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Original research article

Evaluation of the clinical indications, adverse drug reactions, and finasteride use in patients with benign prostatic hyperplasia in Poland

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ABSTRACT

Introduction: Benign prostatic hyperplasia (LUTS/BPH) is one of the most common urinary disorders in elderly men. The symptoms of the disease include prostate gland enlargement, bladder outlet obstruction, and lower urinary tract symptoms (LUTSs). BPH predisposes patients to bladder infections and bladder stone formation and increases their risk of urinary retention, which in turn causes renal failure. Hence, the disease requires surgical treatment. However, over the recent years, the number of surgical interventions performed in pharmacotherapy has significantly reduced because of the increased efficacy of conservative therapy, including combination treatment mostly with 2 groups of drugs, namely, alpha-1-adrenolitics and other 5-alpha-reductase blockers, with a different pharmacological activity [25].

The aim of this study was to evaluate the clinical indications, adverse drug reactions, and finasteride use in patients with diagnosed BPH in Poland.

Materials and methods: We conducted a clinical trial from November 2009 to November 2010 that included 5751 patients who were enrolled in 46 urological centres in Poland. The researchers who conducted the clinical trial were urologists from different regions of Poland. The clinical trial involved 6 follow-up visits. The mean age of the patients was 67 years (range, 45–93 years; median, 67.00; SD, 8.507). The inclusion criteria were as follows: LUTSs, finasteride therapy for at least 2 weeks, age $>$ 40 years, and BPH.

Results: Patients self-reported data on LUTSs, the symptom frequency, concurrent diseases, and intensification of urinary system symptoms. In addition, additional examinations were performed, including prostate-specific antigen test, urinary tract ultrasonography with evaluation of residual urine and prostate, and uroflowmetry. The study did not exclude data on the combined treatment with finasteride and alpha-1-adrenolitics.

Conclusion: Finasteride was demonstrated to be effective, as evidenced by the significant decrease in TPV by 40% even after 12 months. It was also found to contribute to the attenuation of LUTSs, improvement in maximum flow rate, decrease in nocturia, and improvement in QoL.

Introduction

Benign prostatic hyperplasia (LUTS/BPH) is one of the most common urinary disorders in elderly men. Histologically, it is related to stromal and glandular epithelial hyperplasia that occurs in the periurethral transition zone of the prostate that surrounds the urethra [21].

The symptoms of the disease include prostate gland enlargement, bladder outlet obstruction, and lower urinary tract symptoms (LUTSs).

The prostate growth is dependent on the presence of hormones and growths factors. Testosterone is considered to be the most important of these and it is converted within the prostate into its more active metabolite, dihydrotestosterone (DHT), by 5α-reductase blocker, a nuclear-bound steroid enzyme which is localised primarily in the prostatic stromal cell. Therefore, this cell plays an important role in androgen-dependent prostatic growth [21].

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The pathophysiology of clinical BPH is not considered to be dependent on prostate size, reducing the prostate's volume is thought to decrease the constant component of bladder outlet obstruction. Furthermore, it was shown that men with a prostate volume of 30 cm^3 or more have been shown to be 3.5 times more likely to have moderate-to-severe lower urinary tract symptoms and acute urinary retention [2]. Thus, by actively decreasing the size of the prostate through reduction of intraprostatic DHT [17] finasteride plays a significant role in the reduction of long-term risk of progression.

BPH predisposes patients to bladder infections and bladder stone formation and increases their risk of urinary retention, which in turn causes renal failure [6]. The disease is becoming an important problem of a diagnostic-therapeutic and socioeconomic nature, considering the increase in the life expectancy of men; hence, the disease requires surgical treatment [25]. Urination discomfort due to the enlargement of the prostate gland usually appears after 40 years of age and worsens with age. In Poland, approximately 2 million men experience urination discomfort. In 2000, approximately 20,000 patients underwent surgical treatment because of symptomatic BPH. However, over the recent years, the number of surgical interventions performed in pharmacotherapy has significantly reduced because of the increased efficacy of conservative therapy, including combination treatment mostly with 2 groups of drugs, namely, alpha-1-adrenolitics and other 5-alpha-reductase blockers with a different pharmacological activity [24].

The alpha-1-adrenolitics provide an improvement within flow rate but their effects may not decrease the overall risk of BPH-related complications. The 5-alpha-reductase blockers inhibit the enzyme which converts testosterone to dihydrotestosterone – the androgen involved in normal and abnormal prostate growth [21].

