Comparative Efficacy of High vs. Low Dose Cabergoline Treatment Regimen in Inducing Fertile Oestrus in Anoestrous Dogs

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Abstract: Twenty four bitches in anoestrous for >6 months from the last heat with a serum progesterone level >1 ng mL⁻¹ were divided into two groups and subjected to oestrus induction trials using anti-prolactin drug cabergoline at 5 and 1 µg kg⁻¹ body weight respectively, once daily orally for 20 consecutive days. The mean serum progesterone level among them during anoestrus was found to be 0.56±0.01 ng mL⁻¹. Out of 12 animals treated in each group, 10 (83.3%) in group I and 9 (75%) in group II responded by evincing prooestral bleeding. The mean (±SEM) time taken from initiation of treatment to onset of prooestral bleeding in Groups I and II was 13.5±0.50 (p<0.01) and 21.89±0.86 days, respectively. About 25% of animals treated with high dose cabergoline exhibited side effects as against none with low dose. The mean (±SEM) duration of prooestrous and oestrus in the treatment groups was 8.70±0.30 (p=0.05) and 9.56±0.38 days and 8.20±0.29 and 8.33±0.24 days, respectively. The conception rate in relation to the number of animals responding to oestrus induction in the treatment groups was 90 and 88.89%, respectively. The mean (±SEM) gestation length calculated from the last breeding date and litter size in the treatment groups were 62±0.41 and 62.88±0.49, 6.44±0.29 and 6.13±0.23, respectively.

Key words: Bitch, infertility, anoestrous, oestrus induction, cabergoline, conception rate

INTRODUCTION

The oestrous cycle in the bitch is considerably longer than that in most other domestic species and unique in that there is an obligatory anoestrus following the termination of the luteal phase. Bouchard et al. (1991) and Concannon (1993) reported a non-seasonal anoestrus of variable duration (2-10 months) following each oestrous cycle in bitch. According to Feldman and Nelson (1996), anoestrus could be primary (the bitch that never had an ovarian cycle) or secondary (the bitch that had one or more ovarian cycles but subsequently failed to cycle) and it was opined that secondary anoestrus could occur after the onset of endocrine or non-endocrine diseases.

Prolactin appears to play a part in canine interoestrous interval, possibly by affecting gonadotrophin secretion and/or ovarian responsiveness to gonadotrophins. Dopamine is the main endogenous factor inhibiting the release of prolactin and for this reason it is often defined as the prolactin inhibitory factor (Cortese et al., 1997). Suppression of prolactin secretion by administration of dopamine agonists shortened the duration of anoestrus (Van Haften et al., 1989) and induced oestrus in cases of prolonged anoestrus (Arbeiter et al., 1988; Jochle et al., 1987). Davidson (2006) suggested that prolactin secretion by the pituitary might promote anoestrus and hence dopamine agonists such as cabergoline and bromocriptine could be used to shorten anoestrus in both the normal bitch and in bitches with secondary anoestrus of unknown etiology.

Jochle et al. (1987) and Harvey et al. (1997) reported that cabergoline has a more specific action on D2 dopamine receptors of the anterior pituitary gland and therefore has a greater activity and long lasting effect than bromocriptine. Arbeiter et al. (1988) reported development of tolerance to cabergoline with continued therapy and found lesser degree of side effects with lower
The animals in group I and II were administered with cabergoline at 5 μg kg⁻¹ body weight and 1 μg kg⁻¹ body weight, respectively once daily orally for 20 consecutive days. In order to minimize the side effects, the owners were advised to administer the drug along with food. Those bitches which responded to the treatment by evincing proostral bleeding were subjected to exfoliative vaginal cytology to identify the best time for breeding based on anuclear cell index and were bred with apparently healthy, fertile male dogs repeatedly at 72 h interval until refusal of the male. In order to rule out silent heat among those bitches which failed to exhibit proostral bleeding, serum progesterone concentration was again estimated one month after the completion of treatment. Transabdominal ultrasonography (B-mode, 3.5 MHz sector probes) and abdominal palpation were used for pregnancy diagnosis between 20 and 25 days and 30 and 35 days post-breeding, respectively. All the bitches found pregnant were followed up periodically until whelping and the details pertaining to gestation length and litter size were collected. The data obtained were compiled and subjected to Student's t-test to find out statistically significant difference between the groups (Snedecor and Cochran, 1989).

RESULTS AND DISCUSSION

An investigation carried out to compare the efficacy of high vs. low dose cabergoline treatment regimen in inducing fertile oestrous revealed that the serum progesterone level in anoestrous bitches ranged from 0.45-0.65 ng mL⁻¹ with a mean (±SEM) of 0.56±0.01 ng mL⁻¹. Out of the 12 animals treated in each group, 10 in group I (83.34%) and 9 in group II (75%) evinced proostral bleeding. The mean (±SEM) serum progesterone level among bitches failed to exhibit proostral bleeding was 0.59±0.03 ng mL⁻¹.

