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Trans-abdominal Intra-prostatic Injection of Ethanol and Oxytetracycline HCl under Ultrasonographic Guidance as a New Approach for Treatment of Benign Prostatic Hyperplasia in Dogs

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ABSTRACT

The aim of the present study is to assess the efficacy of trans-abdominal intra-prostatic injection of ethanol and oxytetracycline HCl under ultrasonographic guidance for treatment of canine Benign Prostatic Hyperplasia (BPH). Under sedation with xylazine HCl (1 mg kg^{-1} i.v.), aseptic precautions and ultrasonographic guidance, canine BPH was diagnosed in twelve dogs. Ten dogs were allocated randomly into two groups. The results indicated that there was obvious reduction of the prostatic size in both groups after one month of injection and disappearance of the clinical signs. Ethanol is more potent than oxytetracychne HCl as sclerosant in canine BPH. All data about the cases, clinical signs, abdominal and rectal examinations, ultrasonographic findings and postmortem finding were recorded. In conclusion trans-abdominal intra-prostatic injection of either ethanol or oxytetracycline HCl is an easy, quick, effective, safe, minimally invasive and cheap technique for treatment of canine BPH. Ethanol is more potent than oxytetracycline HCl as sclerosant in canines BPH.

Key words: Prostate, dog, ethanol, oxytetracycline, ultrasonography, hyperplasia, trans-abdominal

INTRODUCTION

The canine prostate is a well developed muscular glandular body that compensates the absence of seminal vesicles and bulbourethral glands.

It completely encompasses the proximal portion of the male urethra and neck of the bladder (Victoria and Melonei, 2005).

There is a dorsal groove and an internal septum dividing the prostate into right and left lobes which are subdivided into lobules by finer septa that radiate outwards to the capsule (Dyce *et al*., 1987).

The length, width, height and weight were 1.9-2.8, 1.9-2.7, 1.4-2.5 cm and 4-14.5 g, respectively. If the length, width or height of the prostate gland in adult dogs of large, medium or small breeds exceed 3-3.5 cm, the gland is most probably pathologically enlarged (Berg, 1958).

The most common prostatic diseases are Benign Prostatic Hyperplasia (BPH), intra-prostatic cyst, para-prostatic cysts, prostatic abscess, prostatic calculi, prostatic urethral stricture and neoplasm (Howard, 1975; Safwat, 1989).

About 90% of the dogs with prostatic affections were over 4 years of age (Howard, 1975). Doberman Pinscher was the most common breed with prostate disease (Krawiec and Heflin, 1992). BPH is a spontaneous and age-related disorder of intact male dogs which is associated with clinical signs of sanguinous prostatic fluid, constipation and dysuria (Johnston *et al*., 2000).

The dog is the only species, along with humans, in which prostatic hypertrophy develops spontaneously and almost universally with age. Benign Prostatic Hyperplasia (BPH) is benign enlargement of the prostate glands that is thought to result from hormonal imbalance (Matera and Archibald, 1966).

The occurrence of BPH was studied with different incidence. It was recorded in 87% (Hornbuckle *et al*., 1978), 60% (Weaver, 1978) and 80% (Johnston *et al*., 2000) in all male dogs over 5 years of age.

The disease occurs almost exclusively in men and dogs and is generally considered as a geriatric condition in both species. The hyperplasia may be glandular, fibrous or a combination of the both types and is usually associated with intra-prostatic cysts (Greiner and Johnson, 1983).

The following pathophysiologic sequence of prostatic diseases was suggested (Christie, 1983):

Prostatic hyperplasia→ductile blockage→prostatic fluid stasis→prostatic cyst formation+ infection→prostatitis→prostatic abscess→end-stage prostate disease

The clinical signs of prostatic diseases were listed as follow: tenesmus, difficult micturition, posterior limbs weakness, stiff gait, arched postures, anorexia, abdominal pain, pain upon rectal examination, incontinence, straining, hematuria, anuria, pyuria and sometimes perineal hernia. Spontaneous blood dripping from the penis, without urination is the most common sign for prostatic cysts (Howard, 1975).

Diagnosis of BPH in dogs is based on: case history, clinical signs, abdominal and rectal palpations, laboratory investigations, contrast radiography, ultrasonography and ultrasound guided-needle biopsies. Definitive diagnosis of BPH is frequently based upon histopathologic criteria.

