to 30 days of mating. Pregnancy was confirmed by the presence of anechoic fluid filled sacs with conceptus. Gestational age was estimated by correlating the anechoic gestational sac diameter with the standard graph as recommended by Khan (2004).

Bitches were monitored every two days by ultrasound scanning until abortion or resorption was completed. During these examinations, the total number

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of conceptus and number of conceptus with visible heartbeats were recorded to know the viability of the fetus. These 24 bitches were assigned randomly to three treatment groups and one control group with 6 animals in each group as follows.

In group I bitches were treated with mifepristone (M T Pill 200 mg tablet, Cipla.LTD.) at the rate of 2.5mg/kg body weight orally twice daily until abortion or resorption occurred. Bitches in group II were treated with a combination of cabergoline (Cabgolin 0.25 or 0.5mg tablet Sun pharmaceutical industries, Andheri, Kurla Road, MUMBAI) at the rate of 5ug/kg body weight orally once daily for 10 days and injection of cloprostenol (Vetmate 2ml vial, each ml contains 250µg of Cloprostenol, Vetcare, TTC industrial area MIDC, Thane District, Maharashtra) at the rate of 2.5µg/kg body weight subcutaneously every 48 hours for 2 to 3 times. Injection Atropine sulphate (Tropine, 1ml ampoule containing 0.6mg atropine sulphate) at the rate of 0.04 mg/kg body weight was also administered subcutaneously, 10-15 minutes prior to administration of cloprostenol. Bitches in group III were treated with 3 to 4 doses of cloprostenol at the rate of 2.5ug/kg body weight subcutaneously administered every 48 hours until termination of pregnancy. Atropine sulphate was administered as in group 2. Bitches in group IV received no treatment and formed the untreated controls. They were monitored until the completion of whelping.

Instruction was given to owners of all the treated bitches to examine them thrice daily after the initiation of treatment up to 7 days after the fetal abortion or resorption for the signs of vaginal discharge, nature and duration, fetal expulsion time and duration. After starting of treatment, abortion or resorption of the fetus was observed in bitches using ultrasonography every two days. The completion of abortion was ascertained by the absence of fetal structures and amniotic sacs. The resorption was indicated by reduced volume and echogenicity of embryonic fluid and presence of empty sac. Duration of lochia, colour and smell of lochia observed after abortion or whelping in both groups were recorded. Duration of occurrence of next estrus was calculated in days from previous estrus in misalliance treatment group. Number of pups born in the subsequent whelping. The data collected were subjected to statistical analysis by ANOVA as per Snedecor and Cochran (1989)

RESULTS AND DISCUSSION

In the present study, the incidence of pregnancy and non-pregnancy rates in misalliance bitches was 55.8 and 44.19 per cent, respectively, which was in agreement with the findings of Feldman *et al.* (1993) and Kulasekar *et al.* (2006).

Parity of bitches utilized for this study was 6 nullipara, 7 primipara and 11 pluripara bitches. The mean gestation periods of bitches at the time of initiation of treatment for pregnancy termination were 28.5 ± 2.75 , 27.0 ± 0.68 , 27.67 ± 1.08 , 26.17 ± 1.82 days in mifepristone, cabergoline plus cloprostenol, cloprostenol and control groups, respectively. Onclin and Versteegen (1996) terminated pregnancy in bitches at similar gestational age with cloprostenol and cabergoline plus cloprostenol.

The mean interval from treatment to fetal resorption or abortion and the mean duration of fetal resorption or abortion showed no significant difference between the treatment groups. In the mifepristone treatment, the interval from treatment to initiation of abortion or resorption was 5.67 ± 0.58 days and the duration of abortion was 2.83 ± 0.57 days. Similar results have been reported by Baan *et al.* (2005), Kulasekar *et al.* (2006) and Schafer and Somi (2007) in bitches. The termination of all pregnancies which occurred in this study must be due to the abortifacient effect at the level of the uterus and independent of any additional effects on luteal function, though the progesterone concentration was at higher levels (Concannon *et al.*, 1989).

In the cabergoline plus cloprostenol group the mean interval from treatment to initiation of abortion or resorption was 5.0 ± 0.89 days and the duration of abortion or fetal resorption was 3.33 ± 0.24 days. Similar finding were also reported by Colin and Klaas Post (2002).

The bitches treated with cloprostenol had mean interval of 5.75 ± 0.78 days from treatment to initiation of abortion or resorption and the duration of abortion was 2.22 ± 0.43 days. Similar results were also observed with the cloprostenol by the Fieni *et al.* (1997). With the use of natural prostaglandins comparable results were reported by Feldman *et al.* (1993) and Balasubramanian *et al.* (2003). Prostaglandins were found to have luteolytic effect in the bitch only on repeated administration. Side effects of prostaglandins were a consequence of nonspecific stimulation of smooth

muscles, only last about 20 minutes and tend to wane as the treatment protocol continues. Synthetic prostaglandins have a much greater affinity for the prostaglandin receptors and have a longer half life than natural prostaglandins. The synthetic prostaglandins also cause less smooth muscle contractions, therefore resulting in minimum side effects.

Pregnancy termination was 100 per cent effective in all the treatments either by abortion or resorption. The incidence of resorption or abortion with mifepristone treatment was 84.62 and 15.38 per cent, respectively which were in accordance with the findings of Baan *et al.* (2005) and Fieni *et al.* (2006). In majority of cases resorption occurred when treated during 1st half of gestation period. If the treatment started after 30 to 40 days of gestation period abortion occurred in most of the cases. The incidence of fetal resorption or abortion in the bitches treated with cabergoline plus cloprostenol was in concurrence with the reports of Colin and Klaas Post (2002). In cloprostenol treatment it was similar (100%) to the observations of Balasubramanian *et al.*

(2003). Slightly higher numbers of fetuses were aborted in mifepristone and cabergoline plus cloprostenol groups which might be due to individual variation in gestation length.

The mean duration of lochial discharge was not significant among treatment and control groups. The average inter-estrous cycle interval in treatment groups was significantly shorter ($P < 0.05$) than control group (Table). The inter-estrous cycle interval was shortened by about 30 days in mifepristone group compared with control group. The variation in the length of inter-estrous interval may be attributed to the efficacy of drug on the hypothalamic - pituitary-ovarian axis and subsequent action like shortening of luteal phase and shortening of the anestrus period in bitches as reported by Kooistra *et al.* (1999). In cabergoline plus cloprostenol treated bitches the shorter inter estrus interval might be due to the luteolytic effect of dopamine agonists and / or prostaglandins. In cloprostenol group, the inter estrus interval was shorter which is in agreement with Onclin and Verstegen (1999). The average numbers of pups born in the next whelping are shown in Table.

Table - Post partum reproductive performance of bitches treated for misalliance

S.No	Therapeutic groups	Duration of lochial discharge (Days) Mean \pm SE	Inter estrous cycle interval (Days) Mean \pm SE	Litter size in next whelping Mean \pm SE
1	Mifepristone	5.25 \pm 0.25	116.67 \pm 5.9 ^a	3.5 \pm 0.22 ^a
2	Cabergoline + Cloprostenol	6.0 \pm 0.58	115.83 \pm 2.89 ^a	5.67 \pm 0.33 ^c
3	Cloprostenol	5.33 \pm 0.21	116.5 \pm 2.13 ^a	3.34 \pm 0.55 ^a
4	Control group	4.5 \pm 0.43	146.0 \pm 5.71 ^b	5.0 \pm 0.58 ^b

Means bearing different superscripts column wise differed significantly.

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