Experience of Long-Term Afala Treatment in Benign Prostatic Hyperplasia

A. V. Gudkov

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The use of ultralow doses of antibodies to prostate-specific antigen (afala) for long-term treatment of benign prostatic hyperplasia in patients with moderate symptoms rapidly and effectively reduces irritative and obstructive symptoms, significantly decreases residual urine volume, and increases the rate of urination. Afala therapy is indicated for patients with stage I-II benign prostatic hyperplasia of moderately pronounced symptoms.

Key Words: *adenoma of the prostate; benign prostatic hyperplasia; afala*

Benign prostatic hyperplasia (BPH) develops in almost all elderly men. According to autopsy data, morphological signs of BPH are recorded in 25% men aging 40-50 years, in 50% men aging 50-60 years, in 65% men aging 60-70 years, in 80% men aging 70-80 years, and in 90% men aging 80-90 years [1,6,8]. However, clinical symptoms of the disease appear in only 25-50% individuals with micro- or macroscopic signs of BPH, of them only 50% patients seek medical advice [7,9].

Symptoms of the disease can vary. The severity of symptoms is evaluated by international system of integral evaluation of prostatic symptoms (international prostatic symptom score, IPSS). IPSS does not allow diagnostics of BPH and is a subjective parameter, but this parameter and the data of other examinations (digital rectal examination, ultrasonography of the kidney, urinary bladder, and prostate, uroflowmetry, urine analysis, measurement of blood creatinine and prostate-specific antigen (PSA), and in some cases cytoscopy and biopsy of the prostate) make it possible to create various algorithms of medical interventions in BPH, to objectively evaluate patient's state, and to control the results of therapy. Proceeding from these data, urologist can recommend observation, drug therapy, low-invasive interventions, or radical surgery.

Siberian State Medical University, Federal Agency for Health Care and Social Development, Tomsk

In recent years, the number of patients requiring surgery for BPH steadily tended to decrease. This can be explained by introduction of drug therapy and low-invasive methods of treatment. However, the number of patients receiving treatment increased with the appearance of low-invasive methods [10].

α_1-Adrenoceptor blockers (AB) and 5α-reductase inhibitors are the most widely used drugs for these purposes.

α_1-AB applied for the treatment of BPH are characterized by different selectivity for α_1-receptors and duration of the effect. Clinical efficiency in BPH and safety of all original α_1-AB is similar. They increase the maximum uroflow rate by 1.3-3.5 ml/sec (20-30%) and reduce IPSS by 1.3-4.7 (20-50%) compared to placebo [4]. When prescribing α_1-AB to patients with BPH, one should take into account the effect of these preparations on other organs and systems, in particular, on blood vessels and CNS. Some side effects of α_1-AB (hypotension, especially, orthostatic hypotension, dizziness, undue fatiguability, tiredness, stuffiness in nose, and ejaculation disturbances) often are the causes of treatment refusal.

Finasteride is a competitive selective inhibitor of type II 5α-reductase. Numerous studies showed that finasteride significantly reduced the volume of the prostate by ~20%, increased the maximum uroflow rate by 0.2-1.8 ml/sec, and decreased the total IPSS

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by 0.6-22. The level of PSA decreased by about 2 times under the effect of finasteride. Regular treatment with finasteride for 2 years reduced the incidence of cases of acute urinary retention by 75% and decreased indications to surgery by one-third [10]. At the same time, adverse effects of the drug on sexual life were noted in 12% patients: libido decreased in 3.4-3.7%, ejaculation disturbances and erectile dysfunction developed in 2.7 and 1.7-3.7%, patients, respectively [4].

The known drawbacks and side effects of α_1-AB and finasterides in mono- and combined therapy promoted the creation of afala, a preparation producing no above-listed negative effects. Biological activity of the preparation is related to potentiation of ultralow doses of antibodies. Afala contains affinity-purified antibodies to PSA (mixture of homeopathic dilutions C12, C30, and C200; 0.003 g) and accessory substances (lactose, crystalline cellulose, calcium stearate/magnium stearate, aerosol). The effect of afala is based on the capacity of antibodies to the endogenous regulator to modify (but not block) activity of the target molecule. Experimental studies showed that afala can regulate the balance of growth factors in the prostatic tissue. The preparation stimulates antiproliferative and angiostatic activity of PSA. The mechanism of afala action presumably consists in modification of functional activity of endogenous PSA that regulates the balance of growth factors responsible for metabolism and normal growth of the prostatic tissue. Taking into account that PSA is a factor of BPG pathogenesis, the modulating effect of ultralow doses of antibodies to PSA can be used for normalization of physiological activity of PSA in the presented chain. Afala normalizes the balance of growth factors in the prostate, which leads to an increase in zinc concentration, improvement of metabolism, inhibition of proliferation, suppression of aseptic inflammation, and normalization of diuresis. The pathogenetic mechanism of afala action provides its complex effect on all clinical components of BPH (inflammation, proliferation, diuresis disturbances) comparable to that of complex therapy with α_1-AB and 5α-reductase inhibitors [5].

The preparation was registered in Russia in 2001; however, there are only few reports on its clinical application in BPH.

Here we studied the safety, tolerance, and clinical efficiency of afala (in tablets for peroral treatment) in patients with BPH during long-term treatment.

MATERIALS AND METHODS

The study included 30 patients aging 53-86 years (mean age 71.1±3.4 years) with clinical manifestations of stage I-II BPH.

The patients had serum PSA concentration <4 mg/ml and total IPSS <7 or >18.

All patients received afala monotherapy (2 tablets 2 times a day *per os*) for 7 months. The maximum duration of observation was 10 months.

