

A CLINICAL TRIAL OF THE PROLACTIN INHIBITOR METERGOLINE IN THE TREATMENT OF CANINE PSEUDOPREGNANCY

Estudio Clínico del Inhibidor de la Prolactina Metergolina en el Tratamiento de la Pseudopreñez Canina

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ABSTRACT

Canine pseudopregnancy is a syndrome, characterized by signs such as nesting, weight gain, mammary enlargement and lactation, which appear in nonpregnant bitches 6 to 12 weeks after estrus. The intensity of these signs is extremely variable among bitches. Metergoline is essentially a serotonergic antagonist that inhibits prolactin secretion. A total of 24 cross and pure-bred, overtly pseudopregnant bitches, were randomly allocated to two groups of 10 and 14 animals respectively each: placebo (PL) and metergoline (ME, treated with metergoline 0.1 mg/kg q12h PO for 10 days). On days -1, 7 and 14 (day 0: beginning of the treatment) all the animals were classified into grades of intensity of pseudopregnancy clinical signs (II, I, 0). Presence or absence of treatment side effects were also recorded. On day 7 of the protocol, 5/14 and 3/10 of the bitches of the ME and PL groups, respectively achieved grade I, while 8/14 and 0/10 of the same groups achieved grade 0 (P 0.03). On day 14, 3/14 and 5/10 of the bitches of the ME and PL groups, respectively achieved grade I, while 10/14 and 0/10 of the same groups achieved grade 0 (P 0.01). Side effects were mild and did not lead to termination of therapy in any case. On day 7, they appeared in 1/14 and 0/10 of the animals of the ME and PL groups, respectively (P 0.01). It was concluded that Metergoline proved to be an efficient and safe drug in the treatment of pseudopregnancy in this group of bitches.

Key words: Bitch, pseudopregnancy, metergoline.

RESUMEN

La pseudopreñez en la perra es un síndrome caracterizado por signos tales como realización del nido, aumento de peso, agrandamiento mamario y lactación, que aparece en hembras no preñadas de 6 a 12 semanas luego del estro. La intensidad

de los signos es extremadamente variable en las distintas perras. La metergolina, es esencialmente un antagonista serotoninérgico que inhibe la secreción de prolactina. Un total 24 perras mestizas y de raza, manifiestamente pseudopreñadas, fueron distribuidas en dos grupos de 10 y 14 animales respectivamente: placebo (PL) y metergolina (ME, tratadas con metergolina 0.1 mg/Kg cada 12 h oral durante 10 días). En los días -1, 7 y 14 (día 0: comienzo del tratamiento) todos los animales fueron clasificados en grados de intensidad según los signos clínicos de pseudopreñez (II, I, 0). La presencia o ausencia de efectos colaterales también fue evaluada. En el día 7 del protocolo, 5/14 y 3/10 de las perras de los grupos ME y PL respectivamente, presentaron grado I, mientras que 8/14 y 0/10 de las perras de ambos grupos presentaron grado 0 (P 0,03). En el día 14, 3/14 y 5/10 de las perras de los grupos ME y PL respectivamente, presentaron grado I, mientras que 10/14 y 0/10 de las perras de ambos grupos presentaron grado 0 (P 0,01). Los efectos colaterales fueron leves ocasionaron la terminación de la terapia en ningún caso. En el día 7, aparecieron en 1/14 y 0/10 de los animales de los grupos ME y PL respectivamente (P 0,01). Se concluye que la metergolina demostró ser una droga eficiente y segura para el tratamiento de la pseudopreñez en este grupo de perras.

Palabras clave: Perra-pseudopreñez-metergolina.

INTRODUCTION

Canine pseudopregnancy is a syndrome, characterized by signs such as nesting, weight gain, mammary enlargement and lactation, which appears in non pregnant bitches 6 to 12 weeks after estrus. The intensity of these signs is extremely variable among bitches [2,10]. Pseudopregnancy is now a frequent finding in domestic dogs, with a prevalence estimated to be as high as 50-75 % both in the bibliography and in our clinical

cal practice [10]. The precise etiophysiology of pseudopregnancy is one of the topics of canine endocrinology that still remains to be explained. It is accepted that clinical signs of pseudopregnancy were related to the increased concentrations of prolactin (PRL) induced by an abrupt decline of progesterone (P₄) concentrations in the late luteal phase [4, 11, 15].

Progestins are frequently used in the treatment of pseudopregnancy, although side effects and signs relapse after cessation of the therapy are frequent [13]. Inhibition of prolactin secretion by ergot derivatives has produced a revolution in the treatment of canine pseudopregnancy. The most frequently used prolactin inhibitors are bromocriptine, cabergoline and metergoline [5, 8, 9]. Metergoline is essentially a serotonergic antagonist that in doses higher than 0.3 mg/kg also presents dopaminergic action [3, 6, 7]. Side effects such as anxiety, aggressiveness, depression, hyperexcitation, anorexia, vomiting, nausea and psychotic effects like whining and escaping were reported for metergoline [1, 6].

Unfortunately, prolactin inhibitors such metergoline are not available in the veterinary market of most American countries yet. The present study was designed to test the efficacy and safety of metergoline in the treatment of canine pseudopregnancy.

