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Surgical treatment and ethanol injections in hyperplastic prostate in dogs

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Summary

The aim of the study was to evaluate the effect of two different methods of partial prostatectomy, to evaluate the influence of 96° ethanol injection on hyperplastic prostate and to compare the efficacy of ethanol injection with the efficacy of surgical treatment of the prostate. The study was performed in the years 2001–2003 in the surgical department of Dr. L. Kriaučeliūnas Small Animal Clinic. The surgical treatment (prostatectomy) was performed on 8 dogs using 2 methods: fillet and subcapsular. We compared the effectiveness and postoperative hystological evaluation of bioptats one and two weeks after surgery. We have performed ethanol injection on 5 dogs and evaluated the histological feature of prostatic tissues after injection to measure the effect of ethanol.

The fillet method is technically simpler, shorter and the tissues of the prostate heal more quickly. Ethanol injection induces multi-focular coagulative necrosis, followed by fibrosis and atrophy of the prostate. This way of treatment is simpler and easier because there are no sections through prostate tissues. To avoid a section of the abdominal wall, a transurethral catheter can be used for the ethanol injection.

Keywords: dogs, prostata

Castration is the most common and the most effective way of treatment of prostate hyperplasia in dogs. After castration full and fixed regression of the gland takes place (2). But this method is not suitable, when the dog is purebred and is meant to have the offspring. Sometimes dog owners refuse to perform castration due to psychological reasons. Disorders of dog's metabolism and adiposity often take place after castration. Changes of neurohumoral regulation lead to changes of behavior: such dog can become aggressive, does not ask to go out to urinate (3). The other way of surgical treatment is partial prostate resection, performed using subcapsular and fillet method. Prostate resection sometimes can complicate in stenosis of urethra due to its lesion or scarring formation (3).

Surgical and other methods are tested on dogs previous to use them in human medicine. Among such methods can be mentioned: electrovaporisation (1, 17), transurethral injection of collagenase (11), transurethral photosensibilisation while injecting ethyletiopurpurin (SnET2) intravenously (23), transurethral big intensity focused ultrasound (6, 9), rotoresection (21), transurethral balloon laser hyperthermia (24). Other treatment method of prostatic hyperplasia is pharmaceutical method. The steroidal and nonsteroidal antiandrogens are used. Steroidal antiandrogens are cyproterone acetate, chlormadinone acetate, and medroxyprogesterone acetate. They are blocking androgen receptors and inhibiting 5 - & - reductase (15). Antiandrogen finasteride – synthetic 4 – azasteroid is very suitable for dogs (16). Flutamide is nonsteroidal antiandrogen that blocks dihydrotestosterone receptors of prostate epithelium (12). Tamoxifen is nonsteroidal antiestrogen. It inhibits activity of aromatase and acts on estrogen receptors of prostate epithelium. The gosipol have antisteroidal action, and it is considered, that in future it may possibly be used for treatment of dogs prostate hyperplasia (4).

But the pharmaceutical treatment of dogs prostate hyperplasia have some disadvantage: significante reduction in prostate size occure only over 1-2 month and after withdraval of pharmaceutical, the size of prostate progressively regenerate. Also this treatment method is expensive (with flutamide or finasteride) (12).

Some scientist tired to use injections of Querin bacillus derivatives into tissues of prostate (22). Cold also was tried to apply, using flat applicator during laparotomy (8). Alternative treatment method is also pharmaceutical method. One of them, pharmaceutical

method is temporal; while medicaments are given to an animal, gland is growing down, but when discontinued – process renews, in addition, pharmaceutical method is expensive.

Ethanol injections are applied worldly in treatment of tumors of various organs and diseases, as cysts of thyroid gland, Greivs disease, autonomic functioning nodules of thyroid gland (7), nonresectable tumors of pancreas (26), liver tumors (13), neurinomas of wrist area (20) and other. 96° ethanol induces necrosis and aseptic inflammation and later fibrosis of the organ or tumor where ethanol was injected develops (7, 13, 20, 26). Injections of absolute ethanol into prostate are increasingly used for treatment of benign hyperplasia in human medicine (10, 14, 27). This method was tested with dogs previously.

The aim of the work was to compare the effectiveness of two surgical methods of prostate elimination and the effectiveness of ethanol injections into prostate.

