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Tamsulosin in the treatment of urological disorders - a literature review

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Abstract

Benign prostatic hyperplasia (BPH) is one of the most common diseases in the elderly, affecting almost half of men over 50 years of age and nearly 90% of men over 80 years of age. The most common complication of BPH is acute urinary retention, which significantly

reduces the quality of life of patients. Pharmacological treatment with alpha blockers and 5-alpha reductase inhibitors is the first line of therapy for BPH. Tamsulosin, as a selective alpha-1 receptor antagonist, is one of the preferred alpha blockers due to its relatively lower side effects compared to other drugs in this class. Tamsulosin has linear pharmacokinetic properties and its absorption is sensitive to the presence of food.

The purpose of one study was to evaluate the efficacy and safety of a double dose of tamsulosin (0.8 mg) in patients with BPH who did not respond to the standard dose (0.4 mg) and were not candidates for transurethral intervention. An open-label, randomized, three-stage study included 111 patients who experienced severe symptoms of BPH. Before and after one month of treatment, several parameters were evaluated, including the International Prostate Symptom Score (IPSS), prostate-specific antigen (PSA) level, prostate volume, maximum urine flow (Qmax) and post-void urine volume.

The results of the study showed that all the patients were treated and the mean age of the participants was 63.12 ± 4.83 years. Improvements in Qmax, post-void urine volume and IPSS score were observed in 93 patients ($p < 0.001$). Total IPSS and Qmax improved from 24.03 ± 2.49 to 16.41 ± 3.84 and from 7.72 ± 1.64 to 12.08 ± 2.37 ml/s, respectively.

Finally, a double dose of tamsulosin 0.8 as an alpha-blocker therapy: an effective treatment option for patients with BPH who have failed to respond to standard therapy and who are not candidates for surgical intervention.

Keywords: Tamsulosin, alpha 1-adrenergic receptor antagonists, benign prostatic hyperplasia (BPH)

Introduction

In the course of BPH (benign prostatic hyperplasia), there is a high expression of α1A adrenergic receptors. Tamsulosin selectively and competitively binds to postsynaptic α1-type adrenergic receptors, especially subtypes α1A and α1D, causing relaxation of the smooth muscle of the prostate and urethra, thereby reducing tone. It also increases maximum urine flow rate, paving the way for urine flow by reducing tension on the smooth muscles of the prostate and urethra. Tamsulosin reduces the severity of lower urinary tract symptoms, assessed by the IPSS questionnaire, by 30-40% and also improves urine flow (20-25% increase in Qmax). Previous observations have shown that it takes several weeks to achieve a full clinical effect, but a significant efficacy compared to placebo is observed after several hours to days [12,13].

Alpha-adrenergic receptor antagonists were first used 30 years ago to treat lower urinary tract (LUT) symptoms of benign prostatic hyperplasia (BPH). The main methods of treating LUT have been around for more than 10 years. The introduction of many highly effective preparations on the market has resulted in the number of patients with BPH treated conservatively being ten times the number of patients undergoing surgical treatment. α adrenergic receptor antagonists produce a therapeutic effect despite α1-adrenergic receptors that are continuously stimulated by norepinephrine. The effect is to reduce the tension of smooth muscle fibers in the stroma and capsule of the prostate gland and around the neck of the urinary bladder. The final therapeutic effect is also affected by the activation of mechanisms in the spinal cord and urinary bladder. It should be noted that the therapeutic effect does not negatively affect the degree of contractility of the muscle that ruptures the urinary bladder. Adrenergic receptors constitute a heterogeneous group, consisting of α1 and α2 receptors. A group of a1 receptors subtype A (a1A) are considered prostate specific. The blockade of the receptors of this subgroup is, among other things: to eliminate the dynamic element of subvesical obstruction (BOO) due to the contraction of the smooth muscles in the neck of the bladder and the stroma of the prostate. Drugs from the group of α-adrenergic receptor antagonists differ in their selectivity for certain subtypes of receptors. Initially, quinazoline α blockers (terazosin, alfuzosin, doxazosin) were introduced in the treatment of patients with LUTs caused by BPH (LUTs/BPH). A drug that was introduced later and is still used is tamsulosin [12,13].