The mean (±SEM) serum progesterone level of 0.56±0.01 ng mL⁻¹ noticed among the bitches selected for the oestrus induction trials confirmed that all of them were in the anoestrous stage at the time of the treatment. On induction of oestrous using cabergoline, the prooestrous response was found to be higher (83.34%) at a dose rate of 5 μg than 1 μg kg⁻¹ body weight (75%). On administration of cabergoline at the rate of 5 μg kg⁻¹ body weight once daily orally in anoestrous bitches, Verstegen et al. (1999) and Ajitkumar et al. (2010) could obtain 93.33 and 90% prooestrous response, respectively. Even though Ciril et al. (2007) could obtain a higher (81.50%) prooestrous response on treatment with cabergoline at the rate of 0.6 μg kg⁻¹ body weight daily than with 5 μg (80%) in the present study it was found to be higher on treating with high dose than with low dose.
cabergoline. The mean (+SEM) serum progesterone level of 0.59±0.03 ng mL⁻¹, noticed among bitches failed to exhibit proestrous bleeding on induction of oestrus, ruled out the occurrence of silent oestrus and that all of them continued in the anoestrous stage.

The mean (+SEM) time taken from initiation of treatment to onset of proestrous bleeding in the two treatment groups was 13.50±0.50 (p<0.01) and 21.89±0.86 days respectively. The mean (+SEM) duration of proestrus and oestrus based on cytology in the treatment groups was 8.70±0.30 (p<0.05) and 9.56±0.38 days and 8.20±0.29 and 8.33±0.24 days, respectively. Out of 12 animals treated with high dose of cabergoline, 3 (25%) exhibited nausea, vomiting and inappetence as side effects of treatment. On the other hand, none in the group treated with low dose exhibited the above mentioned side effects.

The mean (+SEM) time taken from the treatment onset to proestrus in animals induced with cabergoline at the rate of 5 μg kg⁻¹ body weight (Group I) was found to be significantly lower (p<0.01) than that in group II (13.50±0.50 vs. 21.89±0.86 days). Gobello et al. (2002) successfully induced oestrus in anoestrous purebred bitches by administering cabergoline at the rate of 5 μg kg⁻¹ body weight orally and according to them, the mean duration of treatment required was 16 days. From the results of the present study, it could be inferred that low dose cabergoline treatment regimen takes more days for inducing oestrus than high dose regimen. Even though the duration of proestrus in group I was found to be significantly (p<0.05) lower than that in group II, the duration of proestrus and oestrus in the induced cycles in both the groups was found to be within the normal range and was in agreement with the previous reports (Jeukeme and Verstegen, 1997; Verstegen et al., 1999; Gobello et al., 2004).

In earlier oestrus induction trials with cabergoline, some side effects such as vomiting had been reported in 10-25% of dogs (Arbeiter et al., 1988; Gobello et al., 2001; Gunay et al., 2004; Dattatray, 2006). In the present study, even though the drug was administered along with food, 25% of animals treated with high dose cabergoline exhibited side effects as against none treated with low dose. This observation is in consonance with the earlier reports of Arbeiter et al. (1988) and Cirt et al. (2007) who found lesser degree of side effects with lower dose of cabergoline.

The accuracy of pregnancy diagnosis by transabdominal ultrasound scanning increased from 88.23-100% when performed between 20, 25 days and 30, 35 days post-breeding and the corresponding values for abdominal palpation were 76.47 and 94.12%, respectively. Out of 10 and 9 animals in group I and II which responded to the oestrus induction treatment 9 and 8, respectively conceived and subsequently whelped uneventfully. The conception rate in relation to the number of bitches responding to the oestrus induction treatment in the two treatment groups were 90 and 88.89%, respectively. The conception rate obtained with high dose in the present study was found to be better than that of Rota et al. (2003) and Gobello et al. (2004) who reported 83 and 82.60% conception rate respectively on oestrus induction using cabergoline at the rate of 5 μg kg⁻¹ body weight. The mean (+SEM) gestation length calculated from the last breeding date and the litter size in the treatment groups were 62±0.41 and 62.88±0.49 days and 6.44±0.29 and 6.13±0.23, respectively. With respect to gestation length and litter size, significant difference could not be detected between the treatment groups.

CONCLUSION

Oestrus induction trials carried out to compare the efficacy of cabergoline treatment at high and low dose rates in anoestrous bitches revealed that the proestrus response and conception rate were better with the high dose regimen which took fewer days for induction but with side effects in 25% of animals treated.

On the other hand, even though the low dose regimen took more days for induction with slightly lower proestrus response and conception rate, none of the animals in this group exhibited side effects. From the present investigation, it could be concluded that even though the high dose cabergoline treatment regimen recorded earlier induction of oestrus with better proestrus response and conception rate, the lower dose regimen was found to be safe with moderate results.

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REFERENCES


