Phytoadaptogen Correction of Clinical and Immunobiological Parameters in Patients with Benign Prostatic Hyperplasia

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Correction of hormonal, immune, interferon, and antioxidant status and genetic abnormalities with a complex phytoadaptogen leads to positive clinical effects in elderly patients with benign prostatic hyperplasia.

Key Words: *phytoadaptogen; benign prostatic hyperplasia; aging; immunomodulating therapy*

The incidence of benign prostatic hyperplasia (BPH) in elderly men remains high. This pathology is considered to be a result of hormone imbalance [10]. On the other hand, the development of BPH can be associated with chronic stress during elderly age: metabolic immunosuppression [8], disorders in free radical oxidation [9], development of genetic abnormalities [7].

The use of 5-α-reductase inhibitors and α-adrenoblockers in the treatment of patients with BPH is often associated with side effects [2]. In the search for new approaches to the treatment of BPH we tried a complex phytoadaptogen preparation Phytomix-40 (PM-40) exhibiting immunomodulating and antioxidant effects in experimental studies [1,5].

The aim of this study was to improve the quality of life for patients suffering from BPH by correction of clinical and immunobiological parameters with PM-40.

MATERIALS AND METHODS

Sixty-three patients with verified diagnosis of BPH aging 70±1 years took part in the study.

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Group 1 (control; *n*=21) consisted of patients receiving no preparation and regularly examined during 6.0±0.5 months. Group 2 (*n*=53) received 3-4 courses of PM-40 in the mean daily dose 45.0 ml. Group 3 (*n*=4) and group 4 patients (*n*=6) received 2 courses of PM-40 in low (5.0 ml) and high daily dose (75 ml), respectively. One course for all doses was 1.5 months.

Clinical examinations included evaluation of the size of the node and the prostate, urodynamic parameters, volume of residual urine, summary score of symptoms according to the international scale (IPPS), and index of quality of life.

Serum hormones (testosterone, estradiol, luteinizing hormone, hydrocortisone) and specific prostatic antigen were measured by enzyme immunoassay. Immune status (content of lymphocytes expressing differentiation antigens CD3, CD4, CD8, CD16, and CD20; activation antigens CD25, HLADr, CD95; adhesion molecules CD11b, CD18, and CD50) was evaluated by immunofluorescent method. IFN status was evaluated by biological method quantitatively (serum, spontaneous, α- and γ-IFN) and qualitatively (*in vitro* effects of drugs and IFN inductors and effect of PM-40 on interferonogenesis in lymphocytes from patients with BPH) [3]. The content of MDA, glutathione, activities of SOD, catalase, and glutathione-S-transferase were evalua-

ted by routine methods. Metaphase lymphocyte preparations were prepared as described previously [6]. Aberrant metaphases, chromatide fragments and exchanges, chromosome fragments and exchanges were counted. The results were statistically processed using Statistica and ANOVA software.

RESULTS

Initial examinations of patients with BPH detected partial androgen deficiency and sex hormone imbalance, hypercortisolism, cell and humoral immunodeficiency, insufficiency of nonspecific defense factors and IFN system, intensification of free-radical processes and endotoxicosis, and increased the level of chromosome aberrations in lymphocytes.

Significant enlargement of the hyperplastic node and prostate was observed in group 1 patients during 6 months of observation. The severity of the symptoms tended to increase. Quality of life index remained low. A relationship between clinical parameters and homeostasis disorders was observed over the course of the disease.

Since clinical and immunobiological parameters deteriorated in groups 3 and 4, we present the results attained in group 2 patients who received the mean effective dose of the drug (45 ml) daily.

Positive changes in clinical parameters were observed in the majority of group 2 patients. The size of the hyperplastic node and the prostate decreased by 27 and 10%, respectively, symptoms were attenuated by 50%, quality of life improved by 34%. The volume of residual urine decreased to normal (from 61.0±5.0 to 48.0±3.0 ml, p=0.044). Maximum velocity of urination increased by 34%, mean velocity of urination by 16%.

Clinical results attest to high efficiency of PM-40 comparable to that of known 5-α-reductase inhibitors and α-adrenoblockers [4]. On the other hand, the use of phytoadaptogen caused no side effects. Patients with BPH subjectively noted improvement of sexual function, improvement of general tone during daytime and sleep at night, stabilization of blood pressure.

Correction of the hormonal status manifested in increased testosterone content (from 10.4±0.8 to 16.8±0.9 nmol/liter, p<0.001), decreased level of estradiol (from 160.0±10.0 to 110.0±10.0 pmol/liter, p<0.001), luteinizing hormone (from 4.2±0.3 to 3.1±0.3 U/liter, p<0.001), and hydrocortisone (from 735.0±46.0 to 534.0±18.8 nmol/liter, p<0.001). The level of specific prostatic antigen decreased from 3.4±0.5 to 2.4±0.4 ng/ml (p<0.001).