MATERIALS AND METHODS

Animals

A total of 24 cross and pure-bred, overtly pseudopregnant bitches, aged 2 to 13 years and weighing 5 to 40 kg, were referred to the Institute of Theriogenology the Faculty Veterinary Sciences from the National University of La Plata during a period of 1 year. The animals, which were otherwise healthy pets, were kept in their normal surroundings (home) during the trial. According to anamnesis, they had had their estrous cycle between 8 and 12 weeks prior to the commencement of the study and they had all been pseudopregnant for a period of 5 to 10 days when they were referred to us and included in the trial.

Management and Treatment Schedules

In a randomized parallel, single-blind controlled design the bitches were randomly allocated to two groups: PL (n= 10) which was treated with a placebo (with food) PO q12hs for 10 days and ME (n= 14) which was treated with metergoline (Contralac, Virbac Brazil) 0.1 mg/kg q12h PO at food time for 10 days. On days -1, 7 and 14 (day 0 beginning of the treatment) all the animals were physically examined and classified by grades (TABLE I). Overt pseudopregnant was categorized as grade II, full remission as grade 0 and an intermediate state was considered grade I. All bitches were in grade II before the beginning of the treatments (day 0). Presence or absence of treatment side effects (vomiting, nausea, anorexia, depression, whining, escaping and aggressiveness) was also recorded on anamnesis forms on the same days.

TABLE I
GRADES OF INTENSITY OF PSEUDOPREGNANCY

Grade	Clinical signs
0	Normal mammary glands
I	Mammary enlargement + serous secretion
II	Mammary enlargement + milk secretion*

*Frequently associated with behavioral changes.

Statistical Analyses

Categorical data for the frequency of bitches achieving Grade 0 in the clinical response, and the presence of side effects were carried out by PROC CATMOD, SAS®; 1988. The mathematical model included the main effects of treatment and day, and the interaction of treatment by day. The mean square of bitch nested within treatment was used as an error term to test the main effect of treatment.

Orthogonal contrasts were used to test differences between treatments (PL vs. ME; day -1 vs. day 7 and 14; day 7 vs. day 14). The results are expressed in least squares means (LSM)±SEM. The level of statistical significance was set at P<0.05 [14].

RESULTS

On day seven of the protocol, 5/14 and 3/10 of the bitches of the ME and PL groups, respectively achieved grade I, while 8/14 and 0/10 of the same groups achieved grade 0 (P<0.03). On day fourteen, 3/13 and 5/10 of the bitches of the ME and PL groups, respectively achieved grade I, while 10/14 and 0/10 of the same groups achieved grade 0 (P<0.01, FIG. 1).

Side effects were did not lead to termination of therapy in any case. They consist of hyperexcitation and nausea. On day seven, they appeared in 1/14 and 0/10 of the animals of the ME and PL groups (P<0.01), respectively. They gradually disappeared during the second week of the protocol.

DISCUSSION

The lack availability of prolactin inhibitor drugs, such as metergoline, in the veterinary market of most American countries, is the main cause of inexperience with use of these drugs by most practitioners. Moreover, progestin treatment, which is known to cause life- threaten side effects is frequently used for canine pseudopregnancy in these countries. In line with previous reports, in this study ME treated group had a quicker involution of pseudopregnancy signs than PL treated animals [1, 5, 7, 12] Side effects appeared in a very low percentage of the treated bitches. It is concluded that metergoline was an efficient and safe drug in the treatment of pseudopregnancy in this group of bitches.

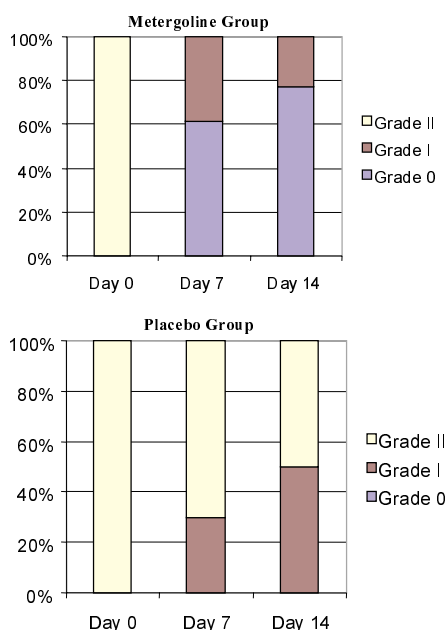


FIGURE 1. CLINICAL RESPONSE TO METERGOLINE. THE TOTAL NUMBER OF ANIMALS IN EACH GROUP IS REPRESENTED AS 100%. FOR EACH TIME POINT THE PROPORTION OF ANIMALS WITH A GIVEN GRADE OF INTENSITY OF PSEUDOPREGNANCY CLINICAL SIGNS IS REPRESENTED BY SPECIFIC COLOR.

CONCLUSIÓN

It is concluded that metergoline was as efficient and safe drug in the treatment of pseudopregnancy in this group of bitches.

ACKNOWLEDGEMENTS

The authors would like to thank Virbac, Brazil for metergoline (Contralac) supply. This research was funded in part by a grant of the Incentive Program for Teaching and Research from the UNLP N° 11/V107 to RLS.

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