Radiographic findings in BPH including: displacement of the bladder cranially and ventrally, displacement of the colon or rectum dorsally, identification of the enlarged prostate in the caudal abdomen as a rounded mass caudal to the bladder and positive contrast urethrogram may show narrowing of the prostatic urethra (Kevin *et al*., 2011).

Ultrasonographic findings in BPH include; the gland retains its shape, symmetry and smooth margin. The echotexture is homogenous and fine, but the echogenicity is slightly hyperechoic. Small anechoic areas may be seen, representing small retention cysts. If the cysts become large and are located at the periphery, they may disrupt the gland outline, in which case acoustic enhancement will be seen in the far field (Kevin *et al*., 2011).

Various treatment modalities were suggested for treatment of BPH in dogs including: Castration and antiandrogen therapy (Read and Bryden, 1995), Transurethral Microwave Thermotherapy (TUMT) (Terai *et al*., 1995), oral treatment with chlormadinone acetate at 2.0 mg/kg/day/7 days (Orima *et al*., 1995; Murakoshi *et al*., 2005), chemoablation using transurethral intraprostatic absolute ethanol injection (20 mL/animal) (Zvara *et al*., 1999; Plante *et al*., 2003), oral

administration of a new steroidal anti-androgen, osaterone acetate at 0.2 mg kg^{-1} (Tsutsu *et al.*, 2000), 5-alpha-reductase inhibitor finasteride (Sirinarumitr *et al.*, 2001), transurethral injection (using prostaject device) of ethyl alcohol (10% of prostate size) (Martov *et al.*, 2004) and intra-glandular injection of ethanol, phenol, polidocanol and oxytetracycline HCl (Mossa and Farag, 1998; Azoz *et al.*, 2001).

The use of prostalyser-1 (natrii chloridi 9.5 g, dimethyl sulfoxide 0.5 g, aquae distill. Ad 1000.0 g) and prostalyser-2 (spiritus aethylicus 96%-76.5 g, DMSO 0.5 g, aq. distill ad 100.0 g) solutions for chemical destruction of the prostate in case of BPH was recommended (Shioshvili *et al.*, 2005) while total prostatectomy, subtotal prostatectomy and castration were preferred by others Freitag *et al.* (2007).

The aim of the present study is to evaluate a new minimally invasive alternative chemical destruction of prostate in case of BPH by trans-abdominal intra-prostatic injection of absolute ethanol or oxytetracycline HCl.

MATERIALS AND METHODS

The present study was carried out on 12 dogs admitted to the surgery clinic. Full case history, animal description and all clinical signs were reported for each dog. Complete physical, abdominal and rectal examinations were carried out.

Ultrasonographic examination was carried out on each case to confirm the diagnosis of benign prostatic hyperplasia. Toshiba ultrasound device connected with 3.7-5 Mh_z convex transducer was used. The dogs were tranquilized with xylazine HCl 1 mg kg^{-1} b.wt. given intravenously. The prostate could be examined in dorsal recumbency. Hair was clipped and shaved lateral to the prepuce, Povidone iodine solution was used as antiseptic then acoustic coupling gel was applied. Sagittal and transverse scans were made. The transducer was placed parallel to the prepuce, perpendicular to the skin and the bladder was located. The transducer was moved caudally to the bladder neck. Angulation of the transducer from side to side would permit the prostate to be located. Transducer pressure may have to be increased to attain the best image.

For prostatic fluid aspiration and drug injection, the scan head was placed longitudinally on either sides of the prepuce. The sterilized biopsy guide was fitted to the transducer and the scanning was repeated. The transducer was angulated until the target place visualized the sterilized biopsy needle was pushed through the biopsy guide and advanced through the abdominal wall while being visualized on the monitor through the movement of the surrounding tissues. After puncture of the prostatic capsule, aspiration of the cystic fluid-if present- was carried out while the transducer was stabilized. Then the sclerosant agent was injected in the prostatic tissues.

Ten of the dogs had BPH, were randomly allocated into following groups for treatment:

- **Group I:** Five dogs were intra-prostatic injected (both lobes) with absolute ethanol (5-10 mL) by using the ultrasound guided needle after aspiration of prostatic fluid if present
- **Group II:** Five dogs were intra-prostatic injected (both lobes) with oxytetracycline HCl (5-10 mL of Pan Terramycin®, Pfizer Co.) by using the ultrasound guided needle after aspiration of prostatic fluid if present. Animals in severe pain post injection (Group I) were given carprofen (Rimadyl® tablets, Pfizer) (4.4 mg kg^{-1}) as pain killer for three days

The treated dogs were followed up every 15 days for 2 months by ultrasound examination. Repeated intra-prostatic injections, whenever required, were carried out after one month of the first injection. The animals were followed up till 6 month post injection by phone calls for any recurrence of clinical signs. All data about each dog were recorded in a special report.