Tamsulosin at a dose of 0.8 mg showed better results in the treatment of patients with lower urinary tract symptoms in the course of benign prostatic hyperplasia than Tamsulosin at a dose of 0.4 mg and was well tolerated [11]. Lower urinary tract symptoms (LUTS) with benign prostatic hyperplasia (BPH) are a common phenomenon in the elderly and, according to studies conducted among men over 40, affect approximately 25% of men over 40. BPH can interfere with daily activities and reduce quality of life, especially when it comes to urinary symptoms. Treatment options include careful observation, lifestyle changes, herbal remedies, prescription drugs, and surgery. Pharmacological treatment is the primary therapeutic approach for many symptomatic BPH patients [2].

The main goals of treatment are to alleviate symptoms in a short period of time, alleviate the side effects of treatment and finally prevent complications to prevent quality of life. Currently, the most effective medical therapies for BPH are alpha 1-adrenergic receptor antagonists (alpha blockers) and 5-alpha reductase inhibitors (5-ARIS) [3]. Alpha blockers increase sympathetic activity and increase urination by relaxing the smooth muscle of the prostate and bladder neck, blocking sympathetic activity. The most commonly prescribed drugs are alpha blockers, including doxazosin, terazosin, prazosin, alfuzosin, and tamsulosin [4].

Tamsulosin, with high affinity for alpha-1a adrenergic receptors, mainly mediates smooth muscle tone of the prostate and bladder, as well as the dynamic component of bladder dysfunction (BOO) and rapidly relieves LUTS. In contrast to other non-selective alpha-blockers, such as doxazosin, alfuzosin and terazosin, tamsulosin is well tolerated due to its prostate selectivity [5]. Tamsulosin appears to respond poorly to diagnostic tests for low blood level disorders and is well tolerated by age. simultaneous appetite and treatment with other drugs. In addition, tamsulosin has been shown to have a weaker interaction with drugs from the 5-phosphodiesterase inhibitor group (tadalafil, vardenafil) than terazosin or doxazosin and to be hemodynamically active [11].

Expand

Lower urinary tract symptoms (LUTS) are the most common urologic symptoms in older adults, and benign prostatic hyperplasia (BPH) is the most common cause of LUTS in older adults. LUTS can be divided into urinary, voiding and post-micturition symptoms, which often affect quality of life (QoL) and activities of daily living. If left untreated, it can cause lower urinary tract complications such as acute urinary retention (AUR), kidney failure,

recurrent urinary tract infections or bladder stones, etc. and may require endoscopic surgery such as transurethral resection.hyperplasia of the prostate or prostate [6] .

A prospective study conducted from November 2022 to July 2023 in several urology clinics in Cairo and Fayoum, Egypt, focused on patients over 50 years of age who have severe lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia. BPH). However, each dose of tamsulosin is 0.4 mg. Initially, 150 patients were admitted, but only 111 completed both visits, resulting in 39 dropouts. Inclusion criteria included at least 3 months of prior tamsulosin monotherapy, International Prostate Symptom Score (IPSS) greater than 19, urine flow less than 10 peak flow (Qmax) less than 10, and inability to undergo surgery due to medical conditions or refusal. Patients receiving treatment other than tamsulosin were excluded. Extensive interviews, examinations, and analyzes were performed, including IPSS, quality of life (QoL), prostate volume, Qmax, and abdominal/pelvic ultrasound at presentation and at the 1-month visit. A responsive group was identified by an improvement in the IPSS of more than 3, after ethical approval [4].

The European Association of Urology (EAU) recommends an initial test of medical history, a validated questionnaire for urological symptom scores, paper volume velocity, bladder comment, physical examination including digital rectal examination (DRE), urinalysis and prostate specific antigen (PSA). to BPH InternationalThe Prostate Symptom Score (IPSS) is the most common evaluation tool in patients complaining of LUTS, and consists of seven questionnaires assessing urinary symptoms (sense of incomplete emptying, interruption, flow and weak urgency), symptoms of urinary retention (frequency, urgency) urination and nocturnal and quality of life [6].

In the study conducted by Mohamed Mahmoud Dogha, a total of one hundred and fifty patients were enrolled in the first visit in 2024. However, only 111 patients completed the two visits and therefore 39 patients were excluded. Total Qmax improved from 7.72 ± 1.64 ml/s to 12.08 ± 2.37 ml/s ($p = 0.001$), and total IPSS symptoms improved from 24.03 ± 2.49 to 16.41 ± 3.84 ($p = 0.001$). The IPSS scores of 93 patients increased by more than 3 and were assigned to the responder group, while the remaining 18 patients, whose IPSS scores did not increase by more than 3, were assigned to the nonresponder group. The general characteristics of patients in both PSA groups were similar. The mean age was 63.12 ± 4.8 years and the mean PSA level was 3.42 ± 0.93 ng/ml [4].

