

Comparative Experimental Evaluation of the Efficacy of Prostamol Uno and Samprost on Rat Model of Chronic Aseptic Prostate Inflammation

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Comparative experimental evaluation of the efficiency of prostatotropic drugs Prostamol Uno and Samprost on the model of the chronic aseptic prostate inflammation in rats was performed. It was established that peptide drug Samprost decelerates sclerotic processes in the prostate gland to a greater extent than herbal preparation Prostamol Uno. Both products equally stimulate secretory activity of the gland. Prostamol Uno, unlike Samprost, prevents the development of reduced sexual motivation, one of the complications of chronic prostatitis.

Key Words: *chronic aseptic prostatitis; rats; Prostamol Uno; Samprost*

Chronic prostatitis is one of the most common urological abnormalities in men [5]. Treatment of abacterial form of the disease diagnosed in the majority of patients (90%) is a difficult problem [12]. Chronic abacterial prostatitis is recurrent. It is often complicated by violation of the copulative function, which markedly reduces quality of life in men [7,16]. More than 20 groups of drugs are currently used for the treatment of this disease. However, no substantiated approaches for the treatment strategy for chronic abacterial prostatitis were proposed [8,15]. Bioregulatory peptides derived from the prostate tissue of mature bulls are among the actively used drugs. They provide organotropic effect on prostate [12]. Samprost is one of these drugs with antiplatelet and anticoagulant properties. Its anti-inflammatory properties are associated with the capacity to increase the synthesis of antihistamine and antiserotonin antibodies and improve microcirculation

in the prostate [4]. Another trend of modern therapy in patients with chronic abacterial prostatitis is the use of plant preparations derived from *Serenoa repens* (sabal palm); one of them Prostamol Uno is widely used in medical practice [3,6]. Its anti-inflammatory effect is determined by inhibition of phospholipase. In addition, Prostamol Uno exhibits marked anti-edema activity, affects the vascular phase of inflammation and capillary permeability, and reduces vascular stasis [3]. Since administration of the drug inhibits type 1 and type 2 5 α -reductase, it is used in the treatment of benign prostatic hyperplasia often accompanying chronic prostatitis.

Here we compared the efficacy of Prostamol Uno and Samprost on rat model of chronic aseptic prostate inflammation.

MATERIALS AND METHODS

Experiments were carried out on 4-month-old male outbred rats weighing 330-500 g ($n=40$), 10 of those served as controls and 10 rats as background. The animals were obtained from the nursery of the Institute of

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Pharmacology. The animals were kept in accordance with the regulations approved by the European Convention for Vertebrate Protection (Strasbourg, 1986).

Chronic aseptic prostate inflammation was caused by suturing its ventral lobe with a silk thread [1]. The surgery was performed under general anesthesia with sodium thiopental (60 mg/kg intraperitoneally). The test drugs were administered to animals for 15 days; the treatment was started 1 month after surgery. Samprost was administered in a dose of 20 mg/kg intramuscularly, Prostamol Uno in a dose of 50 mg/kg intragastrically in 2.5% ethanol solution [10]. Control rats received equivalent volume of the solvent at the same time. Forty-five days after surgery, the sutured ventral prostate lobe was dissected, weighed, and weighting factor was calculated. The volume of the stitched lobe was determined and its density was determined. For histological examination, the right (sutured) part of the anterior prostate lobe was excised, fixed in Carnoy's fluid, embedded in paraffin, and 5- μ sections were prepared. Deparaffinized sections were stained after van Gieson for visualization of the connective tissue. Using computer graphic analysis, the area of epithelial structures and lumens of terminal parts of the glands and the area of collagen fibers in connective tissue layers were measured on the standard area of histological section and the percentage of these structures of the standard section area was calculated. The rest of the sample was used for measuring zinc content by emission spectroscopy [2]. Functional status of the gland was assessed by zinc content, which is an indicator of secretory activity of the prostate [9]. In addition, the presence of zinc in preparations Prostamol Uno and Samprost was determined by emission spectroscopy.

Since copulation disturbances are usual complications of chronic prostatitis, sexual behavior of the examined rats was studied 1 day before taking tissue samples. To this end, the males were housed with estrous females (estrus was induced by administration of folliculin for 4 days). Phase of the sexual cycle was verified by cytology of vaginal smears. The following parameters were recorded for each male over 15 min:

latent period of mounting (time between first female presenting and the first mounting), total number of mountings (attempts to copulate), and the number of copulations [13].

The experimental data were treated statistically using nonparametric Mann–Whitney test and angular Fisher transformation.

RESULTS

Microscopic examination of the ventral prostate lobe in the control group 45 days after suturing revealed dilated and plethoric blood vessels. The connective tissue layers between the acini were wider than in the normal due to both edema/infiltration and growth of collagen fibers. The area occupied by fibers was significantly (3.7 times) greater than in the background group (Table 1) indicating pronounced sclerotic processes. Epithelium of terminal parts was lower than in rats of the background group (Table 1): its area was significantly reduced by 26%. Since the area of acinus lumens in animals of the background and control groups was almost identical, the decrease in the area of epithelium lining the terminal sections of the prostate may indicate atrophy of the epithelium. Thus, 45 days after suturing of the anterior lobe of the rat prostate gland, multiple sclerosis, atrophy, and infiltration of the stroma develop, which are the morphological features of chronic inflammation.