Two of the affected dogs were excluded from the treatment protocol because they were suffered cauda equina syndrome with paraplegia beside BPH. These animals were euthanized on the request of the owners by using high dose of thiopental sodium given intravenously. Postmortem examination was carried out and the affected prostates were excised.

RESULTS

The age of the dogs ranged between 4-14 years. Rottweiler breed was the most common affected dogs. The affected dogs' breed were Rottweiler (4), German shepherd (3), Dopperman (3), Griffon (1) and Bull Mastiff (1).

The most common signs were tenesmus, dysuria, hematuria, anorexia, spontaneous dripping of blood from the penis without urination and constipation.

On rectal examination, the dogs had enlarged prostates. The abdominal examination revealed distension and pain.

Ultrasonographically, the gland retains its shape, symmetry, echotexture and smooth margin. The prostate appeared of large size 4-9 cm in length and 3.5-4.8 cm width with slightly hyperechoic pattern. According to the prostatic length, BPH was classified into three degrees including slight BPH (if the prostatic length is 3-5 cm) (Fig. 1), moderate BPH (if the prostatic length is 5.1-7 cm) (Fig. 2) and severe BPH (if the prostatic length>7.1 cm) (Fig. 4). Out of 12 affected dogs, 4 dogs had intra-prostatic cysts (1-2 cysts). The cyst appeared as anechoic area inside the echogenic prostate and ranged between 0.5-2.7 cm in diameter (Fig. 3, 5). Aspiration of the intra-cystic prostatic

Fig. 1: Ultrasonogram of slight degree of BPH in a 4-year-old German shepherd dog

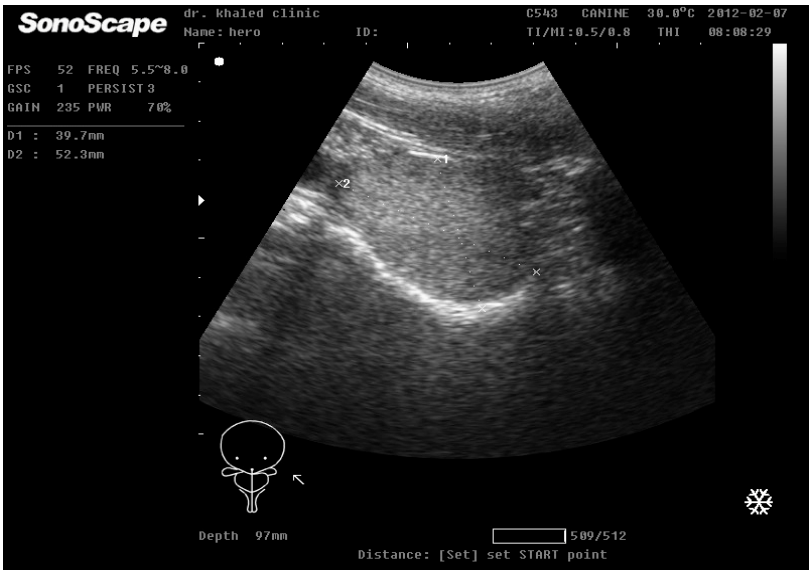

Fig. 2: Ultrasonogram of moderate degree of BPH in a 4-year-old German shepherd dog showing homogenous, fine and slightly hyperechoic echotexture with smooth hyperechoic capsule

