Cabergoline: Ameliorative Drug for Maladies of Canine Reproduction

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ABSTRACT

Prolactin is synthesized from anterior pituitary and secreted highly during the diestrual phase of the estrous cycle in bitches. Various reproductive clinical conditions are arising during diestrual stage of bitches. Manipulation of the diestrual phase of the estrous cycle in a bitch, by a simple administration of anti-prolactin drugs could bring about changes in the diestrus period. Commonly used dopamine agonists in canine practice are cabergoline and bromocriptine. The present communication elaborates the role of prolactin and dopamine agonists in various clinical conditions of bitches.

INTRODUCTION

Prolactin is an anterior pituitary hormone, secreted highly during the diestrual phase of the estrous cycle in bitches. It increases support to the corpus luteum after 32 days of pregnancy and even in non-pregnant bitches. Hence, prolactin is often called as the luteotrophic hormone in bitches. This means that both pregnant and non-pregnant bitches in their diestrual phase have concentrations of prolactin to support the corpus luteum to synthesize progesterone (Concannon *et al.*, 2011). Because of this, all non-pregnant bitches in their diestrual phase

are commonly present in "physiological pseudopregnancy."

If a veterinarian wants to manipulate the diestrual phase of the estrous cycle in a bitch, a simple administration of anti-prolactin could be sufficient. Hypothalamic control of prolactin secretion is unique from other anterior pituitary hormones because it is through inhibition by dopamine that prolactin secretion is controlled. So, anti-prolactin drugs are also called "dopamine agonists."

Commonly used dopamine agonists in canine practice are *Cabergoline and Bromocriptine*. But bromocriptine has more side effects when compared to cabergoline.

CABERGOLINE

Cabergoline is a dopamine receptor agonist with a high affinity for D_2 receptors. It has a direct inhibitory effect on lactotrophs and stimulates the release of dopamine by tubero-infundibular neurons or suppressing secretion of serotonin.

Availability: 0.25 mg and 0.5 mg tablets in different trade names.

Clinical Uses

1. Clinical pseudopregnancy (Clinical pseudocyesis)
2. Medical termination of pregnancy for mismating (MTP)
3. Galactostasis/Galactorrhea
4. Fetal resorption
5. Open cervix pyometra (OCP)
6. Anestrus (Primary anestrus and secondary anestrus)

1. Clinical pseudopregnancy

This is a syndrome observed in non-pregnant bitches and is characterized by clinical signs such as nesting, weight gain, mammary enlargement, and lactation. It typically occurs in non-pregnant bitches about 6 to 12 weeks after estrus. Diagnosis is based on clinical signs, ultrasonography, and radiography. Increased concentration of prolactin and decreased concentration or withdrawal of progesterone are responsible for the development of the symptoms of pseudopregnancy.

The most common ergot compounds used clinically to inhibit prolactin secretion are the dopamine agonists such as cabergoline and bromocriptine. Cabergoline has greater bioactivity, superior D_2 receptor specificity, and a longer duration of action compared to bromocriptine. Cabergoline crosses the blood-brain barrier slightly and has less central emetic effect than bromocriptine. Administration of cabergoline at 5 µg/kg/day orally (PO) SID for 7-10 days could decrease or abolishes the signs of pseudopregnancy.

2. Medical termination of pregnancy (MTP) for mismating

The prolactin hormone increases its support to the corpus luteum (CL) after 32-35 days of pregnancy and maintains the CL functions. Hence, administration of cabergoline at 5 µg/kg/day orally (PO) BID results in a decrease in the function of the CL and a decrease in the concentration of progesterone, resulting in the termination of pregnancy (Parmar *et al*., 2020). Cabergoline should be administered until the expulsion of all the fetuses, which is confirmed by follow-up ultrasonography.

3. Galactostasis/Galactorrhea

Galactostasis refers to the continuous excessive accumulation of milk in the mammary gland with a concurrent lack of secretion. Clinical signs are enlargement of the mammary gland with the presence of residual milk, leading to mild to moderate inflammation activity followed by edema and

discomfort. Administration of cabergoline at 5 µg/kg/day orally (PO) SID for 7-10 days could decrease the milk secretion.

3. Fetal resorption

Fetal resorption is a process that occurs when a live fetus deteriorates and decomposes during the early stages of pregnancy in dogs. Bitches may not have any visible signs other than a greenish-black vaginal discharge, which may also be licked by the dog and not observed by the pet owner. Ultrasonography can confirm fetal resorption by imprinting of the zonary placenta and any fetal remnants present in the uterine horns. The condition can be treated by administration of cabergoline at 5 µg/kg/day orally (PO) BID for 7 days. After 7 days of treatment, no remnants should be visualized in the horns.

4. Canine open cervix pyometra:

Pyometra is a hormonally mediated diestrual disorder characterized by the accumulation of purulent material in the uterine horns of intact, sexually mature bitches. It is diagnosed based on clinical signs, ultrasonography, and radiography. Cabergoline is also one of the treatment options for pyometra, administered along with antibiotics, anti-emetics, and antiulcer drugs.

Dose: 5 µg/kg/day orally (PO) BID for 7 days. The basic principle involved is the decrease of progesterone concentration by blocking the secretion of production from the anterior pituitary.

5. Anestrus

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 or whelping (Verstegen *et al.*, 1999). For both types of anestrus, cabergoline could be administered at a dose of 5 µg per kg body weight once daily (SID) for 15 days, along with vitamin E supplementation, to induce fertile estrus in bitches.

The precise mechanism of action by which dopaminergic agonists are able to initiate estrus is not yet clear, but it has been hypothesized that, 1. Inhibition of neurotransmitters responsible for negative feedback effect on pulsatile release of gonadotropin releasing hormone (GnRH). 2. Dopaminergic agonists directly stimulate the hypothalamic-pituitary axis. 3. An indirect effect caused by a decrease in prolactin concentration or a peripheral effect of prolactin on the ovaries appears less likely

CONCLUSION

Dopamine agonist (cabergoline) considered to be the more reliable drug for the management of various clinical conditions which are arising during the diestrual phase of the bitches. Easy availability of this drug in the local market and less side effect added advantage to the practicing veterinarians.

Table 1: Approximate calculation of cabergoline dosage for canine

Body weight	Dose rate	Availability	Dose given (µg)	Dividing the tablets (into powder)	No. of tablets/ Parts of tablet (SID)	No. of tablets/ Parts of tablet (BID)
43-50 Kg	5 µg per Kg. b.wt	**CABGOLIN** DOSTIHEAL CABOTIN DOSTINEX CABERLIN VIGOLINE	215-250	-	1 tab/day	1 tab- 0 -1 tab per day
35-42 kg			175-210	1 tablet divided into 4 parts	3 parts/day	3 parts- 0- 3 parts per day
26-34 kg			130-170	1 tablet divided into 3 parts	2 part/day	2 parts- 0- 2 parts per day

21-25 kg		0.25 mg (250 µg) 1 strip contain 4 tablets 1 tablet-Rs.45	105-125	1 tablet divided into 2 parts	1 part/day	1 part- 0- 1 part per day
16-20 kg			80-100	1 tablet divided into 3 parts	1 part/day	1 part- 0- 1 part per day
11-15 kg			55-75	1 tablet divided into 4 parts	1 part/day	1 part- 0- 1 part per day
5-10 kg			25-50	1 tablet divided into 8 parts (Make the tablet into powder and divide)	1 part/day	1 part- 0- 1 part per day

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