COMBINATION THERAPY FOR BENIGN PROSTATIC HYPERPLASIA (BPH).

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Abstract. Timely initiation of treatment of benign prostatic hyperplasia (BPH) with the combined drug duodart (which includes a double inhibitor of 5α-reductase - dutasteride and an α1a-adrenergic receptor blocker - tamsulosin hydrochloride) in patients with prostate cell proliferation stops, and then cell apoptosis begins. This leads to improved urination, a decrease in the volume of prostatic hyperplasia, an improvement in the quality of life of patients and the avoidance of surgery.

Benign prostatic hyperplasia (BPH) is the most common disease in older men, which is based on the increasing infravesical obstruction caused by prostatic hyperplasia. The disease develops slowly and progresses with age.

According to autopsies, the first signs of BPH are found in 8% of men aged 31 to 40 years. In men older than 60 years, BPH occurs in 60-70%, and after 80 years - 90%. The clinical symptoms of the disease include obstructive and irritative symptoms, which are combined into lower urinary tract symptoms (LUTS). Presented in 2001 in Geneva in the materials of the European Urological Association, data from a survey of patients with symptoms of urination disorders in BPH, indicate that 58% of men deliberately reduce fluid intake in the evening; 41% avoid visiting places where there is no toilet; 31% refuse to travel long distances; 20% try to leave the house less often.

According to the UN, the population over the age of 60 by the end of the twentieth century increased by more than 3 times compared to its middle. Given the trend of population aging, we can assume an increase in the relevance of the problem of diagnosis and treatment of BPH.

Achievements in the study of the etiology and pathogenesis of benign prostatic hyperplasia (BPH) have led to the creation of a number of drugs, the use of which has proved to be so effective that it can be assumed with great confidence that in the 21st century, patients with BPH will be treated mainly with medication, with a high quality of life, and evidence-based prevention of BPH will become a reality.

Conservative therapy for BPH has recently made a significant breakthrough and is designed for a long period - months, and sometimes even years.

Currently, conservative therapy for BPH is based on two main groups of drugs - alpha-blockers and 5-alpha reductase inhibitors.

At present, it has indeed been established that during the development of BPH, the activity of 5-alpha reductase (5AR) increases in the transition zone, where the development of BPH occurs.

Indications for treatment with 5AR inhibitor drugs are clinical signs of prostate enlargement and disturbing symptoms that do not have serious complications.

Duodart is a combination of two components with complementary mechanisms of action that help relieve symptoms in patients with benign prostatic hyperplasia (BPH): a dual 5α-reductase inhibitor, dutasteride, and an α1a-adrenergic receptor blocker, tamsulosin hydrochloride.

Dutasteride inhibits the activity of 5α-reductase isoenzymes of the 1st and 2nd types, under the influence of which testosterone is converted into 5α-dihydrotestosterone (DHT), the main androgen that causes hyperplasia of the glandular tissue of the prostate.

Up to 90-95% of the testosterone produced in the body is in the blood plasma in an inactive state, since testosterone is bound to albumin and globulin, and only 5-10% of it is not bound to plasma proteins - free testosterone.

Testosterone penetrating into the cells of the prostate gland, under the influence of the enzyme 5-reductase (4Ar), turns into the most active form of 5-DGP, which, by binding to the corresponding protein receptors, activates the synthesis of substances called growth factors that enhance the growth and maturation of parenchyma cells and stroma of the prostate (Habib and Grant, 1996).

Tamsulosin inhibits α1a-adrenergic receptors in the smooth muscle of the stroma of the prostate and bladder neck. Approximately 75% of α1-adrenergic receptors in the prostate gland are α1a receptors.

It is expected that the pharmacodynamic properties of dutasteride and tamsulosin in the form of a combined preparation will not differ from the properties of dutasteride and tamsulosin used simultaneously as separate components.

Dutasteride lowers DHT levels, reduces the size of the prostate gland, improves lower urinary tract symptoms and increases the rate of urination, and reduces the risk of acute urinary retention and the need for surgery.

The maximum effect of daily doses of dutasteride on the reduction of DHT concentrations is dose-dependent and occurs within 1-2 weeks. After 1 and 2 weeks of taking dutasteride at a dose of 0.5 mg per day, the average values of serum DHT concentrations decreased by 85% and 90%, respectively.

In patients with BPH who received 0.5 mg dutasteride per day, the average decrease in DHT levels was 94% after 1 year and 93% after 2 years, the average increase in serum testosterone levels was 19% both after 1 year and after 2 years. of the year. This is an expected consequence of 5α-reductase inhibition and does not result in any of the known adverse events.

Tamsulosin increases the maximum urinary flow rate by reducing the smooth muscle tone of the prostate and urethra and therefore reduces obstruction. Tamsulosin also reduces the complex of symptoms of filling and emptying, in the development of which the instability of the bladder and the tone of the smooth muscles of the lower urinary tract play a significant role. α1-blockers can lower blood pressure by reducing peripheral resistance.