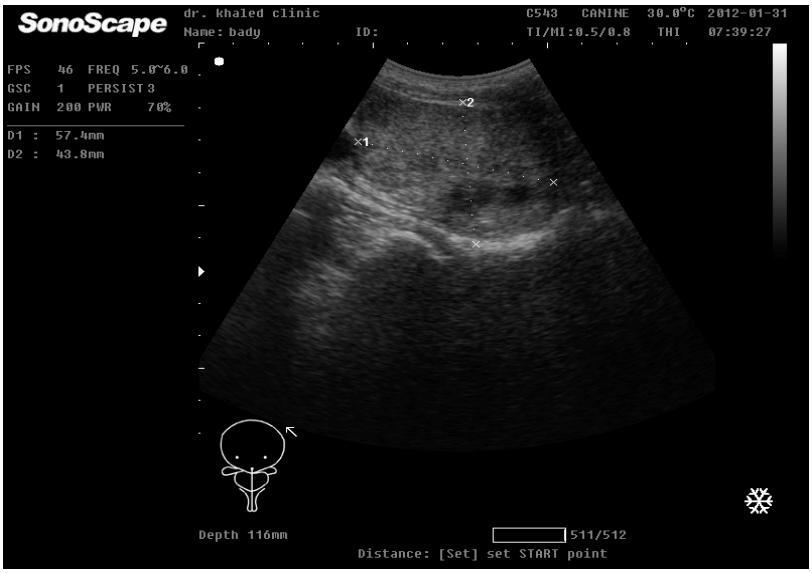

Fig. 3: Ultrasonogram of moderate degree of BPH in a 6-year-old German shepherd dog showing two intra-prostatic cysts (arrows)

fluid was carried out revealing pale yellow or sanguineous prostatic fluid, odorless fluid with varying degree of cloudiness. The amount of fluid ranged between 1-8 mL.

In group (I), the injected dogs responded well after one month except one case which had severe hyperplasia 9×4.5 cm and required reinjection with absolute ethanol. All dogs had nearly normal

Fig. 4: Ultrasonogram of severe degree of BPH in 10-year-old Rottweiler dog

Fig. 5: Ultrasonogram of moderate degree of BPH in a 5-year-old German shepherd dog showing large intra-prostatic cyst

sized prostate (3.5-4×3.5 cm) after two month post injection (Fig. 5-7). The prostate became more echogenic and had thicker capsule than before injection. Hematuria and dripping of blood from the penis stopped third day of injection. Signs of pain in the form of rising of the tail, stiff gaits, arched back and anorexia were noticed second day of injection and disappeared after two to three days. The urine flow and appetite were improved after one week of injection.

Fig. 6: Ultrasonogram of 5-year-old German shepherd dog after aspiration of the cystic fluid and intra-prostatic injection of absolute ethyl alcohol

Fig. 7: Ultrasonogram of 5-year-old German shepherd dog after 45 days of intra-prostatic injection of absolute alcohol showing approximately normal- sized and hyperechoic prostate gland

In group (II), the injected dogs had smaller prostate (4.4-4.7×3.5-3.9 cm) than before injection (Fig. 8-10) but the glands did not retain its normal size and intra-prostatic cysts were reformed after one month of injection in one dog. The prostate became more echogenic and had thicker capsule than before injection. Hematuria and dripping of blood from the penis stopped third day of injection. No signs of pain were reported after injection. The urine flow and appetite were

Fig. 8: Ultrasonogram of moderate degree of BPH with intraprostatic cyst in a 5-year-old German shepherd dog

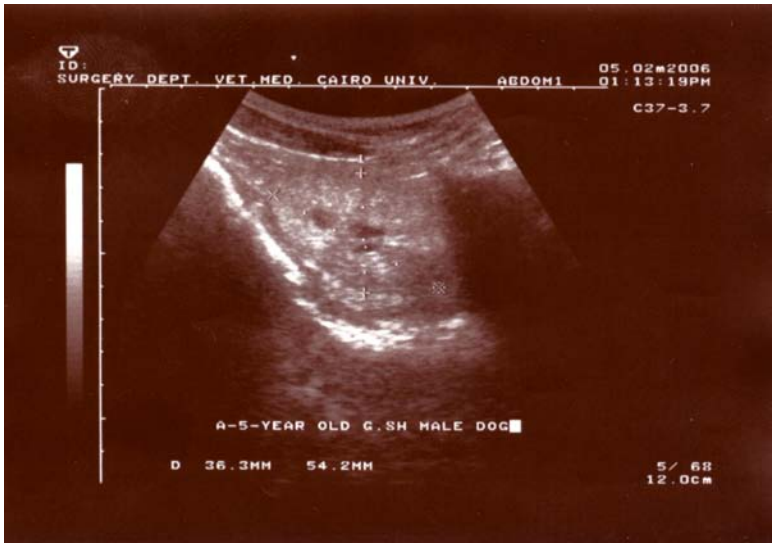

Fig. 9: Ultrasonogram of 5-year-old German shepherd dog after 15 days of intra-prostatic injection of oxytetracycline HCl showing decreased-sized and hyperechoic prostate gland with regression of the intraprostatic cyst

improved after one week of injection. Out of five dogs, three dogs were reinjected with oxytetracycline after one month of the first injection. After two months, the clinical sings disappeared and the prostatic size was decreased but still did not attain its normal size.

