

Short Communication

EFFECT OF OSATERONE ACETATE ON SERUM TESTOSTERONE LEVELS AND SEMINAL PARAMETERS IN DOGS WITH BENIGN PROSTATIC HYPERPLASIA

T.R.Dhivya, P.Sridevi*, K.Kulasekar and P.Kumarasamy

Department of Animal Reproduction, Gynaecology and Obstetrics,
Madras Veterinary College, Chennai-600 007.

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ABSTRACT

This study was carried out with the aim to investigate the effect of Osaterone acetate (OSA), an antiandrogen on blood testosterone levels and the seminal parameters in dogs with benign prostatic hyperplasia (BPH). OSA treatment of dogs with BPH showed no significant changes in mean volume, concentration, live and dead and sperm motility. However, a transient increase in sperm abnormality was noticed by month 2 which gradually decreased to pretreatment levels by month 4 - 5. Similarly, a significant and transient decline in the mean testosterone levels were noticed following OSA administration indicating that the transient decrease in the testosterone level might be responsible for a transient increase in the sperm abnormality. No adverse effects were noticed following OSA administration and 100 per cent of the dogs experienced complete clinical remission of BPH and stayed in remission throughout the 6 month trial period.

MATERIALS AND METHODS

Two hundred and sixteen male dogs of different breeds, aged > 4 yrs brought to Madras Veterinary College Teaching Hospital with symptoms of dysuria, recurrent urinary tract infection, tenesmus and constipation were screened for BPH using ultrasonography. Sixteen dogs positive for BPH formed the experimental animals for the study. Group I dogs

were subjected to medical therapy using antiandrogen 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. Group II dogs served as untreated controls.

*Corresponding Author: Associate Professor, Department of Clinics, Madras Veterinary College, Chennai-600 007.

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Blood samples were collected thrice a day at 8.00 AM, 10.00 AM and 2.00 PM from the cephalic / saphenous vein for testosterone estimation and the mean value was regarded as the value of the day. Samples were collected prior to treatment and thereafter at weekly intervals for two weeks and then at monthly intervals for a period of six months. Serum was separated and stored at -20°C for testosterone estimation at a later date. Dogs were evaluated eight times during the treatment period as stated above together with ultrasonography.

Semen collection by digital manipulation was accomplished by using sterile gloved hands. The prepuce was pushed gently behind the bulbous glandis and pressure was exerted behind the bulbous glandis with fingers. The semen was collected in a sterile glass semen collection vial. The dog was released once the penis became flaccid and the prepuce returned to the normal position. Semen evaluation was carried out prior to treatment and during the follow up period to study the effect of the drug on seminal parameters.

RESULTS AND DISCUSSION

The mean prostatic volume (cm³) during pre treatment, week 1, week 2, month 1, month 2, month 3, month 4, month 5 and month 6 in the OSA treated group was 72.00 ± 5.30, 55.63 ± 6.43, 44.27 ± 7.09, 33.80 ± 1.68, 35.30 ± 3.32, 34.60 ± 3.51, 37.50 ± 4.40, 38.60 ± 4.85, 39.30 ± 4.90 cm³ respectively. Within the OSA treated group a significant ($P \leq 0.05$) decline in mean prostatic volume was found throughout the evaluation periods following treatment when compared to the pre treatment levels. The mean prostatic volume in pre treatment and the week

1 evaluation period of the OSA treated group were not significantly different from that of the control group. However, from week 2 onwards till month 6 the prostate volume was significantly lower ($P \leq 0.01$) in the OSA treated group when compared to the control group indicating that OSA rapidly and markedly reduced prostatic volume in dogs with BPH. OSA also caused a marked improvement in the prostatic echogenesity to a normal pattern within the first 7- 14 days of treatment in all the 3 dogs that had intra prostatic cysts at the start of the treatment.

In view of the large individual variations in the size of the prostate gland among the dogs, the reduction in prostatic volume induced by OSA was evaluated in terms of percentage reduction of the prostate volume. It was found that the percentage reduction was 30.20 by week1, 46.84 by week 2, 53.68 by month 1, 52.65 by month 2, 51.55 by month 3, 48.76 by month 4, 44.43 by month 5 and 43.43 by month 6 post treatment indicating that the percentage reduction in prostatic volume induced by OSA during the trial was seen within the first week of treatment with peak reduction observed by month 1.

With regard to the effect of OSA on sperm abnormality it was found that there was no significant difference in the mean volume, concentration, live and dead and sperm motility between the OSA treated and control group of dogs with BPH indicating that the OSA did not affect these parameters. However, a significant increase in the major sperm abnormality was noticed by month 2 (6.25 ± 0.66), which gradually declined to significant levels by month 5 (4.00 ± 0.58) and reached the pre treatment

levels by month 6 (4.50 ± 0.65), while a significant increase in the minor sperm abnormality was noticed by month 2 (5.75 ± 1.43), which persisted till month 5 (4.25 ± 0.63) and gradually declined to 3.25 ± 0.48 on month 6 which was statistically similar to pre treatment levels of 3.50 ± 0.65 . Major sperm abnormalities included dag defects, double heads, double tails and detached heads while minor sperm included bent tail and looped tails

The mean testosterone level prior to OSA administration was 3.34 ± 0.54 ng/ml, the peripheral blood testosterone level one week after OSA administration was maintained at 1.94 ng/ml or lower showing a clearly decreased level compared to the level prior to administration ($P \leq 0.05$). However, the level slightly increased by month 4 to reach 2.65 ± 0.15 ng/ml by month 5 which was statistically similar to the pre treatment levels. Although a significant and transient decline in the mean testosterone levels were noticed when compared to the pre treatment levels, this decline was within the normal limits reported for testosterone in dogs (0.1- 4 ng / ml) (Mischke *et al.*, 2002 and Koch *et al.*, 2000).

The results of the present study concurred with the findings of Tsutsui *et al.* (2001), who reported that the transient decrease in the testosterone level might be responsible for a transient increase in the sperm abnormality. The changes in the secretory discharge in the epididymis brought about by the reduced testosterone levels might have resulted in the increased incidence of abnormality in the sperm tail region as observed in the present study. The finding that the OSA used in the treatment of BPH helped to maintain

normal plasma LH levels (Tsutsui *et al.*, 2000) without adversely affecting the function of the testis and pituitary LH cells (Murakoshi *et al.*, 1992) could be the contributing factor for the normal testosterone levels (in spite of the transient decline) and maintenance of normal semen quality in the present study.

Summary

Although oral OSA administration was found to transiently decrease the peripheral blood testosterone level it did not markedly affect the semen quality suggesting that OSA is clinically applicable as a therapeutic drug for BPH in breeding dogs. The lack of adverse effects makes it suitable as a therapeutic drug for BPH in older dogs with anaesthetic risk for surgery.

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