ABSTRACTS

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EFFECT OF AN INJECTABLE CABERGOLINE FORMULATION ON SERUM PROLACTIN (PRL) AND MILK SECRETION IN EARLY POSTPARTUM BEAGLE BITCHES

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Introduction - Cabergoline (Galastop®) is currently used as an oral formulation to reduce or eliminate mammary secretion in pseudopregnant bitches using treatment protocols which include daily administration for periods of 4-6 days (come da registrazione). An injectable formulation of cabergoline (Galastop® Iniettabile) was recently evaluated for marketing purposes. This paper describes the results of a clinical & pharmacodynamic study conducted with the injectable formulation of cabergoline administered to lactating Beagle bitches and its effects on serum prolactin concentrations and mammary milk secretion.

Materials and methods - The study was conducted on 5 adult Beagle bitches of 1-5 years of age and 8-13 kg body weight. Each bitch was inseminated using semen of an adult, healthy male Beagle dog and followed up during pregnancy. On day 3, 4 and 5 postpartum (PP) a 5.0 cc blood sample was collected AM and PM; on day 6 a 0.1 ml/kg placebo (vehicle only) was administered, and on day 9 a similar amount of injectable cabergoline formulation (containing 15 mcg/ml) was administered. All treatments were made SC between the shoulder blades, in the morning. Blood samplings were continued AM and PM until day 12 PP and then only PM until day 17 PP (table n° 1). During the 14-day study period the experimental bitches were checked twice daily to monitor weight, health status, milk production and occurrence of side effects due to treatment. Puppies’ body weight was checked twice daily and, if necessary, their nutrition was integrated with a commercially available canine milk replacement (Sherley’s Lactol) 4 times daily until the third week of age. Milk production was assessed subjectively on each bitch by looking at mammary status and trying to express milk from each teat, using the following score:

- 4) milk flows out in large quantity just by touching the teat;
- 3) milk can be expressed in large quantity when squeezing the teat;
- 2) milk can be expressed by squeezing the teat;
- 1) small amounts of milk can be expressed by squeezing the teat;
- 0) no milk can be expressed by squeezing the teat.

Serum PRL was assayed using an ELISA technique (Milenia Biotech Gmnbh Bad Nauheim, Germany) specific for canine PRL, which has a range of calibration of 0.4-80 ng/ml and a minimum detectable concentration of 0.4 ng/ml. Data were analyzed with a one-way ANOVA using each bitch as her own control and considering the study period as the variation factor; the Tukey’s test was used to check for statistical significance of different values observed with ANOVA, and the Pearson’s correlation test was used to check for presence of correlation among all parameters studied.

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Table n° 1 – Experimental protocol to check the effect on an injectable cabergoline preparation (1.5 mcg/kg administered on postpartum day 9) on serum prolactin and milk secretion in 5 lactating Beagle bitches. Temporal sequence of administration of placebo (day 6 post-partum = PP), cabergoline (day 9 PP), and timing of blood samplings to assay serum prolactin.

Results - All parturitions occurred spontaneously at term. Litter size was 2-4 puppies/bitch, for a total of 16 puppies for the 5 bitches; 3/16 puppies died within the first 3 days of life due to congenital malformations. Puppies were re-distributed among bitches in order to have at least 2 suckling pups/bitch. Milk production was drastically reduced when comparing the basal and placebo periods to the treatment period. The decrease in milk production from day 9 PP on was significant for all glands (P<0.001) (Figure n° 1). PRL secretion decreased significantly from values of > 50 ng/ml on the morning of day 9 PP (prior to treatment) to an average value of approximately 10 ng/ml (in 3/5 bitches serum PRL was undetectable). While serum PRL seemed to show a circadian rhythm prior to treatment (high AM, low PM, Figure n° 2), such a rhythm disappeared after treatment and PRL values took 3 days to be restored at a value comparable to the lower end of the daily range (evening value) prior to treatment (Figure n° 2). Puppies were fed with artificial milk starting on the 1st day of treatment, and their body weight kept growing regularly throughout the experimental period. No central or local (injection site) side effects were observed in any bitch following administration of placebo, and in 4/5 bitches following administration of the treatment; one of the treated bitches had a local reaction at the injection site which did not necessitate treatment and disappeared on its own after 2 days.
Injectable cabergoline administered at the dose of 1.5 mcg/kg SC was able to cause a drastic reduction of serum PRL (80% reduction when comparing pre-treatment and post-treatment values) and also a drastic fall in milk secretion. These results confirm earlier studies (1,2) in which it was observed that only 1/3 of the dose is needed to achieve a clinical effect when using the injectable compared to the oral preparation. The effect of the drug was long-lasting as it took at least 3 days for serum PRL to go back to pre-treatment values. Therefore, should a bitch need a second treatment, this can be done 48 or 72 hours after the first one. The injectable cabergoline formulation was safe and well tolerated.

References