Benign prostatic hyperplasia (BPH) is a progressive disease characterized by worsening symptoms over time and, in some cases, the need for surgery. Given the associated risks of surgery and prolonged catheterization, our study explored the use of a double-dose tamsulosin solution for temporarily less fit patients.

Tamsulosin is highly selectiveα1 blocker reduces the contraction of smooth muscle in the prostate, urethra and bladder neck, thereby reducing resistance to urine. It has a greater affinity for α1A receptors than for α1B receptors. Therefore, it has fewer cardiovascular effects and does not interfere with antihypertensive drugs [7].

Uroflowmetry parameters such as maximum flow rate (Qmax), mean flow rate (Qavg) and post-void urine volume (PVR), as well as the International Prostate Symptom Scale (IPSS) were used to evaluate the improvement of lower urinary tract symptoms[7].

To be compared to othersα1 blockers, Tamsulosin have fewer side effects, such as dizziness, lightheadedness, syncope after the first dose and orthostatic hypotension. According to the study, there was no statistically significant difference in blood pressure between people treated with Tamsulosin and those treated with placebo. On the other hand, Tamsulosin often causes delayed or retrograde exclamation. This is done by blocking receptors in the vas deferens and bladder neck, which prevent the internal sphincter from contracting during ejaculation. Other less common side effects include headache, weakness and rhinitis-like symptoms, which are probably caused by inhibition of serotonin release in the central nervous system[8]

Many studies have used doses of 0.2, 0.4, 0.6, and 0.8 mg for the efficacy and safety of tamsulosin in the treatment of BPH. An initial study by Abrams and colleagues for efficacyand is designed to help tamsulosin safety and to determine the optimal dose of treatment[10] Placebo, 0.2, 0.4, or 0.6 mg of tamsulosin once a month for 1 day. The greatest reduction in symptoms in men receiving 0.4 or 0.6 mg, compared to 0.2 mg and placebo[10] Two drinks also showed the greatest improvement in uroflow compared to placebo. There were no dose-related changes in vital signs or laboratory variables[10]

Conclusion

Long-term treatment with tamsulosin leads to a reduction in maximum pressure in the

prostatic urethra and an improvement in both urinary retention in the bladder and its emptying. It is believed that the beneficial therapeutic effect of tamsulosin is due to the blockade of α1A adrenergic receptors, especially in the neck of the bladder, as well as in the stroma of the urethra and prostate. Cooperation is required by other mechanisms, namely the blocking of α1-adrenergic receptors on cholinergic nerve endings at the level of the urinary bladder and/or peripheral ganglia, leading to a reduction in acetylcholine release and consequently a reduction in voluntary contractions of the detrusor muscle. [11].

The introduction of generic drugs (generic drugs) to the market led to a reduction in treatment costs. The most important factor limiting the use of α1-adrenergic receptor antagonists is undoubtedly the occurrence of side effects and impaired drug tolerance. Patients treated with alpha-blockers may experience side effects (such as dizziness and headache, weakness, increased heart rate, orthostatic hypotension, fainting) from the effects of these drugs on the cardiovascular system [11]. Side effects include: the use of tamsulosin, which is not related to the cardiovascular system, indicating ejaculation disorders. Retrograde ejaculation, reduced volume or lack of ejaculation results from blockade of α1A and α1D adrenergic receptors in the vas deferens, bladder neck and/or seminal vesicles [11].

Tamsulosin, an extended-release uroselective drug, has a significantly lower risk of orthostatic hypotension and is therefore preferred in the general practice of BPH pharmacotherapy. It is believed that non-uroselective preparations are more likely to cause adverse reactions in the cardiovascular system (including hypotensive effects). But the good blood-lowering effects are somewhat common side effects. These include: orthostatic hypotension, dizziness, fatigue, headache and cardiac arrhythmias (mainly tachycardia). Considering that the risk of cardiovascular complications in this group of patients increases with age, it is worth considering the adjustment of a uroselective drug, ie, tamsulosin [13].

Disclosure

Conceptualization, Błażej Kaczmarek, Aleksandra Dorosz;

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