ANDROGEN DEPRIVATION THERAPY USING OSATERONE ACETATE IN DOGS WITH BENIGN PROSTATIC HYPERPLASIA

T.R. DHIVYA[1], P. SRIDEVI[2]*, K. KULASEKAR[3] AND P. KUMARASAMY[4]

Department of Clinics, Madras Veterinary College, Chennai - 600 007

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ABSTRACT

Benign Prostatic Hyperplasia (BPH) positive dogs were randomly treated with Osaterone acetate (OSA, n=10, 7 days, p.o.), and 6 BPH positive dogs served as untreated controls. Following treatment, the time taken for the remission of clinical signs ranged from 2-30 days with significant reduction in prostatic volume from month 2 to month 6 of the treatment. No adverse effects were noticed following OSA administration and all the treated dogs experienced complete clinical remission and stayed in remission throughout the 6 month trial period. This indicated that OSA rapidly and markedly reduced prostatic volume in dogs with BPH.

Keywords: Benign Prostatic Hyperplasia, BPH**,** Osaterone acetate, Canine, Dog

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a highly prevalent age related condition in dogs with more than 80% of the intact males over 5 years being affected (Johnston *et al.,* 2000). It arises spontaneously in the gland as a consequence of ageing and endocrine influence and may begin as early as 2-3 years of age, becoming cystic over 4 years of age. Whilst its pathogenesis remains unresolved, dihydrotestosterone (DHT) is considered important in promoting hyperplasia. Androgen action alone, however cannot explain BPH but other factors like estradiol and various mitogenic growth factors are also implicated in its pathophysiology. Chronic inflammation may additionally play a role in disease progression (Olson *et al*., 1987). Castration is the most effective treatment, with prostatic size decreasing by 50-70% and clinical signs disappearing within 3 weeks of surgery. Conversely medical treatment is often considered in cases where the risk of anaesthesia and surgery is unacceptable, if the affected dog is required for breeding, or if owner do not wish their dog to be castrated. This study investigates the effect of a relatively new drug Osaterone acetate (OSA) on the prostate volume in dogs with BPH.

[1]M.V.Sc. Scholar, [3]Professor, Department of Veterinary, Gynaecology and Obstetrics; [2]Professor; [4]Professor and Head, Department of Bioinformatics Centre and Aris Cell; *sridevi@tanuvas.org.in

MATERIALS AND METHODS

Sixteen dogs (n=16) diagnosed positive for BPH based on clinical symptoms, radiography and ultrasonography were utilized for the study and were divided into two groups of 10 (Group I) and 6 (Group II) each. Group I dogs were subjected to medical therapy using Osaterone acetate (YPOZANE®; VIRBAC Animal Health, France). The drug, available in the form of tablets in four dosage units viz.1.875, 3.75, 7.5 and 15 mg and designed to suit the animals of a wide range of body weights was administered orally at a target dose of 0.25 mg/kg body weight once a day for 7 consecutive days. The group II dogs served as untreated controls.

The ultrasonographic measurement of prostatic volume was taken prior to treatment and at weekly intervals for two weeks and thereafter at monthly intervals for a period of 6 months post treatment. At each visit of the patient, clinical signs relating to BPH were monitored, and clinical scores were obtained by summing the scores for the five clinical signs viz. blood discharge without micturition, constipation/

Table 1: Prostatic volume (Mean±SE, cm^3) **in osaterone acetate treated** (OSA) **and control** (C) **group of dogs with Benign Prostatic Hyperplasia.** Wk 0 - Pre treatment values, Mo - Months

Gp	Wk 0	Wk 1	Wk 2	Mo 1	Mo 2	Mo 3	Mo 4	Mo 5	Mo 6
OSA	72.0 ±5.3^{a}	55.6 ±6.4^{b}	44.3 ±7.1^{bc}	33.8 ±1.7^{c}	35.3 ±3.3^{c}	34.6 ±3.5^{c}	37.5 ±4.40^{c}	38.6 ±4.8^{c}	39.3 ±4.9^{c}
C	64.0 ±4.5^{a}	65.5 ±3.03^{a}	66.7 ±2.5^{a}	64.5 ±2.4^{a}	66.3 ±2.9^{a}	66.0 ±3.4^{a}	64.00 ±3.65^{a}	62.2 ±5.3^{a}	62.3 ±4.9^{a}

$p<0.05$, Means bearing different superscripts in a row differ significantly

tenesmus, hematuria/presence of blood in semen, urinary problems, difficulty in emptying the bladder and incontinence. To each of these, a score ranging from 0 to 3 was given, depending on severity (Albouy *et al*., 2008). The clinical recovery or complete remission was defined as a clinical score of 0 combined with a reduction in prostatic volume. The extent of clinical recovery following treatment with OSA was compared between groups and the efficacy of the drug on prostatic volume at various intervals after treatment was compared using One- way ANOVA.

RESULTS AND DISCUSSION

Dogs with BPH showed a mean score of 6.81 from a maximum clinical score of 12. The time taken for remission of clinical signs ranged from 2 to 30 days with 10, 20, 10, 20, 20 and 20% of dogs showing remission within 5, 6, 8, 14 and 30 days of OSA treatment, respectively. By the end of trial, OSA induced clinical remission in all the dogs. In a similar study, OSA reduced clinical signs in 75% dogs by day 14 with largest reduction of 88% by day 120. The complete clinical recovery was recorded in 50% dogs by day 14, and had induced clinical remission in 84% dogs by the end of the 6 month trial (Albouy *et al.,* 2008).

The mean prostatic volume declined ($p<0.05$) within first week of treatment with OSA and continued to decline statistically till month 1 post-treatment (Table 1). In control group, no significant changes in mean prostatic volume were observed throughout the evaluation period. From week 2 onwards till month 6, the prostate volume was lower ($p<0.05$) in OSA treated group when compared to control. A marked improvement in prostatic echogenecity to a normal pattern within first 7-14 days of OSA treatment was observed in the 3 dogs that had intra-prostatic cysts at the start of treatment. The impact of OSA treatment could be attributed to its potent antiandrogenic activity that included inhibition of androgen binding to androgen receptors and to other mechanism such as reduction of the androgen receptors, reduction of 5α reductase and inhibition of testosterone transport into prostatic cells (Tsutsui *et al*., 2000).

During the follow up visits after 6 month trail period, one dog showed signs of relapse characterized by an increase in prostatic volume and blood discharge with micturition. Treatment was subsequently started using the same drug for the second time. Within the first week of treatment the prostatic volume decreased to 43 cm^3 from the volume of 54 cm^3 observed prior to the treatment with no further complaint of blood discharge, thus indicating that dogs with relapse can be effectively retreated with OSA. However, the long-term adverse effects of OSA needs further study. In a study, signs of relapse in a gradual manner over a course of 120 days in 16% dogs was reported among the total dogs that exhibited complete remission of BPH (Albouy *et al.,* 2008).

In conclusion, a short 7-day course of OSA proved an effective and safe therapeutic regimen for BPH in dogs for a period of 6 months.

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