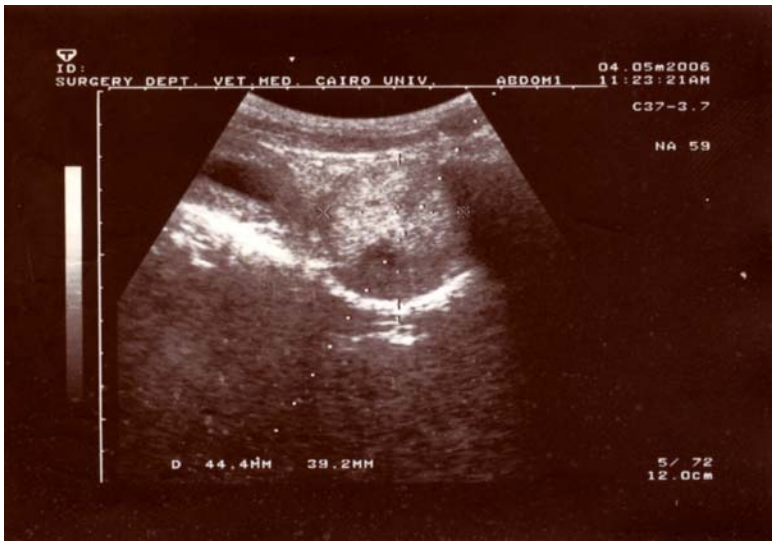

Fig. 10: Ultrasonogram of 5-year-old German shepherd dog after 3.5 month of intra-prostatic injection of oxytetracycline HCl showing decreased-sized and hyperechoic prostate gland with regression of the intraprostatic cyst

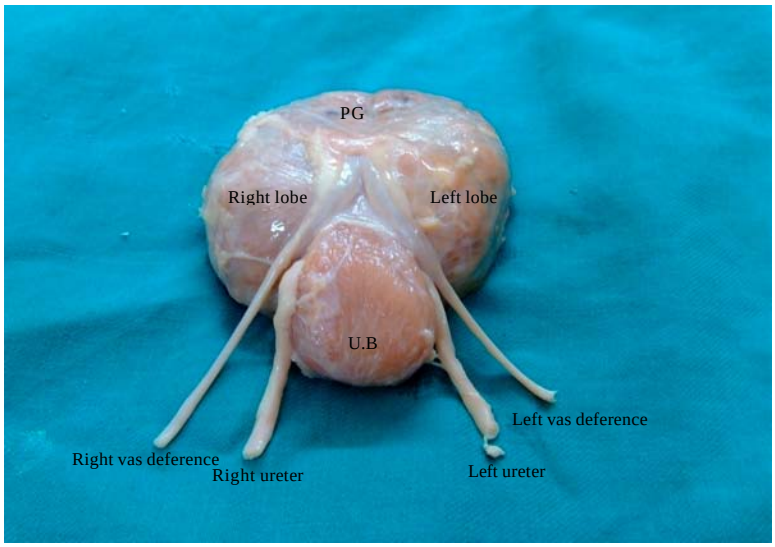

Fig. 11: Gross appearance of BPH: urinary bladder (U.B) and bilaterally symmetrically enlarged prostate gland (PG)

Postmortem examination revealed symmetrical glandular hypertrophy, smooth prostatic surface (Fig. 11), narrowing of the intraprostatic urethra, congested urinary bladder, moist cut surface with greasy secretion and cystic lesions containing prostatic fluid. The prostate gland weighted 150 and 180 g and measured 8.5-9×4-4.5 cm in both dogs.

DISCUSSION

Benign prostatic hyperplasia is a major disease in dogs and men and its non surgical therapy is a major area of interest. Therefore, old dogs with spontaneous BPH are useful animal models for the etiological and pharmacological researches of human BPH (Cai *et al*., 2003).