In rats receiving prostaticotropic drugs against the background of the surgery, hyperemia and infiltration of gland tissue were moderately expressed. The area of collagen fibers was reduced by 2 and 2.9 times, respectively, in comparison with the control (Table 1). These parameters in both experimental groups did not differ significantly from the background. The area of epithelium in acini when administered both Prostamol Uno and Samprost did not increase in comparison with the control and was reduced in comparison with the background, which suggested that the drugs did not inhibit the development of atrophic processes. The areas of acinus lumen in the two groups were similar, except that in animals receiving Prostamol Uno. This

TABLE 1. Morphometric Parameters of the Prostate in Rats with Chronic Prostatitis Treated with Prostaticotropic Drugs (%), $X \pm m$)

| Parameter | Background | Control | Prostamol Uno | Samprost |
|---------------------------|------------------|-------------------------------|-------------------------------|-------------------------------|
| Area of collagen fibers | 0.89 \pm 0.31 | 3.30 \pm 0.26 ⁺ | 1.61 \pm 0.41 [*] | 1.12 \pm 0.12 [*] |
| Area of acinus epithelium | 25.48 \pm 3.23 | 19.08 \pm 0.95 ⁺ | 16.90 \pm 1.09 ⁺ | 17.80 \pm 1.33 ⁺ |
| Area of acinus lumen | 48.20 \pm 2.48 | 42.82 \pm 4.22 | 52.74 \pm 2.20 ⁺ | 45.74 \pm 1.60 |

Note. Here and in Tables. 2, 3: $p < 0.05$ in comparison with ^{*}control, ⁺background.

TABLE 2. Weight, Volume, Density, and Zinc Content (mg/%) in the Ventral Prostate Lobe of Rats with Aseptic Chronic Inflammation Treated with Prostatotropic Drugs ($X \pm m$)

| Group | Weight of prostate, mg | Weight ratio, mg/g | Prostate volume, cm ³ | Density of the prostate, g/cm ³ | Relative content of zinc (100 mg /% of gland) |
|---------------|------------------------|--------------------|----------------------------------|--|---|
| Background | 384.00±12.13 | 0.83±0.03 | 0.42±0.03 | 0.92±0.02 | 0.84±0.13 |
| Control | 390.00±19.32 | 0.78±0.08 | 0.38±0.03 | 1.05±0.01 ⁺ | 0.44±0.10 ⁺ |
| Samprost | 357.00±22.31 | 0.82±0.05 | 0.36±0.04 | 0.99±0.02 [*] | 1.03±0.23 [*] |
| Prostamol Uno | 345.50±18.95 | 0.77±0.05 | 0.36±0.04 | 0.96±0.02 [*] | 1.12±0.13 [*] |

parameter although did not differ from the control, but surpassed the background values (Table 1).

Thus, administration of the test prostatotropic drugs against the background of surgery reduced the formation of collagen fibers in the gland interstitium, which attests to their anti-sclerotic effect (more pronounced in Samprost).

The weight, weight ratio, and volume of the ventral prostate lobe in controls were similar to background values 45 days after suturing (Table 2). Increased density by 14% compared to the background may be associated with the increased cellularity due to infiltration. The area of collagen fibers also increased. In both experimental groups, this indicator decreased in comparison with the control and did not differ from background values, which can be a result of anti-inflammatory effects of the drugs.

Forty-five days after suturing of the ventral prostate with a silk thread, zinc content significantly decreased (almost 2-fold in comparison with the background values, Table 2). In other laboratory animals, hypofunction of the prostate was also revealed after suturing it with a thread [1]. In rats receiving Samprost and Prostamol Uno, zinc content was significantly increased in comparison with controls, which can indicate stimulation of the secretory activity of glands. Zinc content in Samprost and Prostamol Uno is 1.4-1.6 and 0.7-0.8 mg/%, respectively. In light of this, secretory activity of the gland in animals treated with drugs increases probably not only due to the therapeutic effect of the drugs, but also due to introduction of exogenous zinc.

Analysis of sexual behavior showed that all animals of the background group made attempt to copulate with estrous females within 15 min of the experiment. In the control group, the number of active male rats was significantly lower: 80%. In the group of rats treated with Samprost, inactive animals were also detected (Table 3), but the differences were statistically insignificant. Against the background of Prostamol Uno administration, all male rats have been attempting to mate. In animals with chronic prostatitis, latent period of mounting characterizing libido was 44% longer than in rats of background groups (Table 3), which attests to reduced libido. These results confirm published data that chronic prostatitis can be associated with reduced sexual desire [11,14]. Against the background of Samprost administration, latent period of mounting did not significantly differ from the control and background values. On the contrary, Prostamol Uno stimulated sexual desire. Thus, the latent period of mounting was significantly reduced compared to the control (by 2.6 times). The total number of mountings and the number of mating in the two groups were similar. Therefore, the drugs had no significant effect on copulatory function.

Thus, using the model of chronic aseptic inflammation we had shown that administration of Prostamol Uno and Samprost stimulated secretory activity of the prostate and inhibited sclerotic processes in the prostate tissue. The latter effect was more pronounced in the group of animals treated with Samprost. At the same time, preparations had no significant effect on the development of atrophic processes. Sexual motiva-

TABLE 3. Sexual Activity in Male Rats

| Group | Number of active animals, % | Latent period of mounting, sec | Total number of mountings | Number of copulations |
|---------------|-----------------------------|--------------------------------|---------------------------|-----------------------|
| Background | 100 | 114.70±61.73 | 14.70±2.49 | 0.30±0.15 |
| Control | 80 ⁺ | 164.00±38.63 ⁺ | 18.13±4.24 | 0.13±0.13 |
| Samprost | 90 | 184.33±91.61 | 15.89±2.91 | 0.56±0.24 |
| Prostamol Uno | 100 | 62.80±8.73 [*] | 15.90±2.12 | 0.60±0.22 |

tion of male rats increased against the background of Prostatamol Uno administration.

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