Simultaneous treatment with α_1-AB and 5α-reductase inhibitors was excluded.

In all patients complex medical examination was performed. It included history taking, physical examination, blood pressure measurement, questionnaire filling (IPSS and IIEF-5), digital rectal examination, transabdominal ultrasonography of the kidney and urinary bladder, transrectal ultrasonography of the prostate (TRUS), laboratory tests (complete blood count, total analysis of the urine, biochemical blood tests: total protein, glucose, creatinine, urea, bilirubin, PSA), consultation of related specialists, ECG, and multifocal biopsy of the prostate (if indicated).

Clinical efficiency of afala was evaluated by the positive dynamics of the main diagnostic criteria and parameters, such as total subjective self-evaluation of general patient's state during examination (improvement, worsening, without changes, side effects); dynamics of the total IPSS and IIEF score, quality of life (QoL); blood pressure control; uroflowmetry, residual urine volume; TRUS of the prostate; PSA level.

RESULTS

The results of primary examination yielded the following characteristic of the studied patient's group. Most patients (60%) were at the age of 60-80 years. The history of the disease varied from 2 to 20 years (mean 7.0±6.3 years). The severity of clinical symptoms according to IPSS was 11-18 (mean 14.5±2.4) and quality of life score varied from 3 to 6 (mean 4.8±0.5). Nocturia was observed in all patients (from 1 to 8 times, mean 4.8±2.8 times). The volume of the prostate by TRUS data was 14-120 cm^3 (mean 57.8±14.6 cm^3); patients with prostate volume 40-80 cm^3 predominated (70%). Residual urine volume varied from 0 to 230 ml (mean 156±47 ml). No residual urine was found in 16.7% patients, in 63.3% this parameter was below 100 ml, and in 20% it surpassed 100 ml. All patients complained of weakened urine stream. According to uroflowmetry data, the maximum uroflow rate was 5-12 ml/sec (mean 8.2±2.9 ml/sec); serum PSA concentration varied from 0 to 4.7 ng/ml (mean 2.0±1.7 ng/ml). We included one more patient with PSA level >4 ng/ml and higher volume of the prostate into the studied group; he underwent multifocal biopsy of the prostate several months ago and no malignancies were found. The following concomitant diseases were found: essential hypertension (36.7%), chronic prostatitis (20%), type 2 diabetes

TABLE 1. Dynamic of Studied Parameters in Patients Treated with Afala and Efficiency of Treatment (*M*±*m*)

Parameter	Time of observation, months					Efficiency, %
	initial	1	3	6	7	
IPSS	14.5±2.4	8.3±0.5*	8.2±0.5	8.3±0.4	8.2±0.2**	+56.7
QoL	4.8±0.5	2.8±0.2*	2.7±0.2	2.5±0.1	2.5±0.1**	+53
Maximum uroflow rate, ml/sec	8.2±2.9	12±1.8*	11.8±1.9	12.3±2.1	13.8±2.5**	+68
Residual urine volume, ml	156±47	114±56*	96.4±48	87.2±39	70.2±35**	+56.3
Volume of prostate, cm^3	57.8±14.6	54.6±15.9	57.8±15.1	58.5±14.2	56.9±15.7	+0.1
PSA, ng/ml	2.0±1.7	1.8±0.6	2.1±1.1	2.3±1.2	2.5±1.1	-25

Note. *$p<0.05$, **$p<0.001$ compared to initial values.

mellitus (10%), hemiparesis after stroke (3.3%). One patient underwent palliative transurethral resection of prostatic adenoma 10 years ago. Some patients (10%) received α_1-AB for more than 2 years before inclusion into the study; other patients received no treatment for BPH. We recommended stopping α_1-AB treatment during the study to patients receiving these drugs.

The efficiency of treatment was evaluated every month, the data were compared with the initial values (Table 1).

The positive effect of afala was subjectively noted by patients on days 5-7 of treatment. Residual urine volume decreased by 56,3% over the observation period. As soon as after 4 weeks, the following parameters changed and then remained at the same levels: IPSS decreased by 56.7%, nocturia decreased by 47.4%, QoL improved by 53%, maximum uroflow rate increased by 68.5%. No significant changes in prostate volume were noted. By the end of the study, a slight (insignificant) increase in PSA level was noted. None patients dropped out over the whole period of the study, no complications or side effects were noted.

The patients receiving α_1-AB and stopped this treatment during the study reported no worsening of their general state during afala therapy.

Dynamic observation over 17% patients, in whom afala therapy was started and completed by 3 months earlier than in others and who received no treatment in the follow-up period, revealed no progression of the disease.

In one patient, transurethral resection of prostatic adenoma was performed after completion of afala course, despite stabilization of the process and even subjective and objective improvement attained as a result of afala treatment. Residual urine volume remained relatively high (150 ml) in this patient and he was completely unsatisfied by his quality of life.

The results of our study confirmed previous data [2,3]. Serum level of PSA increased in 3 patients. By the end of the study, this parameter increased by 2-3 times and surpassed 4 ng/ml and in one patient it attained 5.7 ng/ml despite positive dynamics of clinical symptoms. These patients were thoroughly examined for prostatic cancer, including polyfocal biopsy of the prostate and MRI with contrasting. No malignant tumors were detected.

Thus, afala is an effective preparation for long-term treatment of patients with stage I-II BPH. It decreases irritative and obstructive symptoms, reduces residual urine volume, and increases the rate of urination.

No side effects and complications were noted against the background of afala treatment. At the same time, further studies of this preparation are required for evaluation of the optimal doses and duration of treatment course and for evaluation of its effect on PSA level.

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