The most common clinical signs associated with BPH are tenesmus and constipation. This could be explained by the prostatic enlargement which partially occludes the lumen of the rectum. Hematuria could be explained by the severe straining associated with BPH. Similar explanations were mentioned (Greiner and Johnson, 1983; Victoria and Melonei, 2005).

In this study, out of 12 cases, four cases of BPH had intra-prostatic cyst. This could be explained by the ductile blockage and stasis of the prostatic fluid that produce intra-prostatic cyst. Similar, pathophysiologic sequence was described before (Christie, 1983).

The aspirated prostatic fluid was pale yellow with varying degree of cloudiness. The fluid was differentiated from urine by its lack of uriniferous odor.

Ultrasonographically, BPH could be differentiated from cystic prostate, neoplastic prostate or prostatic abscess by its symmetric prostatomegaly and echogenicity. In addition, prostatomegaly seen with cystic prostate, neoplastic prostate or abscess is generally larger than that seen with hyperplastic prostate.

Recent studies were used expensive and sophisticated techniques as laser therapy (Muschter, 2008) and three-dimensional conformal radiation therapy (Zhao *et al*., 2011) on the treatment of BPH. In the present study, an easy, cheap, rapid and safe method was used under ultrasound guidance by intra-prostatic injection of either ethanol or oxytetracycline HCl as sclerosants. These agents produce hemorrhagic infarction in the glands within one week followed by coagulative necrosis within one month post injection, then by fibrous replacement of necrosis and moderate atrophic changes of prostatic acini after 2 months (Azoz *et al*., 2001).

Although oxytetracycline HCl is less painful than absolute ethanol as intraprostatic injections, absolute ethanol is more potent than oxytetracycline HCl for chemical destruction of prostate in case of BPH. Similar finding was recorded (Azoz *et al*., 2001).

Both oxytetracycline HCl and ethanol produce chemical destruction of the prostate glands in case of BPH after one to two month of injection which results in obvious reduction in the prostatic size that improves the urine flow. In addition these drugs have antibacterial action which controls the infection if it is present.

Trans-abdominal intra-prostatic injection under ultrasound guidance is an easy and accurate method because of the difference in acoustic impedance between the prostate gland and the needle allows it to be accurately visualized in the prostate as a bright image within the prostatic parenchyma.

In conclusion, Trans-abdominal intra-prostatic injection of either oxytetracycline HCl or ethanol is an easy applicable, safe, quick, cheap, less invasive and effective approach for treatment of canine BPH and consequently in human BPH especially in high risk or sexually active patients after further study.

REFERENCES

Azoz, M., K. Farag and A. Soumaya, 2001. Experimental study of effect of intraglandular ethanolamine oleate, polidocanol and oxytetracycline HCl injections in canine benign prostatic hyperplasia. Med. J. Cairo Univ., 69: 159-165.

Berg, O.A., 1958. The normal prostate gland of the dog. Acta Endocrinol., 27: 129-139.

Cai, R.F., Y.G. Cui, L.X. Hua, Y. Jia, D.Z. Ma and X.H. Wang, 2003. Experimental research on spontaneous benign prostatic hyperplasia in old dogs. Zhonghua Nan Ke Xue, 9: 651-657.

Christie, T.R., 1983. Prostate Gland and Testes. In: Current Techniques in Small Animal Surgery, Bojrab, M. (Ed.). 2nd Edn. Leaand Febiger, Philadelphia.

Dyce, K.M., W.O. Sack and C. Wensing, 1987. Textbook of Veterinary Anatomy. 3rd Edn W.B. Saunders Company, UK., Pages: 437.

Freitag, T., R.M. Jerram, A.M. Walker and C.G. Warman, 2007. Surgical management of common canine prostatic conditions. Compend Contin Edu. Pract. Vet., 29: 656-660.

Greiner, P.T. and G.R. Johnson, 1983. Diseases of the Prostate Gland. In: Textbook of Veterinary Internal Medicine, Diseases of the Dog and Cat, Stephen, J. (Ed.). 2nd Edn., W.B. Saunders Company, Philadelphia.

Hornbuckle, W.E., D.M. MacCoy, G.S. Allan and R. Gunther, 1978. Prostatic disease in the dog. Cornell Vet., 68: 298-305.

Howard, D.R., 1975. Prostatic Disease and Prostatectomy. In: Current Techniques in Small Animal Surgery, Bojrab, M.J. (Ed.). Ist Edn. Leaand Febiger, Philadelphia.

