Our experience with the treatment of benign prostatic hyperplasia (BPH) with Tamsulosin

Cervenakov I, Fillo J

Abstract

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Background: **Alpha$_1$-blockers decrease the tension, ease the tonus of smooth muscles and thus alleviate the voiding and storage symptoms of the lower urogenital tract.**
Objectives: **The goal of this study was to assess objectively the improvement of the voidings and storage difficulties in 72 randomly chosen patients suffering from Benign Prostatic Hyperplasia (BPH) prior to, and in the course of 15 months of treatment with this alpha$_{1-b}$locker in a dose of one capsule of tamsulosin daily after meal.**
Methods: **During the periode of three years (1997—1999), we have treated and studied 72 patients suffering from lower urinary tract symptoms (LUTS). The age of the patients ranged from 55 to 80 years with the median age of 71 years. The patients were examined physically, by laboratory methods, by ultrasonography (USG) and by uroflowmetry. Anamnestic data were justified by the application of the IPSS questionnaire and blood pressure tests (BP). The eventual volume of residual urine, as well as the condition of the kidneys were checked by USG. The Q_{max} values were measured by uroflowmetry prior to, and during treatment (0—3 weeks — 6 months). We have continued with this treatment even after 6 months, but we have discontinued the biochemical, haematological and urofowmetrical assessments. On the other hand, we have continued with quartely examinations of urine, digital rectal examinations (DRE), measuring of BP and IPSS evaluation. PSA was checked at least once a year. Our patients were checked in this way for 12 to 18 months (median of 15 months). One capsule of tamsulosin was administered daily after meal.**
Results: **The prostatoselective alpha$_1$-blocker tamsulosin is a well-tolerated medication applied in the treatment of BPH. We did not have to discontinue the treatment with any of the**

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Abstrakt

Červenákov I., Fillo J.:
Naše skúsenosti s liečbou benígnej prostatickej hyperplázie (BPH) tamsulosinom
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Pozadie problému: Alfa$_1$-blokátory znižujú napätie a uvoľňujú spazmus hladkého svalstva, a tým zlepšujú ťažkosti dolných močových ciest.
Cieľ sledovania: Cieľom štúdie bolo zistiť objektívne zlepšenie obštrukčných a iritačných ťažkostí u 72 náhodne vybraných pacientov s benígnou prostatickou hyperpláziou (BPH) pred liečbou a počas 15-mesačnej liečby alfa$_1$-blokátorom (tamsulosin 0,4 mg) jedna kapsula denne po jedle.
Metódy sledovania: Počas 3 rokov (1997—1999) sme sledovali a liečili 72 pacientov s BPH. Vek pacientov bol 55—80 rokov (medián 71 rokov). Pacientov sme fyzikálne, laboratórne, USG a uroflowmetricky vyšetrili. Anamnestické údaje sme objektivizovali IPSS dotazníkom a určením krvného tlaku (TK). Veľkosť a eventuálny reziduálny moč, ako aj stav obličiek sme kontrolovali USG vyšetrením. Ďalej sme sledovali Q_{max} uroflowmetrickými vyšetreniami pred liečbou a počas kontinuálnej liečby (0—3 týždne — 6 mesiacov). Tamsulosin sme podávali 1 kapsulu denne po jedle. 6 mesiacov sme pokračovali v liečbe, ale nerobili sme biochemické, hematologické vyšetrenia a uroflowmetriu. Pokračovali sme vo vyšetrení moču, digitálnom rektálnom vyšetrení (DRV), vyšetrení TK a hodnotení IPSS. PSA sme kontrolovali aspoň raz ročne. Takto sme sledovali pacientov 12—18 mesiacov (medián 15 mesiacov).
Výsledky: Alfa$_1$-prostatoselektívny blokátor tamsulosin je dobre tolerovaný liek pri BPH. Ani u jedného pacienta sme nemuseli prerušiť liečbu počas nášho sledovania. Rovnako dobre sa znáša v dávke jedna kapsula denne ráno alebo večer po jedle bez ortostatických poruchových symptómov. Kvalita života sa zlepšila o 3 symptómové jednotky, TK sa prakticky nezmenil, IPSS symptómový index pre BPH klesol o 6,8 skóre a Q_{max} sa

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patients during the 15 months of assessment. It is equally well tolerated at a dose of one capsule of tamsulosin daily, administered after the morning or evening meal without any orthostatic defect symptomatology. The quality of life has improved by three symptomatic units; the blood pressure remained practically unchanged, the IPSS score for BPH decreased by 6.8 score and the Qmax was upgraded from 10.1 ml/s to 14.9 ml/s. This finding remained practically unchanged during the 15 months of assessment and later.

Conclusion: **In the course of the recent years, the conservative treatment of BPH by phytotherapeutics but mainly by alpha$_1$-blockers have resulted in a considerable reduction of transurethral resections of the prostate (TURP), and of the transvesical "open" prostatectomy (PE open). This reduction down to 50 % can be observed nearly all over the world. The presence of alpha$_1$-a, alpha$_1$-b, alpha$_1$-d receptors in the lower urinary tract is a good prerequisite for successful treatment of voiding and storage symptoms. In the assessment of the effects of a 15-month continuous treatment by tamsulosin, we have registered a considerable improvement in the quality of life (QOL), an increase in the Q_{max}, and decrease in the IPSS score. The age of patients under or over 60 years as well as their weight did not play significant roles. We have not registered any interaction with other medications generally used by older patients.** ***(Ref. 30.)***

Key words: benign prostatic hyperplasia, therapy, alpha$_1$-blockers.

zvýšil z 10,1 ml/s na 14,9 ml/s. Tieto výsledky pretrvávali s nesignifikantnými odchýlkami 15 a viac mesiacov neprerušovanej liečby.

