Clinical Study of the Efficiency and Safety of Afala in Patients with Benign Prostatic Hyperplasia

K. V. Savel'eva, M. V. Kachanova, V. N. Pavlov*, R. A. Kazikhinurov*, M. Yu. Frolov, A. B. Mukhin**, V. V. Udut***, Z. A. Yurmazov***, Yu. L. Dugina, S. A. Sergeeva, and O. I. Epshtein**

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 148, Suppl. 1, pp. 54-56, August, 2009
Original article submitted August 1, 2008

The use of afala in patients with benign prostatic hyperplasia and moderate urination disturbances reduced the symptoms of the disease, improved urodynamic parameters, and increased quality of life. Clinical efficiency of afala was comparable with the efficiency of *Serenoa repens* extract (reference preparation).

Key Words: *benign prostatic hyperplasia; prostate-specific antigen; ultralow doses*

Lower urinary tract symptoms (LUTS), clinical manifestation of benign prostatic hyperplasia (BPH), are typical complains of male patients over age 50 years [2,4]. These symptoms include difficulty of urination, weak and interrupted urinary stream, a sensation of incomplete bladder emptying, nocturia, *etc*. [6,7]. LUTS can led to sleep disturbances and erectile dysfunction, and as a result to considerable impairment of quality of life [1,6].

Surgical treatment is most effective in BPH, but it is associated with a number of complications [5] and can be contraindicated to elderly patients because of concomitant diseases. Moreover, many patients refuse surgical treatment and prefer less traumatic drug therapy, especially in cases of mild and uncomplicated urination disorders. Thus, in view of high prevalence of BPH and the need in drug therapy in this condition, the search and development of new drugs for conservative treatment of BPH symptoms are an urgent problem of pharmacology.

Here we report the results of clinical study of the efficiency and safety of afala (ultralow doses of antibodies to prostate-specific antigen) in comparison with *Serenoa repens* (*S. repens*) extract in patients with BPH.

Materia Medica Holding Research-and-Production Company, Moscow; *Bashkir State Medical University, Federal Agency for Health Care and Social Development, Ufa; **Volgograd State Medical University; ***Institute of Pharmacology, Tomsk Research Center, Siberian Division of Russian Academy of Medical Sciences, Tomsk

MATERIALS AND METHODS

The study included 186 male patients aging 63.9±0.6 years with a history of BPH 5.3±0.3 years: 132 patients received afala and 54 patients received *S. repens*. The groups were comparable by initial characteristics.

Design of the study: randomized open comparative study in parallel groups. The inclusion criteria were: age 40-75 years; BPH verified by transrectal ultrasonography (TRUS); moderate symptoms of urination disturbances: 8-20 according to IPSS questionnaire (International Prostate Symptom Score); maximum uroflow rate 5-15 ml/sec, prostate volume >25 cm^2, residual volume of the urine <150 ml, serum concentration of prostate-specific antigen <4 ng/ml, and signed informed consent form. Patients who underwent surgical interventions for prostatic or urinary bladder pathologies and patients with severe concomitant diseases were excluded from the study.

The patients were randomly divided into 2 groups: group 1 patients received afala (2 tablets 4 times a day) and group 2 patients received *S. repens* extract

0007-4888/09/1482-0305

(320 mg once a day). The duration of treatment in both groups was 16 weeks.

The efficiency and safety of treatment were evaluated after 4, 8, 12, and 16 weeks. The efficiency of treatment was evaluated by IPSS [3,5], uroflowmetry, TRUS [5]; the safety of the test preparations was assessed by the incidence and severity of undesirable effects against the background of therapy and dynamics of laboratory parameters.

The significance of differences between the means was evaluated by Student's *t* test for dependent and independent variables.

RESULTS

Therapy with afala reduced the severity of LUTS and improved urodynamic characteristics and patient's quality of life. Significant changes in IPSS (total score), quality of life index (QoL), and uroflowmetry parameters: maximum and mean uroflow rates (Q_{max} and Q_{av}, respectively) were observed as soon as by the 4th week of treatment: total IPSS and QoL decreased by 12.9 and 13.5%, respectively, and Q_{max} and Q_{av} increased by 10.8 and 9.2%, respectively. At later terms (after 8 and 12 weeks) clinical parameters continued to improve, the maximum changes were observed by the end of week 16 (Tables 1-3).

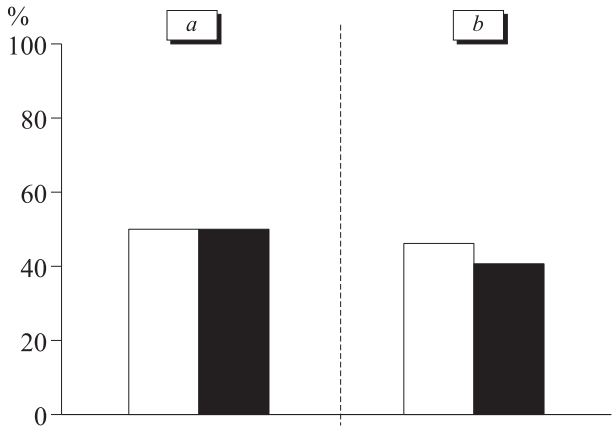

Fig. 1. Number of patients with mild LUTS (IPSS<8; *a*) and minor urination disturbances (Q_{max}>15 ml/sec; *b*) in the studied groups after 16-week treatment. Open bars: afala; dark bars: *S. repens*.

