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RESULTS OF USING ADENO RITZ IN BENIGN PROSTATIC HYPERPLASIA IN YOUNG MEN

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ABSTRACT

To analyze the effect of Adeno ritz at a dose of 320 mg once a day on sexual function compared to tamsulosin at a dose of 0.4 mg once, in men with lower urinary tract symptoms (LUTs) complicated by benign prostatic hyperplasia.

Introduction: Therapy of erectile dysfunction (ED) against the background of benign prostatic hyperplasia (BPH) in patients aged 40-50 years requires more focus when choosing a drug to jointly eliminate or reduce the symptoms of the lower urinary tract (LUTs), correct the volume of the prostate, improve urination and the quality of life of the patient. The long-term goals of these measures are to persistently improve symptoms, prevent disease progression, maintain the achieved urination rate, reduce the volume of the prostate, and, of course, reduce the risk of acute urinary retention and the need for surgical intervention [1, 2].

Many well-known schemes of conservative administration of patients with ED on the background of BPH remain controversial to this day, due to the fact that the combined use of α-blockers and 5α-reductase inhibitors often become impossible due to concomitant diseases. Most often, the occurrence of side effects is associated with the action of alpha-blockers, especially in patients with a burdened somatic status. For example, in the treatment of hypertension, tamsulosin enhances the effect of antihypertensive therapy and provokes orthostatic collapses. In combination with complex therapy with phosphodiesterase inhibitors, orthostatic hypotension may also occur. A known side effect of alpha-blockers is a violation of sexual function in the form of retrograde ejaculation, which makes a significant discomfort in the lives of many patients [3]. Undesirable effects are also characteristic of the second, most well-known group of drugs — 5α-reductase inhibitors, which most often affect sexual function, reducing

libido, causing erectile dysfunction (ED) and, less often, ejaculation disorders or a decrease in sperm volume [4-5]. The process of initiation and progression of the proliferative activity of the prostatic tissue can be greatly aggravated by some concomitant diseases, such as obesity, insulin resistance, type 2 diabetes mellitus, and metabolic syndrome [6]. An important factor in the progression of BPH is the constant active influence of androgens on its functional tissue. It is known that α1-adrenoreceptors are directly involved in the action of intracellular effectors that affect the volume and tone of the smooth muscle elements of the prostate, which explains the obvious result of their activation [7].

In BPH without ED, the most effective treatment option is a combination of an α1-adrenoblocker and a 5α-reductase inhibitor. In BPH with ED, a two-and three-component combination with the inclusion of a phosphodiesterase-5 inhibitor provides a significant improvement in erectile function and BPH-related LUTs. It has been shown that multicomponent therapy regimens are not accompanied by a significant increase in the frequency of adverse reactions [8].

Among the drugs used for the treatment of BPH, herbal preparations occupy a special place. Nowadays, active research is being conducted on the basis of herbal extracts, which are considered more gentle and safe for use in some groups of patients who are forced to receive conservative therapy for a long time. The most well-known such preparations are extracts of pumpkin Pepo (pumpkin seeds), Hypoxis rooperi (South African star grass), extract of the bark of the African plum africanum (bark of the African plum), rye and some rye herbs (rye pollen) and extract of the dwarf palm serenoa serrulata (fan-leaved palm). Of the above-mentioned herbal preparations, the hexane extract of S. serrulata is evaluated as a drug with recognized efficacy and safety [9].

They inhibit the synthesis of prostaglandins in the prostate; reduce the secretion of sex hormone-binding globulin in the liver; have a cytotoxic effect on prostate cells; have a blocking effect on androgen receptors; inhibit the proliferation of prostatic epithelium induced by growth factors, and also reduce the activity of 5α-reductase [10]. It is believed that hexane extracts with. creepers inhibit the synthesis of prostaglandins and leukotrienes by blocking the arachidonic acid cascade, reduce the expression of various genes involved in the inflammatory process, stimulate the expression of anti-inflammatory factors, reduce the number of immune cells (B-lymphocytes, etc.) and the concentration of interleukin 1β, tumor necrosis factor α. Hexane extracts with. creeping has an effect not only on the activity of 5a-reductase, but also on various phases of androgen metabolism and inhibits the binding of dihydrotestosterone to androgen receptors, which explains its anti-estrogenic effect, which, in addition, is also due to a decrease in the number of estrogen receptors in the prostate and a decrease in prolactin stimulation of hyperplastic processes [11]. Another mechanism of action attributed to Serenoa serrulata extract is the modulation of apoptosis via growth factors: it reverses the apoptosis/proliferation ratio seen in BPH tissue [12, 13].

