Prooxidant-Antioxidant Balance in the Prostate and Blood of Rats with Sulpyride-Induced Prostatic Hyperplasia Corrected with Prostatilen

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We studied the effects of 30-day injections of sulpyride and treatment with Prostatilen on the development of prostatic hyperplasia and LPO in rats. Sulpyride induced proliferation of lateral lobes, increased the content of lipid hydroperoxides and glutathione peroxidase activity in the gland; in the blood this preparation increased lipid hydroperoxide concentration and decreased glutathione peroxidase and total antioxidant activity. Prostatilen prevented the development of hyperplasia and normalized the prooxidant-antioxidant balance in tissues, except total antioxidant activity of the blood.

Key Words: *benign prostatic hyperplasia; lipid peroxidation; sulpyride; Prostatilen*

Benign hyperplasia is the most prevalent prostatic disease, more incident than prostatic cancer and prostatitis. Pathomorphology of benign prostatic hyperplasia is well studied, but the molecular mechanisms of its development remain not quite clear. For example, the data on changes in LPO, a universal component of the pathological processes in prostatic hyperplasia are contradictory [8,11].

Prostatilen, a complex of water-soluble bioregulatory peptides from cattle prostate characterized by a specific organotropic effect, is successfully used in the therapy of prostatic diseases [6], but the effects of this drug on free radical processes are little studied.

We investigated physiological parameters of the prostate and the prooxidant-antioxidant balance in sulpyride-induced hyperplasia and during Prostatilen treatment.

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MATERIALS AND METHODS

The study was carried out on 26 random-bred male rats (180-240 g) kept in accordance with the regulations of the European Convention for Protection of Vertebrates Used for Experimental and Research Purposes (Strasbourg, 1986).

Prostatic hyperplasia was induced by daily intraperitoneal injections of sulpyride (Eglonil, solution for injections, Sintelabo Laboratory) in a dose of 40 mg/kg for 30 days [12]. Prostatilen (Biofarma) was injected once daily intramuscularly in a dose of 1 mg/kg [1] for 30 days simultaneously with sulpyride. Rats receiving daily intramuscular injections of isotonic saline served as the control.

The animals were decapitated under light ether narcosis 24 h after the last injection, the blood was collected for separating the serum, lateral lobes of the prostate were isolated and weighed; their volume was evaluated on a plethysmometer (Ugo Basil). Homogenate was prepared on 100 mM Tris-HCl buffer (pH 7.4) in 1:5 ratio by grinding the tissue in liquid nitrogen.

Lipid hydroperoxides (LHP) [10], proteins [9], and selenium-dependent glutathione peroxidase (GP)

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TABLE 1. Effects of Sulpyride and Sulpyride+Prostatilen on Physiological Parameters of Prostatic Lateral Lobe, Protein Content, and Prooxidant-Antioxidant Balance in the Prostate and Blood ($M \pm m$, n=5-10)

Parameter	Group		
	control	sulpyride	sulpyride+Prostatilen
Prostatic lateral lobes			
weight, mg	112±10	241±26*	141±10^{+}
weight coefficient, g/g×10^{-3}	0.500±0.037	1.077±0.117*	0.639±0.039*$^{+}$
volume, ml	0.109±0.009	0.228±0.049*	0.158±0.015
total protein, mg/g tissue	110.0±5.6	146±7*	116±8.2^{+}
LHP, nmol MDA/g tissue	13.97±1.00	20.59±1.39*	16.45±0.83^{+}
GP activity, nmol NADPH/min/ml	2738±144	4713±250*	3787±291*$^{+}$
Serum			
LHP, nmol MDA/g tissue	0.567±0.041	0.937±0.073*	0.657±0.037^{+}
GP activity, nmol NADPH/min/ml	3049±207	2412±172*	2711±141
AOA, %	52.10±2.15	44.06±2.88*	44.80±2.12*

Note. p<0.05 compared to: *control, $^{+}$sulpyride.

activity with H_2O_2 as the substrate [5] were measured in the homogenates. Serum LHP [7], GP activity [5], and antioxidant activity (AOA) [3] were measured. The results were statistically processed using Student's t test.

RESULTS

Administration of sulpyride for 30 days increased the absolute weight, weight coefficient, and volume of the lateral lobes by 109-115%; protein content increased by 33%, which attested to the development of prostatic hyperplasia in rats (Table 1).

Long-term treatment with sulpyride induces hypersecretion of prolactin [12,13] determining prostatic cell growth and death [13]. Hyperprolactinemia in rats induces hyperplasia of the prostatic lateral lobes, which are very liable to this pathology [12,13].

The development of prostatic hyperplasia was paralleled by an appreciable increase in LHP content in the prostate (by 47.4%) and serum (by 65.3%) (Table 1). Accumulation of LPO products in the serum was associated with a decrease in AOA (by 15.4%) and GP activities (by 20.9%), while in the prostate it was associated with a significant increase in GP activity (by 72.1%) in comparison with control animals. The detected increase of selenium-dependent GP activity in sulpyride-induced prostatic hyperplasia can be caused by enzyme induction in response to increased LHP concentration or activation caused by modification of the hormone status [4].

Treatment with Prostatilen in parallel with sulpyride injections prevented the development of prostatic hyperplasia. The absolute weight of prostatic lateral lobes decreased 1.72 times in animals treated with Prostatilen in comparison with untreated rats, the weight coefficient decreased 1.69 times, volume 1.44 times, and protein content 1.26 times. The content of LHP in prostatic tissue and blood decreased by 20.1 and 29.9%, respectively, and by absolute values virtually did not differ from LHP levels in the controls. Activity of GP in the prostate in response to Prostatilen decreased by 19.6%, while in the blood it increased by 12.4%, that is, the shifts exhibited a trend towards normalization of the activity for these tissues. Prostatilen had no effect on AOA, an integral parameter of the nonenzymatic antioxidant system in the blood.

Hence, 30-day sulpyride treatment leads to the development of prostatic hyperplasia and shifts in the prooxidant-antioxidant balance in prostatic tissue and blood towards prooxidants. This alteration of the prooxidant-antioxidant status reflecting the development of oxidative damage [2] can be one of the main causes of prostatic hyperplasia. Prostatilen exhibited a marked antihyperplastic effect and normalized the prooxidant-antioxidant balance, presumably due to improvement of the enzymatic antioxidant system.

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