Material and methods

The studies were performed according to 06.11.1997 „Law for the care, treatment and management of animals of the Republic of Lithuania" No 8-500 (published in „Valstybės žinios", No 108, November 28, 1997), the order No 4-16 „Regarding usage of laboratory animals in scientific experiments", published January 18, 1999, the order No 155 of the Minister of Health „Regarding good Laboratory Practice (GLP) rules for non-clinical (experimental) laboratory investigations", published April 12, 1999 and the permission No 3 of Director of the State Food and Veterinary Service, given May 06, 2003.

In the surgical department of Dr. L. Kriaučeliūnas Small Animal Clinic 8 dogs 5-8 years of age were used for surgical treatment and 5 dogs 5-9 years of age were used for ethanol injection. All dogs were clinically healthy and showed no signs of prostate diseases. Prostate glands were examined rectally and ultrasonographicly. During rectal examination, all prostates were movable, smooth and moderately firm, but not hard in texture, median raphe was palpable. Almost all prostates were found in the abdominal cavity. Ultrasound showed homogenous texture, normal to slightly hyper echoic. After surgical ablation, prostate tissues specimens were examined histologicaly. Normal histological structure, epithelial hyperplasia or epithelial hyperplasia with small cysts was found.

One lobe of prostate was operated using fillet method – almost all parenchyma of the gland was removed with the capsule, leaving only about 5 mm layer around the prostatic part of the urethra. The remaining open tissues of prostate were covered with periprostatic fat and omentum. The other part of prostate was operated using subcapsular method of gland elimination – parenchyma was eliminated from the center to the outer side, mostly lateral and dorsolateral parts, leaving 2-3 mm layer of parenchyma near capsule. The gland was closed, leaving as small cavity as possible and eliminating redundant walls of prostate (25). To evaluate the healing, tissues for histological assay were taken after 1 and 2 weeks.

Ethanol injections were performed in two ways. During operation for two dogs six 1.5 ml injections of 96% ethanol were made: two injections (proximally and caudally) into each lobe in dorsal parts and one injection into each lobe in ventral parts. The leek of ethanol was absorbed with sterile tampons immediately. Dorsal parts were reached by keeping urinary bladder and turning it into one or another side respectively, and raising it slightly. The places of injections were not cauterized with electrocoagulator for these dogs. For the other three dogs the smaller dose – 1 ml of ethanol was injected into 6 places, and the place of injection was cauterized with electrocoagulator immediately.

To relieve the urination, the catheter was plunged into urinary bladder during three successive days for the all dogs (for those that were operated and for those that received ethanol injections). Injections of the analgesic (Novasul) were performed. Five day later the catheters were removed.

Pathological material of prostate from euthanized dogs was taken in order to evaluate the healing processes. The material for histological examination was taken after 3 days, 2 week, one month, and two months after the injection of ethanol. The sonography was performed before and after the operation.

Results and discussion

In the pathological material, which was taken from that lobus of prostate where fillet method was applied, after two weeks, few remaining outflow tubules were seen. These ducts were covered with intermediate (in the place of opening into urethra) and cubical epithelium. Stroma between the ducts was thickly infiltrated with lymphocytes and macrophages. The inflammatory cells were found also in the lumen of some ducts. The adipose tissue was also thickly infiltrated with inflammatory cells and lots of erythrocytes were concentrated in some places. Young granulation tissue was formed between remaining tissues of prostate and adipose tissue. (fig. 1a). Using this method, there were less blood masses between the remaining part of the gland and adipose layer covering the surface of resection and connective tissue formed more quickly. Technically duration of this surgical method was shorter, even hardly reachable tissues are easily eliminated; there is no need to near margins of the gland. A little clot of blood forms in the place of the section and it quickly resolves. Forming of connective tissue of the scar is quicker and not so thick. This tissue vanishes and do not deform the remaining gland. There are such limitations: urethra may be touched and it can cicatrize. The gland can gain mobility because of accretion with surrounding tissues.