Normalization of immunological parameters was observed after courses of PM-40 (Fig. 1): increase in total count of T cells (CD3), helper-inductors (CD4), decrease in the count of T-suppressors (CD8), recovery of humoral immunity (CD20 and HLADr) and natural resistance (CD16 and CD11b), increase in the expression of IL-2 receptors (CD25) and in the content of leukocytic adhesion molecules (CD11b, CD18, CD50).

The effect of PM-40 in the medium dose on IFN status manifested in a decrease in serum IFN concentration to the normal level and recovery of induced production of α- and γ-IFN by peripheral blood lymphocytes (Table 1). Increased sensitivity of BPH patients to IFN and its preparations was

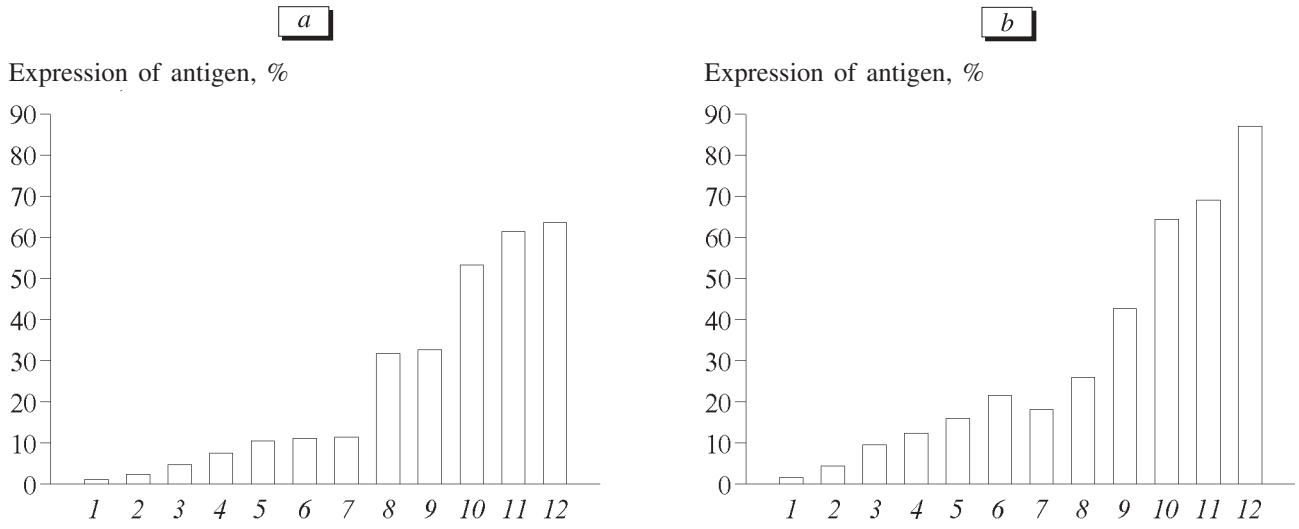

Fig. 1. Changes in immune status parameters of patients with benign prostatic hyperplasia (BPH) under the effect of the mean daily dose (45 ml) of Phytomix-40. *a*) before therapy; *b*) after 7 months of treatment. *1*) CD4/CD8; *2*) CD25; *3*) CD20; *4*) HLADr; *5*) CD16; *6*) CD95; *7*) CD11b; *8*) CD8; *9*) CD4; *10*) CD18; *11*) CD3; *12*) CD50.