Materials and methods. In the Urgench branch of the Republican Specialized Scientific Medical Center of Urology (RSMCU) in the period from January 2019 to June 2022, a study was conducted that studied the clinical efficacy of the drug Duodart (dutasteride + tamsulosin 0.5 / 0.4 mg) in patients with LUTS due to BPH. Data were compared before and after administration of cardura. The study involved 75 patients aged 61 to 78 years, the observation period was 6 months. The effect of taking the drug on the severity of LUTS according to the IPSS scale, the size of the prostate gland according to ultrasound and TRUS,

the volume of residual urine, the functional capacity of the bladder, blood pressure, and the presence of side effects were evaluated.

The inclusion criteria for the study were:

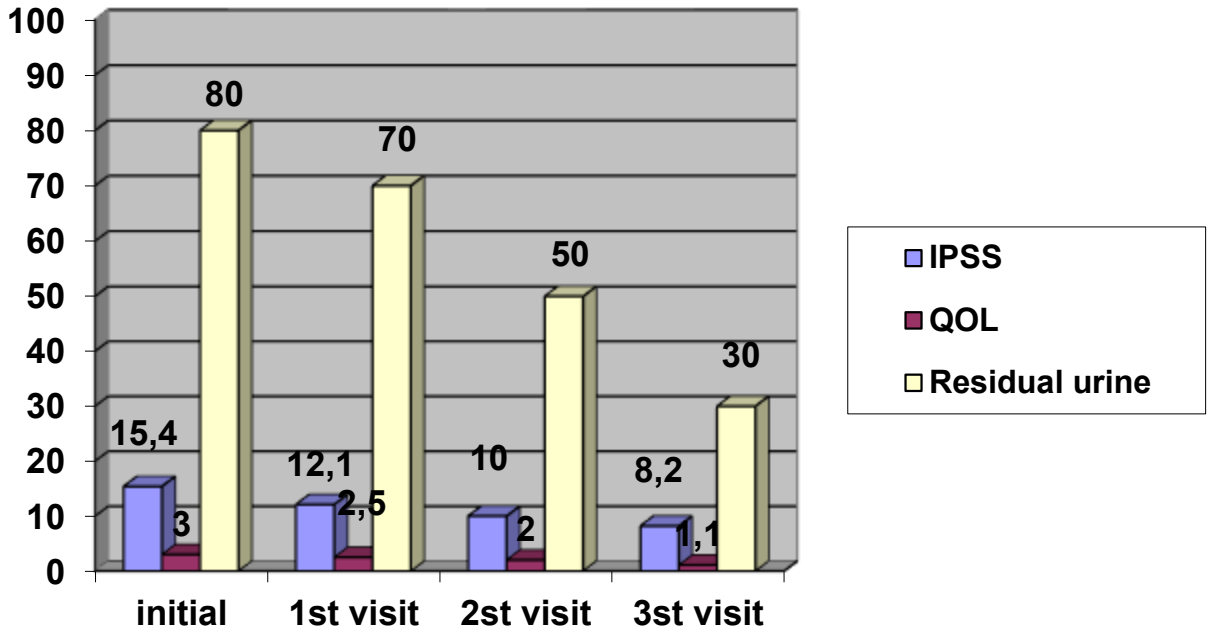
- outpatients and inpatients with LUTS due to BPH
- age over 60 years
- severity of symptoms on the IPSS scale from 8 to 20 points (average 15.4)
- the volume of residual urine is not more than 100 ml
- the patient's quality of life is not more than 4 points (average - 3.2)
- confirmation of the diagnosis of BPH by rectal examination.

The drug was taken according to the following scheme: daily (after dinner) oral administration of duodart with an average symptomatology on the IPSS scale. During the study, follow-up was divided into 3 visits, 1st visit one month after the start of treatment, 2nd visit 3 months later, 3rd visit 6 months later.

During the study, 3 patients dropped out of it: due to the development of undesirable effects (one had a sharp decrease in blood pressure, two had stool disorders).

Results. During the observation period, there was a significant decrease in irritative and obstructive symptoms due to BPH. The severity of symptoms on the IPSS scale decreased from 15.4 to 8.2 points, the patient's quality of life (QOL) decreased from 3.0 to 1.1 points, residual urine volume from 80 ml to 30 ml on average.

Prostate volume on TRUS decreased from 70 ml to 40 ml on average.



As a result of the study, we obtained a significant reduction in such risk factors for the progression of the disease as the volume of residual urine, the volume of the prostate gland, and also noted an improvement in the quality of life of patients.

Conclusion. Conservative treatment of patients with BPH with the combined drug duodart (dutosteride + tamsulosin) leads to an improvement in urination parameters, reduces the amount of residual urine and, most importantly, to improve the patient's quality of life. Thus, the combined treatment of patients with BPH with 5a-reductase inhibitors and a-blockers is

highly effective, because it affects the two leading links in pathogenesis of urination disorders in hyperplasia prostate - infravesical obstruction and detrusor hypoxia. This improves cystic circulation, increases the capacity bladder, significantly reduced irritative symptomatology, which positively affects the quality the lives of the sick.

Our experience with the use of a-blockers with inhibitors

5α-reductase showed a significant improvement urodynamics of the lower urinary tract.

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