In the other side of the gland, where subcapsular method was applied, between the capsule and left during elimination gland structures thick accumulations of fibrin with fragmented erythrocytes were found. These accumulations were already overgrown by the young granulation tissue; a lot of inflammatory cells, lymphocytes, macrophages, and in some places neu-

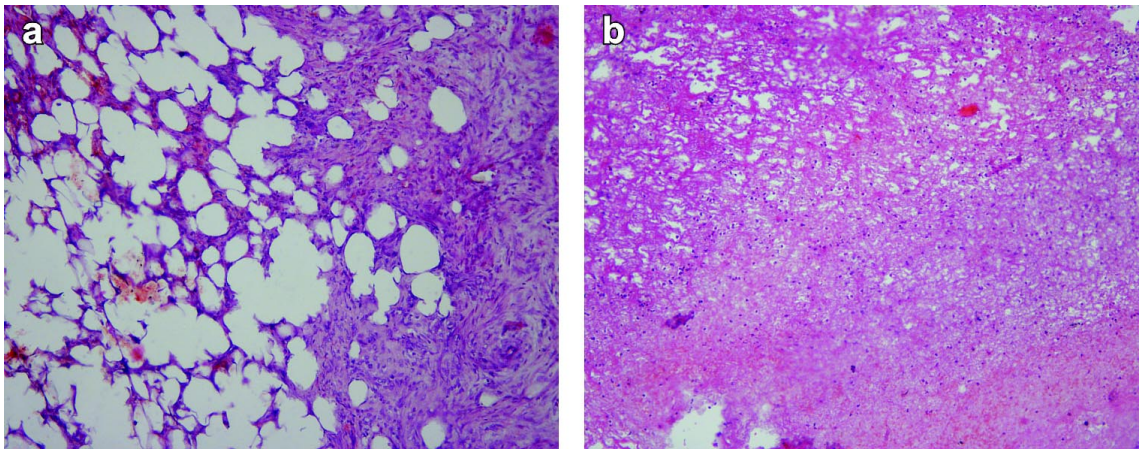

Fig. 1. Prostate histological view after 2 weeks after surgical ablation of prostate. a – Fillet method. Young granulation tissue formed in the remaining prostate parenchyma is seen. This tissue is growing into the periprostatic adipose tissue, which section place after eliminating of the parenchyma has been covered with; b – subcapsular method. Starting to develop masses of fibrin with sparse cells of inflammation are seen between remaining prostate part and the capsule of gland (HE, 10 × 20)

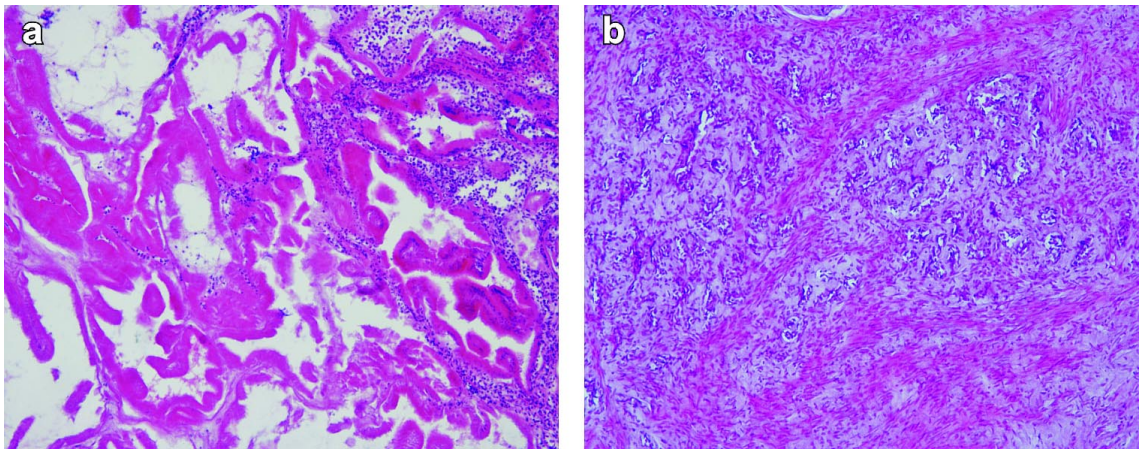

Fig. 2. The ethanol effect on prostate tissue. a – 3 days after ethanol injection. Coagulation necrosis of prostate glandular parts and stroma is seen – tissues are sharply basophilic, area of necrosis is surrounded by inflammation cells; b – 2 month later. Conspicuous fibrosis and atrophy of prostate is seen (HE, 10 × 20)