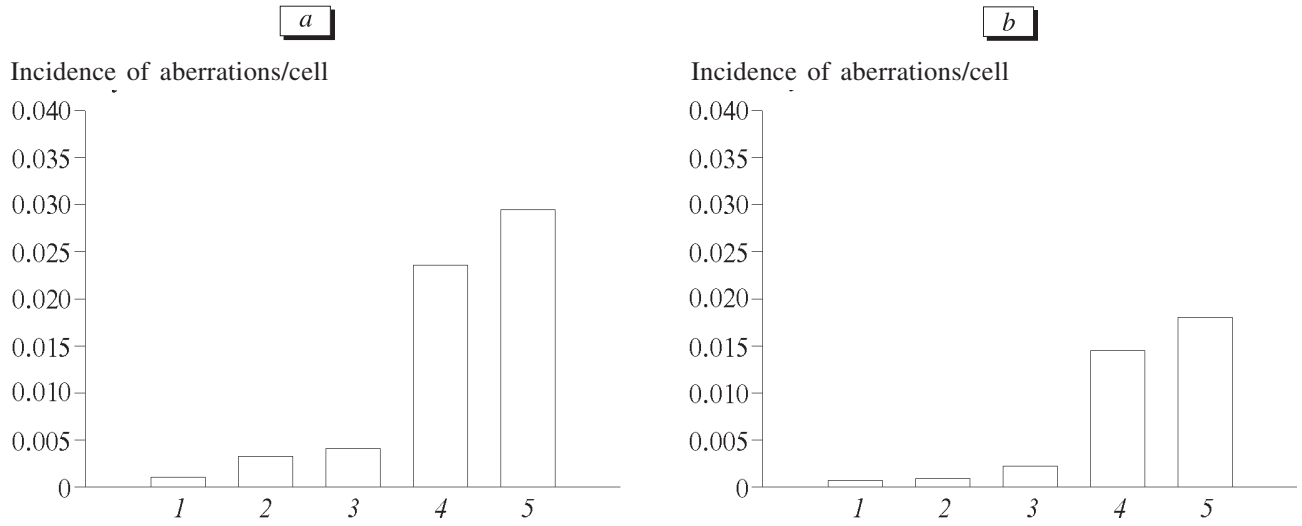

Fig. 2. Changes in cytogenetic parameters in BPH patients under the effect of the medium dose (45 ml/day) of Phytomix-40. *a*) before therapy; *b*) after 7 months of treatment. *1*) chromatide exchanges; *2*) chromosome exchanges; *3*) chromosome fragments; *4*) chromatide fragments; *5*) aberrant metaphases.

noted. On the other hand, 100% patients remained as sensitive to PM-40 after treatment as before it.

Addition of PM-40 to therapy for BPH led to inhibition of LPO, which manifested in a significant decrease (normalization) in MDA level (from 8.2±0.8 to 5.2±0.2, $p<0.05$). Catalase, glutathione, and glutathione-S-transferase were notably activated. This indicated reduction of endotoxicosis, preventing the development of the endogenic intoxication syndrome and promoting improvement of the quality of life.

A decrease in the total level of chromosome aberrations and some types of exchange aberrations and aberrations leading to the formation of fragments was observed after the end of PM-40 course. The incidence of chromosome exchanges decreased almost 3-fold ($p<0.001$, Fig. 2). After the course of PM-40 therapy this parameter was below the common population value for the corresponding age in Russia ($15.62\times10^{-4}\pm1.01\times10^{-4}$) and lower than in control subjects having no contacts with adverse industrial, ecological, or communal factors ($13.3\times10^{-4}\pm1.8\times10^{-4}$).

Hence, age-associated increase in the level of toxic products of free-radical oxidation seems to lead to programmed genetic disorders triggering changes in neurohumoral regulation causing, for example in elderly men, androgen deficiency and hypercortisolism. It seems that the developing immunosuppression supplements the picture of chronic stress. Imbalance of sex hormones activates 5-α-reductase, which promotes hyperplastic processes in the prostate. Hydrocortisone stimulates proliferation of prostatic cells, α-adrenoreceptors activity, and epinephrine release. The resultant benign prostatic hyperplasia and increased tone of smooth-muscle structures of the base of the urinary bladder, posterior urethra, and prostate lead to uri-

TABLE 1. Changes in IFN Status Parameters of BPH Patients under the Effect of Phytomix-40 in the Medium Dose (45 ml/day)

Interferon reaction of leukocytes	Normal value for adults, U/ml	Number of patients with normal IFN level, %		IFN titers, U/ml, *M*±*m*	
		before therapy	after 7-month therapy	before therapy	after 7-month therapy
Serum IFN	≤4	40	76	8.8±1.2	4.3±0.5*
Spontaneous IFN	<2	100	100	<2	<2
α-IFN	≥64	12	28	27.8±5.3	66.9±16.7**
γ-IFN	≥16	12	60	8.1±2.5	18.9±3.7*

Note. *$p<0.001$, **$p<0.004$ compared to the corresponding value before therapy.

nation disorders deteriorating the quality of life in elderly men suffering from BPH.

Clinical efficiency of PM-40 in the treatment of patients with BPH (decrease in the size of the gland and normalization of urodynamics) are presumably due to correction of age-associated disorders in immunobiological values. Leveling of sex hormone imbalance and hypercortisolism promotes the decrease in 5-α-reductase activity, sensitivity of α-adrenoreceptors playing an important role in the pathogenesis of BPH, and leads to reduction of the hyperplastic processes. All this improves quality of life in BPH patients, promotes more smooth development of age-associated stress reactions, and indicates a geroprotective effect of the preparation.

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