Comparison of the results in the afala and *S. repens* groups showed that these preparations were comparable by their efficiency (Tables 1-3). In patients

TABLE 1. Parameters Evaluated by IPSS Questionnaire during Therapy (*M*±*m*)

Parameter	Preparation	Initial	Duration of therapy, weeks			
			4	8	12	16
Total IPSS	Afala	14.7±0.3	12.8±0.3***	11.1±0.4***	9.4±0.4***	8.2±0.4***
	S. repens	14.2±0.4	11.7±0.5***	10.2±0.4***	9.0±0.4***	8.0±0.4***
Quality of life index (QoL)	Afala	3.7±0.1	3.2±0.1**	2.6±0.1***	2.2±0.1***	1.7±0.1***+
	S. repens	3.5±0.1	2.9±0.1**	2.5±0.1***	2.3±0.1***	2.1±0.1***

Note. Here and in Tables 2 and 3: *p<0.05, **p<0.01, ***p<0.001 compared to initial values; +p<0.05 compared to *S. repens*.

TABLE 2. Parameters of Uroflowmetry during Therapy (*M*±*m*)

Parameter	Preparation	Initial	Duration of therapy, weeks			
			4	8	12	16
Maximum uroflow rate, ml/sec	Afala	10.2±0.2	11.3±0.3**	12.9±0.3***	13.8±0.4***	14.8±0.4***
	S. repens	10.4±0.3	11.2±0.4*	12.4±0.5***	13.5±0.4***	14.1±0.4***
Mean uroflow rate, ml/sec	Afala	6.5±0.2	7.1±0.2**	7.9±0.2***	8.2±0.2***	9.0±0.2***
	S. repens	6.1±0.3	7.0±0.3***	7.7±0.3***	7.9±0.3***	8.2±0.3***

TABLE 3. Results of TRUS during Therapy (*M*±*m*)

Parameter	Preparation	Initial	After 16-week therapy
Volume of the prostate, cm^3	Afala	44.6±1.3	41.9±1.3**
	S. repens	44.7±2.0	39.3±1.8**
Residual urine volume, ml	Afala	31.0±3.2	12.9±1.7***
	S. repens	38.4±4.1	21.4±4.0***

receiving afala, the improvement of the quality of life was somewhat more pronounced (Table 1). The decrease in the total IPSS (decrease in the severity of urination disturbances) in patients receiving afala and *S. repens* was 44.2 and 43.7%, respectively, the decrease in QoL was 54.1 и 40.0%, the increase in Q_{max} was 45.1 и 35.6%, and the increase in Q_{av} was 37.4 и 34.4%. The volume of residual urine (by TRUS data) also significantly decreased by 58.4 and 44.3% in the afala and *S. repens* groups.

By the end of week 16, LUTS severity in 50% patients decreased from moderate to mild (IPSS<8) and only slight urination disturbances were observed (Q_{max}>15 ml/sec, Fig. 1). According to international recommendations, no drug treatment of BPH, but only dynamic observation (watchful waiting policy) is indicated for these patients [5].

No undesirable events, including changes in laboratory parameters, were noted during afala treatment: complete blood count, biochemical parameters, including serum concentration of prostate-specific antigen, and clinical analysis of the urine corresponded to normal before and after therapy. In patients receiving *S. repens,* undesirable events were also absent.

Thus, our study demonstrated clinical efficiency and safety of afala in patients with medium-severity urination disturbances caused by BPH. Clinical efficiency of afala was comparable with the efficiency of *S. repens* extract (reference preparation). The safety of afala treatment in patients with BPH was also demonstrated.

REFERENCES

1. B. Burger, W. Weidner, and J. E. Altwein, *Eur. Urol*. **35**, No. 3, 177-184 (1999).
2. M. J. Barry, S. Beckley, P. Boyle, *et al*., *Proceedings of the International Consultation on BPH. WHO* (1992), p. 13.
3. M. J. Barry, F. J. Fowler Jr., M. P. O'Leary, *et al., J. Urol.,* **148**, No. 5, 1549-1557 (1992).
4. S. J. Berry, D. S. Coffey, P. C. Walsh, and L. L. Ewing, *Ibid*., **132**, No. 3, 474-479 (1984).
5. J. J. de la Rosette, G. Alivizatos, S. Madersbacher, *et al., Eur. Urol*. **40**, No. 3, 256-263 (2001).
6. S. J. Frankel, J. L. Donovan, T.I. Peters, *et al., J. Clin. Epidemiol.,* **51**, No. 8, 677-685 (1998).
7. E. Shapiro and H. Lepor, *Urol. Clin. North. Am.,* 1995. **22**, No. 2, 285-290 (1993).