Use of cabergoline to treat primary and secondary anestrus in dogs

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Objective—To determine whether cabergoline would be safe and effective for induction of estrus in dogs with primary or secondary anestrus.

Design—Prospective case series.

Animals—Six privately owned otherwise healthy purebred dogs with primary or secondary anestrus.

Procedure—Dogs were treated with cabergoline (5 µg/kg [2.3 µg/lb], PO, q 24 h) until 2 days after the onset of proestrus. Follicular development was assessed by means of cytologic examination of vaginal smears; ovulation was assessed by measuring serum progesterone concentration 3 weeks after the onset of estrus. Five bitches were mated during behavioral estrus.

Results—All dogs had normal estrus periods, and all 5 dogs that were mated whelped normal litters. Mean duration of cabergoline treatment was 16 days. None of the dogs had any adverse effects associated with cabergoline administration.

Conclusions and Clinical Relevance—Results suggest that administration of cabergoline is safe and effective for treatment for primary and secondary anestrus in dogs. (J Am Vet Med Assoc 2002;220:1653–1654)

Abnormalities of the anestrus period are common in dogs. Persistent anestrus is classified as primary or secondary, with primary anestrus defined as a lack of estrus by 18 to 24 months of age, depending on the size of the bitch, and secondary anestrus defined as a lack of estrus within 12 months after the preceding estrus period.1,2

Treatment of primary and secondary anestrus should be directed toward identifying and treating the underlying cause. However, estrus induction may be attempted when an underlying cause is not found. Unfortunately, reliable protocols for induction of estrus in dogs have been difficult to devise because of a lack of understanding of the hormonal and follicular events responsible for termination of anestrus. Estrus induction traditionally has involved administration of gonadotrophic hormones or synthetic gonadotrophin-releasing peptides, which induce release of endogenous gonadotrophic hormones from the pituitary gland.3 Comparison of the efficacy of different hormonal protocols is difficult because of the unknown history of the bitches used and the various criteria used to judge success (eg, induction of behavioral estrus, evidence of ovulation, full-term pregnancy). Moreover, there are problems relating to availability, quality, potency, and consistency of hormone preparations. In addition, different synthetic hormone agonists may have different potencies.

During the past 2 decades, various authors have reported that dopaminergic agonists can be used to induce estrus in dogs.4,5 Dopaminergic agonists are ergot derivatives that inhibit prolactin secretion by stimulating secretion of dopamine or suppressing secretion of serotonin.6,7 Currently, 2 dopaminergic agonists are commercially available: bromocriptine and cabergoline. Cabergoline has been shown to be safer and more potent than bromocriptine, probably because it more specifically binds to D2 hypothalamic and pituitary receptors.8 The precise mechanism of action by which dopaminergic agonists are able to initiate estrus is not yet clear, but it has been hypothesized that dopaminergic agonists directly stimulate the hypothalamic-pituitary axis.9,9 An indirect effect caused by a decrease in prolactin concentration or a peripheral effect of prolactin on the ovaries appears less likely.

Most previous studies10–12 of the use of dopaminergic agonists to induce estrus in dogs have involved healthy bitches. Therefore, the possibility exists that the drugs will not be effective in dogs with persistent anestrus. The purpose of the study reported here, therefore, was to determine whether cabergoline would be safe and effective for induction of estrus in dogs with primary or secondary anestrus.

Materials and Methods

Animals—Six privately owned otherwise healthy purebred dogs with primary or secondary anestrus were used in the study. Two of the dogs had primary anestrus, including a 22-month-old Pekingese and a 30-month-old Labrador Retriever. The remaining 4 dogs had secondary persistent anestrus, including a 3-year-old Dachshund that had not had any signs of estrus for the preceding 18 months, a 2.5-year-old Labrador Retriever that had not had any signs of estrus for the preceding 13 months, a 3.5-year-old Fox Terrier that had not had any signs of estrus for the preceding 17 months, and a 3-year-old Fox Terrier that had not had any signs of estrus for the preceding 24 months.

All dogs were confirmed to be in anestrus on the basis of results of cytologic examination of a vaginal smear, vaginoscopy, and measurement of serum progesterone concentration (< 1.5 ng/ml).12,13 The dogs remained in their home environment during the study, except at the time of examinations. Consent forms were signed by all owners.

Experimental protocol—Dogs were treated with cabergoline® (5 µg/kg [2.3 µg/lb], PO, q 24 h) until 2 days after the onset of proestrus (ie, vulvar swelling and bloody vaginal dis-
charge); cabergoline was administered with food. Vaginal
smears were collected daily from the onset of proestrus until
the onset of diestrus and examined cytologically to follow
follicular development. Five dogs were mated during behav-
ioral estrus. Blood samples were collected 3 weeks after
the onset of behavioral estrus, and serum progesterone concen-
tration was measured to confirm ovulation (progesterone
concentration, > 2 ng/ml).2,21
The induced estrus period was considered normal if
dogs had normal follicular development (determined by
means of cytologic examination of vaginal smears) and oву-
lated (as evidenced by a serum progesterone concentration
> 2 ng/ml). Number of days of treatment with cabergoline and
any adverse effects were recorded.

Results
None of the dogs had any adverse effects during
treatment with cabergoline, and all had normal estrus
periods. Duration of the estrus period in the 4 dogs
with secondary anestrus was similar to duration of the
previous estrus period. Mean duration of treatment
with cabergoline was 16 days (range, 4 to 34 days). In
3 dogs with secondary anestrus, the duration of treat-
ment was short (4, 5, and 8 days), whereas in the
remaining dog the duration was 28 days. In the 2 dogs
with primary anestrus, duration of treatment was
much longer (18 and 34 days). All 5 dogs that were
mated during behavioral estrus became pregnant and
whelped normal litters.

The Pekingese with primary anestrus had previ-
ously been examined by a dermatologist because of
vulvar fold dermatitis secondary to hypoplasia of the
vulva. In this dog, the vulva increased in size following
treatment with cabergoline, and this change persisted
following discontinuation of administration, permit-
ting resolution of the dermatitis.

Discussion
Results of the present study suggest that adminis-
tration of cabergoline is a safe and effective treatment
for primary and secondary anestrus in dogs. Mean
duration of treatment in these dogs was similar to
duration in previous studies involving administra-
tion of cabergoline to healthy bitches. As with previous
studies involving healthy bitches, cabergoline
administration resulted in a normal estrus period. The
reason why duration of treatment was relatively short
in 3 dogs in this study and longer in the remaining 3
could not be explained, although breed and individual
differences in response to treatment could possibly
have played a role.

None of the dogs in the present study had any
adverse gastrointestinal effects associated with caber-
goline administration, whereas dogs in previous stud-
ies had mild adverse effects. Administration of caber-
goline with food may account for the lack of adverse
effects in the present study.

Although this treatment should be tested in a larg-
er number of dogs with persistent anestrus, results of
the present study suggest that it is a promising tool for
improving reproductive performance in dogs.

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