Some studies have described a significant improvement in the International Index of

Erectile Function score following treatment with Serenoa serrulata extracts. If we take into consideration that retrograde ejaculation and reduced ejaculate volume related to α-blockers, and erectile dysfunction and decreased libido related to 5α-reductase inhibitors are frequently associated with dissatisfaction in medically treated BPH patients, Serenoa serrulata extract may become a viable alternative in selected cases [14,15,16,17]. Phytotherapy was recently added to the European Association of Urology guidelines. Clear data that Serenoa serrulata extracts significantly reduce nocturia by comparison with placebo are cited. However, the guideline committee states that it is still unable to make specific recommendations about phytotherapy for male LUTS owing to the heterogeneity of the products and the methodological problems associated with meta-analyses[18].

S. repens extract has the properties of an α1-adrenoreceptor blocker. Anticholinergic agents are widely used for the treatment of overactive bladder; therefore, the inhibition of muscarinic receptors may be a new pharmacological effect of extracts on the lower urinary tract to relieve the irritating and obstructive symptoms of dysuria in BPH and LUTs [19]. One of the preparations containing the largest amount of free fatty acids is the hexane extract of S. repens - Adeno ritz ("GM Pharmaceuticals Ltd ", Georgia).

Most of the short-, medium- and long-term studies showed statistically significant improvement in total international prostate symptom score (IPSS) during 6, 12 or 24 months of follow up [20,21]. When the irritative and obstructive IPSS subscores were separately evaluated, a decrease in both was seen. This combined action of Serenoa repens extract may offer at least a theoretical advantage over α-blocking therapy [20, 22].

Materials and methods: The study included 64 men aged 47 to 63 years (mean age 54.3±2.1 years) with benign prostatic hyperplasia, with various manifestations of erectile dysfunction. 57 patients out of a total of very low rated their erectile function scores. All patients underwent transrectal ultrasound of the prostate, finger rectal examination and urine analysis according to Nechiporenko. Patients were randomized in two multicenter trials using the same study protocols. In each group, patients were randomized as follows: the first group (n = 34) received Adeno ritz, at a dose of 320mg once a day. The second (n=30) tamsulosin 0.4 mg once, using the IPSS scale (International Prostate Symptom Score), the IIEF-5 total score (International Index of Erectile Function) and QoL (quality of life), as the main evaluation criteria.

Results: The study included a 16-week period for each group. The assessment of sexual function was carried out according to the results, side effects and general condition of the patients.

Table 1. Comparative patient rates after 16 weeks of treatment

Parameter	**Tamsulozin 0.4 mg** (n = 30)	**Adeno ritz 320 mg** (n = 34)
lowered the indicator IPSS	n = 27(39%)	n = 12(34%)

improved the QoL	n = 13(44%)	n = 16(47%)
IIEF-5 indicators	11-16	17-22
Impact on the disease progression	-	+
Selectivity	-	+
Anti-inflammatory effects	-	++
Action speed	+++	+
Adverse events in sexual life	+	-
Inhibition of growth factors	-	+

Both drugs reduced the IPSS (-34% and -39%, respectively), subjectively improved the quality of life (by 47 and 44%), IIEF-5 indicators were 17-22 in the first group and 11-16 in the second group. In the second group, there was no improvement in the quality of erectile function. A significant number of patients were found to have retrograde ejaculation, frequent abnormal ejaculations when straining the abdominal press during the act of defecation, despite a significant improvement in imperative anxiety, when taking tamsulosin. In relation to the drug Adeno ritz, no pronounced side effects were recorded. At the end of treatment, 21 (61%) patients from the first group noticeably felt an improvement in erectile function, noted an increase in libido and an increase in the amount of ejaculate released, together with a decrease in urination disorders and discomfort in the perineum.

Conclusion: Adeno ritz 320mg, with a single dose per day, is well tolerated by patients, and there is no negative effect on the cardiovascular system and visual organs compared to tamsulosin. Adeno ritz, in contrast to tamsulosin, has a more pronounced anti-inflammatory effect, reduces the progression of BPH and does not cause violations of the sexual function of men, which are observed with the use of α1-blockers. Adeno ritz in patients with undetected symptoms of BPH, in the initial stages of adenoma, as well as in persons who consider it mandatory to maintain sexual function at 16 weeks or more, can reduce the symptoms of the lower urinary tract and improve erectile function in men of significantly younger age with benign prostatic hyperplasia.

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