Finasteride (MK-906) is chemically 17β-(N-tert-butyl-carbamoyl)-4-aza-5α-androst-1-en-3-one, approved in the United States in 1992 for the treatment of BPH [23]. This competitive inhibitor of 5α-reductase type 2 with 10-fold high affinity than type 1 forms a stable complex with enzyme. It was confirmed that the clinical dose of 5 mg/day in human beings decreases the prostate DHT level by 70–90%. Furthermore, it results in decreased prostate volume and improved urinary flow rate [12].

The alpha-1-adrenolitics are considered as second group of drugs which is used in combination treatment, they are for example: alfuzosin, doxazosin, tamsulosin and terazosin. The noradrenaline acts at α_1-adrenergic receptors (α_1-AR) in the neck and sphincter of the urinary bladder. It promotes contraction and urinary retention and it controls the smooth muscles in the prostate capsule and prostate urethra [7]. The selective α_1-adrenergic receptors relieve the obstruction by relaxing the smooth muscle in the prostate and bladder neck. Furthermore, they do not affect the detrusor muscle of the bladder wall [21].

Alfuzosin is a quinozoline-based α_1-adrenergic receptors antagonist which has a similar affinity for all α_1 receptor subtypes [14]. Terazosin and doxazosin, the advent of selective α_1-drugs, the structural analogue of prazosin, originally developed as antihypertensive agents [14]. Tamsulosin hydrochloride is a competitive antagonist of α_1 adrenergic receptor with 10-fold more selectivity for α_{1A}-receptor subtype compared with α_{1B}-receptor subtype, approved for use in the treatment of BPH [13].

BPH occurs in 70% of men older than 60 years and in 90% of men older than 80 years. Clinical trials conducted among men with ages ranging from 60 to 70 years confirmed that LUTS/BPH occurred in 80% patients. According to numerous statistical data, BPH symptoms occur in approximately 31% of men older than 50 years and in at least 50% of men older than 60 years [8]. Nearly all men are considered to develop microscopic BPH by the age of 90 years [3,5].

The aetiology and pathogenesis of LUTS/BPH are not completely known; nevertheless, the following factors have been demonstrated to greatly influence the progression of the disease: older male age, hormonal imbalance, and nonhormonal growth factors reaction [13].

The self-reported evaluation, physical examination, laboratory test, and imaging examination were very useful in obtaining diagnosis.

Generally, patients with LUTS/BPH symptoms present to the clinic when their quality-of-life (QoL) is affected or when painful urination worsens [18].

Aim of the study

The aim of this study was to evaluate the clinical indications, adverse drug reactions, and finasteride use in patients with diagnosed BPH in Poland.

Material and methods

The clinical trial was conducted from November 2009 to November 2010. A total of 5751 patients who were enrolled in 46 urological centres in Poland participated in the clinical trial. The researchers who conducted the trial were urologists from different regions of Poland. The clinical trial involved 6 follow-up visits. The most frequently reported discomforts were as follows: frequent urination in 81.29% (n = 4675) of the patients, excessive need to urinate at night (nocturia) in 83.11% (n = 4780), decreased size and strength of the urinary stream in 74.82% (n = 4303), and beginning

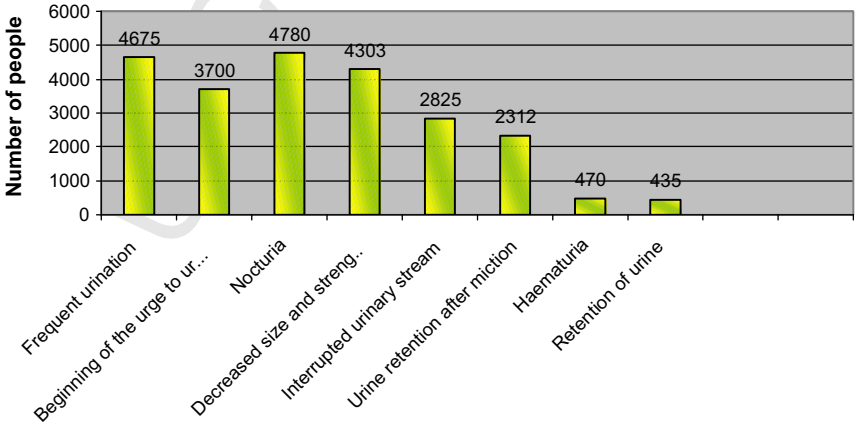

Fig. 1. Discomforts self-reported by the patients during the first appointment.

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