Short-Term Oral Treatment of Canine Benign Prostatic Hypertrophy with Chlormadinone Acetate

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ABSTRACT. Ten beagle dogs (4–8 years of age) with benign prostatic hypertrophy were treated daily for 7 or 14 days by a daily oral administration of chlormadinone acetate (CMA), an anti-androgenic preparation, at a dose of 0.5 or 2.0 mg/kg/day. The groups of dogs treated with CMA at a dose of 2.0 mg/kg showed a greater reduction of the prostatic volume during 7 or 14 days of treatment than the group treated with 0.5 mg/kg of CMA. At 56 and 84 days after the start of CMA treatment, prostate volume was reduced to 63 and 79% of the pre-administration volume, respectively. No marked decrease in plasma LH or testosterone was found after the CMA treatment. These results indicate that the therapeutic effects of 7-day oral treatment with CMA at 2.0 mg/kg/day in dogs with BPH last for about three months or longer without side effects.—**KEY WORDS:** anti-androgen, canine, prostatic hypertrophy.

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Benign prostatic hypertrophy (BPH) in the dog is known to occur in dogs which are older than four years [2]. The clinical signs include hematuria, diarrhea, rectal obstruction and dysuria [3]. This disease has generally been treated by gonadectomy in the dog. Recently, the treatment of BPH in the dog by oral long-term treatment with, or injection of, chlormadinone acetate (CMA), an anti-androgenic preparation has been reported [1, 6]. The authors have previously reported that an oral administration of CMA daily for 28 days at a dose of 2.0 mg/kg/day was effective in treating BPH in the dog: the prostate volume decreased to approximately 40% of the pre-treatment condition and the clinical symptoms, including hematuria, disappeared within 10 days after the treatment [4]. In this study, the effect of short-term oral administration of CMA on prostate volume was examined in dogs with BPH.

Ten beagle dogs with BPH, 4 to 8 years old (mean $\pm$ S.E.; 6.4 ± 1.2 years), were used. These dogs were obtained from the beagle colony in our university after X-ray examination of the prostate. The exact size and volume of the prostate were measured by computed tomography (CT). The weight of the prostate was obtained by means of the formula of Tunn *et al.* [8]. The dogs were diagnosed having as BPH based on the prostate weight (g)/body weight (kg) ratio above 1.6 [9]. The ration the dogs used in this study ranged between 1.6 and 2.1 (mean $\pm$ S.E.; 1.9 ± 0.2). The prostates in all dogs were thus diagnosed as hypertrophied.

In 6 dogs CMA (Prostal 25®, Teikoku Hormone Mfg., Co., Ltd., Japan) was orally administrated daily for 14 days either at a dose of 0.5 mg/kg/day (Group I, $n=3$) or 2.0 mg/kg/day (Group II, $n=3$). The other 4 dogs (Group III) were treated with CMA for 7 days at a dose of 2.0 mg/kg/day. It was orally administrated continuously for 14 days. In Groups II and III, changes in prostate volume were examined until 84 days after the initial CMA treatment. The concentrations of CMA, luteinizing hormone (LH) and testosterone (T) in peripheral blood plasma were measured to investigate the effects of CMA on the endocrine function of the pituitary and the testis. Blood was sampled from the cephalic vein with heparin at intervals of 3 days until 28 days after the initial treatment.

The plasma CMA level was examined by a GC-MS method [7]. Measurement of LH and T in plasma was carried out by radioimmunoassay as previously described [4]. In Group III changes in prostate volume and plasma CMA, LH and T levels were examined until 141 days after the initial CMA treatment.

The mean levels of plasma CMA in the BPH dogs in Groups II and III (2.0 mg/kg/day) increased markedly after the initial administration of CMA compared to Group I (0.5 mg/kg/day) (Fig. 1). The volume of the prostate parenchyma was decreased concurrently with the reduction in plasma CMA (Figs. 1 and 2). In Group III plasma CMA rapidly decreased after the treatment but

Fig. 1. Changes in the mean ($\pm$ S.E.) values for plasma CMA (—●—●) and prostatic volume (○----○) in dogs with BPH after the start of oral treatment with CMA at a dose of 0.5 mg/kg/day (Group I, $n=3$), 2.0 mg/kg/day (Group II, $n=3$) daily for 14 days and 2.0 mg/kg/day (Group III, $n=4$) daily for 7 days.

Fig. 2. CT photographs of the maximum cross section of the prostate in a dog with BPH before (A) and after (B) the oral treatment with CMA at a dose of 2.0 mg/kg/day (Group III, $n=4$) daily for 7 days. The prostatic parenchyma after CMA treatment was greatly reduced compared with that before CMA treatment. AC, abdominal cavity; P, prostate; R, rectum.

Fig. 3. Changes in the mean ($\pm$ S.E.) levels of plasma LH ($\bullet$ — $\bullet$) and testosterone ($\circ$ — $\circ$) in dogs with BPH after the start of oral treatment with CMA at a dose of 0.5 mg/kg/day (Group I, $n=3$), 2.0 mg/kg/day (Group II, $n=3$) daily for 14 days and 2.0 mg/kg/day (Group III, $n=4$) daily for 7 days.

the prostate volume was decreased at 56 and 84 days after the start of the treatment to almost the same degree as in Group II. The volume diminished to 63% and 79% of the pre-treatment volume, respectively.

The mean levels of plasma LH and T in the BPH dogs in Groups I and III were transiently high during or after the CMA treatment (Fig. 3), but the increase in neither LH nor T was significant. The dogs in Group II did not show such a change in LH and T as observed in Groups I and III (Fig. 3).

Murakoshi *et al.* [6] have obtained marked reduction in prostate volume by long-term administration of 2.5 mg/kg/day of CMA in dogs with hormone-induced BPH. This has also been achieved by 28-day oral administration of 2.0 mg/kg/day of CMA in dogs with spontaneous BPH by the present authors [4]. The present study demonstrated that continuous 7-day oral administration of CMA at 2.0 mg/kg/day in dogs with BPH produced marked reduction in the prostate volume and a prostate-shrinking effect which lasted until 84 days after the treatment. It was therefore considered that continuous 7-day oral administration of CMA at 2.0 mg/kg/day in dogs with BPH caused early disappearance of the clinical symptoms and a continuous prostate-shrinkage effect for more than three months.

The authors previously found that the gonadal secretion of androgen was inhibited in dogs by the administration of 2.0 mg/kg/day of CMA for 28 days [4]. In this study, the plasma LH and T levels were not significantly decreased. This suggests that the endocrine function of the pituitary and the testis were not greatly affected by 7- or 14-day oral administration of CMA. It was reported that CMA causes prostatic atrophy by a direct effect which inhibits the

uptake of T in the rat prostate [5].

Brass *et al.* [1] proposed a single or repeated intramuscular injection of 2.5 mg/kg of CMA in the treatment of BPH dogs manifesting clinical signs, but found a case of recurrence as observed in dogs treated orally with CMA [2]. It therefore seems necessary to establish a simple, effective and recurrence-free treatment method with CMA.

The results of the present study indicate that the therapeutic effects of 7-day oral treatment with CMA at 2.0 mg/kg/day in dogs with BPH last for about three months or longer without side effects.

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