trophiles were seen in their periphery. Part of the left during elimination gland structures was fragmenting now. Massive young granulation tissue was forming (fig. 1b). The capsule of the gland remains separated when eliminating parenchyma. A big cavity filled with blood remains in such way. Later it overgrows with connective tissue. The anatomical structure of the organ is preserved, but in the cavity (between the capsule and the remaining part of prostate) exudate and blood aggregate abundantly and later massive connective tissue forms. The advantages of subcapsular method are these: minor defect of the gland, better mobility of the gland; small affected areas can be eliminated and the healthy tissue can be left for regression after castration. Limitations are these: the method is more difficult technically, operation lasts longer, a cavity forms in the gland, where blood and clots of blood aggregates, the process of healing lasts longer, forming of scar tissue takes more time and it can deform the gland.

Ethanol injections. One dog from I group was euthanized 3 days later after ethanol injection. As it was mentioned, we have used the major doses of ethanol for dogs of this group and injection sites were not cauterized – the ethanol reflux occurred, and it caused extensive aseptic peritonitis. For other dog we find only minimal aseptic peritonitis.

The dogs from II group (for these dogs we have used lesser doses of ethanol, and injection site was cauterized), showed not clinical sings of peritonitis, and during autopsy, peritonitis was not observed. Two dogs from the second group were euthanized after one and after two months and one was left for further observation. Complications after operation were not observed in these dogs. On the other day after operation all the dogs urinated with blood addition and this lasted for 4 or 5 days. Not significant raise of body temperature was observed in one dog and it lasted for 2 days. Common condition of the dogs was good: all dogs showed normal appetite and there were no signs of pain. Complications after operation were not observed in these three dogs, only raise of body temperature was observed in one dog and it was not significant.

In samples taken three days after the injections histological massive aggregations of coagulative necrosis were observed – epithelium and connective tissue were clearly basophilic in color, the nuclei of the cells were not found. The zones of necrosis were surrounded by large zones of inflammatory cells (neutrophiles, single lymphocytes) and hyperemia (fig. 2a). In the histological preparations prepared from the pathological material taken 1 month after the ethanol injections the atrophy of the gland was observed, the

whole gland was involved; there were average number of inflammatory cells in the connective tissue. Acinusi were not big, cells were low, a lot of connective tissue was seen. In the histological preparations prepared from the pathological material taken 2 month after injections still smaller acinusi were observed, their lumen were still more narrow; the histological view was identical to the view senile gland involution (or after castration). Significant decreases in size of the gland were observed during sonograpfhy (fig. 2b). One dog was left for further observation. This dog lives for three years already and shows not clinical symptoms in connection with hyperplastic prostate.

As far back as 1988, Littrup and collegues injected ethanol transperineally into dog prostates. After ethanol injections, a massive coagulation necrosis in dogs' prostates was observed and later full atrophy of the glands took place (18). Histological view of the gland was identical to senile atrophy and atrophy after castration. It is considered that coagulation necrosis of prostate tissues develops not only because of direct effect of ethanol, but also because of lesion of blood vessels (10). Whereas transurethral catheter was used, the capsule of the gland was not violated there was no influence on the sphincter and epithelium of the urethra and the section through tissues of abdominal wall is not used (10, 27). In 2004, the Russian scientists also tried this method with dogs and they injected ethanol through transurethral catheter (19).

We injected ethanol through capsule of prostate and cauterized the place of injection with electrocoagulator, because the ethanol leaked form the place of injection inducts strong aseptic inflammation of abdomen wall and surrounding tissues.

This method is less invasive and effective, widely available, inexpensive. The similar method is transurethral enzymic elimination of prostate, injecting into dogs' prostate the mixture, which consists of Triton X, hialuronidase, collagenase and gentamicine. Such injection induced atrophy of gland stroma and cystic dilatations of acinuses, but did not have any influence to surrounding tissues. This method is offered to use in human medicine (5, 11).

In comparing the two surgical methods, the fillet method is technically simpler, shorter and the tissues of prostate heal more quickly.

96° ethanol injection causes stabile fibrosis and atrophy of prostate tissues.

After each ethanol injections into prostate, to cauterize the injection site is necessary, to avoid reflux of ethanol from injection site and aseptic peritonitis. This way of treatment is simpler and easier in comparing with surgical methods, because there are no sections through tissues of prostate.

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