Johnston, S.D., K. Kamolpatana, M.V. Root-Kustritz and G.R. Johnston, 2000. Prostatic disorders in the dog. Anim. Reprod. Sci., 60-61: 405-415.

Kevin, J.K., M. Hester and G. John, 2011. Diagnostic Radiology and Ultrasonography of the Dog and Cat. 5th Edn. Saunders, Elsevier Limited, UK., pp: 175-185.

Krawiec, D.R. and D. Heflin, 1992. Study of prostatic disease in dogs: 177 cases (1981-1986). J. Am. Vet. Med. Assoc., 200: 1119-1122.

Martov, A.G., D.A. Pavlov, V.I. Kirpatovskii and IuV. Kudriavtsev, 2004. Intraprostatic injection of 96% ethanol in experimental animal model. Urologiia, 6: 21-26.

Matera, E.A. and J. Archibald, 1966. Prostate Gland. In: Canine Surgery, Spreull, J.S.A. and J. Archibald (Edn.). 1st Edn. American Veterinary Publications, Evanstone.

Mossa, F. and K. Farag, 1998. Experimental study of local injection of ethanol and phenol in benign prostatic hyperplasia (canine Model). Sci. J. Az. Med. Facul., 19: 853-859.

Murakoshi, M., R. Ikeda, N. Fukui and T. Nakayama, 2005. Relationship between prostatic atrophy and apoptosis in the canine spontaneous benign prostatic hyperplasia (BPH) following chlormadinone acetate (CMA). Urologiia, 6: 18-23.

Muschter, R., 2008. Laser therapy for BPH. Aktwelle Urol., 39: 359-368.

Orima, H., M. Shimizu, T. Tsutsui, E. Kawakami and A. Ogasa, 1995. Short-term oral treatment of canine benign prostatic hypertrophy with chlormadinone acetate. J. Vet. Med. Sci., 57: 139-141.

Plante, M.K., A.L. Gross, J. Kliment, M. Kida and P. Zvara, 2003. Intraprostatic ethanol chemoablation via transurethral and transperineal injection. BJU Int., 91: 94-98.

Read, R.A. and S. Bryden, 1995. Urethral bleeding as a presenting sign of benign prostatic hyperplasia in the dog: A retrospective study (1979-1993). J. Am. Anim. Hosp. Assoc., 31: 261-267.

Safwat, E.A., 1989. Differential diagnosis of prostatic diseases in the dog with special regard to ultrasonographic guided needle biopsy. Ph.D. Thesis, Faculty of Veterinary Medicine, Assiut University, Egypt.

Shioshvili, T.I., G.Z. Chokhonelidze, T.A. Shulaia, E.D. Kazaishvili and T.V. Gogoladze, 2005. Chemical destruction of the prostate by Prostalyser-1 and Prostalyser-2 solutions: An experimental study in dogs. Urologiia, 6: 18-23.

Sirinarumitr, K., S.D. Johnston, M.V. Kustrit, G.R. Johnston, D.K. Sarkar and M.A. Memon, 2001. Effects of finasteride on size of the prostate gland and semen quality in dogs with benign prostatic hypertrophy. J. Am. Vet. Med. Assoc., 218: 1275-1280.

Terai, A., Y. Arai, I. Yamamoto, H. Onishi, K. Oishi and O. Yoshida, 1995. Newly developed transurethral radiofrequency thermotherapy device for benign prostatic hyperplasia: A pilot study in canine prostate. Int. J. Hyperthermia, 11: 627-635.

Tsutsu, T., T. Hori, M. Shimizu, H. Orima, E. Kawakami and S. Fukuda, 2000. Regression of prostatic hypertrophy by osaterone acetate in dogs. J. Vet. Med. Sci., 62: 1115-1119.

Victoria, A. and O. Melonei, 2005. Introduction to Veterinary Anatomy and Physiology 1st Edn., Elsevier Limited, UK.

Weaver, A.D., 1978. Discrete prostatic (paraprostatic) cysts in the dog. Vet. Record, 102: 435-440.

Zhao, P., S. Lu and Y. Yang, 2001. Three dimensional conformalradiation therapy of spontaneous BPH in canines. Oncol. Res., 19: 225-235.

Zvara, P., E. Karpman, R. Stoppacher, A.C. Esenler and M.K. Plante, 1999. Ablation of canine prostate using transurethral intraprostatic absolute ethanol injection. Urology, 54: 411-415.