Závery: Za posledných niekoľko rokov, konzervatívna liečba BPH fytoterapeutikami, ale najmä alfa$_1$-blokátormi značne znížili počet transuretrálnych resekcií prostaty (TURP) a transvezikálnej „otvorenej" prostatektómie (PE open) takmer na celom svete až o 50 %. Prítomnosť receptorov alfa$_1$-a, alfa$_1$-b a alfa$_1$-d v dolnom urogenitálnom trakte dáva predpoklad na úspešnú liečbu obštrukčných a iritačných symptómových ťažkostí pri BPH. Pri sledovaní a kontinuálnej 15-mesačnej liečbe tamsulosinom sme zaznamenali značné zlepšenie kvality života, zvýšenie Q_{max} a pokles IPSS skóre. Vek pacienta (pod a nad 60 rokov), ako aj hmotnosť nie sú rozhodujúce. Interakciu s inými liekmi bežne používanými u starších pacientov sme nezaznamenali. *(Ref. 30.)*

Kľúčové slová: benígna prostatická hyperplázia, liečba, alfa$_1$-blokátory.

Benign prostatic hyperplasia (BPH) is a symptomatic ailment of the lower urinary tract. Lower urinary tract symptoms (LUTS) are present in the male population at higher age. According to Beery et al. (1984) they can be histologically detected in 8 % of males already in the fourth decade of their life (30—40 years) and in 90 % of the male population in their nineth decade (80—90 years of age). About 70 % of the male prostate is formed by the stroma and 30 % is of epithelial character. In BPH, the a ratio of stroma vs epithelial tissue increases and can reach a ratio of up to 5:1 (Horňák, 2000). The substantial part of the prostate consists of smooth muscle innervated predominately by the sympathetic nervous system. The presence of alpha$_1$-receptors was confirmed in the region of the trigonum vesicae and the bladder neck, as well as, in the proximal urethra, but especially in the smooth muscle of the prostate and its capsule. However, alpha$_1$-blockers were applied for the first time in hypertension cure (Balažovjech, 1999; Ruffolo et al., 1999), alpha$_1$-blockers decrease the tension and ease the smooth muscles tonus thus alleviating the voiding and storage of LUTS (Kliment, 1995; Djuvan, 1999).

Patients and methods

At our Department we have studied 72 randomly chosen patients suffering from LUTS. The age of the patients ranged from 55 to 80 years; median 71 years. Treatment and observation median 15 months (12—18). The patients were physically examined by abdominal and external examination, DRE and the BP were measured. The blood of each patient was checked haematologically by biochemical screening, oncomarkers were tested and serological examinations were carried out. In each patient USG of the kidneys, urinary bladder and prostate were carried out and the size as well as the density of the prostate were established. Qmax was measured uroflowmetrically and the anamnestic data were justified by the application of the IPSS questionaire. For the establishment of a more precise orthostatic tolerance, 32 pts were given one capsule of medication every day after the morning meal whereas the remaining patients were given one capsule after the evening meal. The prerequisites for the inclusion into the study were IPSS values above 14 score. The capability of the prostate more than 25 g, postmicturition residual volume of less than 120 ml, Q_{max} under 10.5 ml/s, blood creatinine under 150 mmol/l, negative oncomarkers, no urolithiasis and infection in the urinary tract and without surgical intervention on prostate and bladder in the past and a QOL index higher than 3 score. We have decided to check the pts as follows: a) Complete examination as described in the text. Treatment by tamsulosin. b) First control after 3 weeks — all examinations as at the beginning of the treatment (a) with the exception of the blood tests and c) Complete examination as described under a) at the beginning of the treatment and evaluation after 6 months of continuous medication with tamsulosin.

A: O, B: 3 weeks, C: 6 months, D: 15 months — no significant difference repeated results after 6 months.

Results

Time span: from January 1997 to December 1999. Number of patients (n): 72.

Age of patients: from 55 to 80 years (median 71 years). Aborted therapy: 0 patients.

Treatment and observation: median 15 months.

A: before onset of cure.

Quality of life (QOL): Mostly dissatisfactory

IPSS Score 19—25 (average 21).
Blood pressure (BP): 145/90±35/15
Q_{max}: average 10.1 ml/s;
B: 3 weeks after onset of cure.
Quality of life: mostly satisfactory
IPSS decreased by 5.7 score
Blood pressure: 145/90±30/10
Q_{max}: increased by +3.9 ml/s, average value 14.0 ml/s;
C: after 6 months of continuous therapy.
Quality of life: pleasing
IPSS: decreased by -6.8 score
Blood pressure 145/90±30/10
Q_{max}: increased +4.8 ml/s average total value 14.9 ml/s;
D: after 15 months of continuos therapy. No significant differences as compared with C were detected.

Patients tolerated the treatment without any problems. The dosage of one capsule of tamsulosin after the morning or evening meal was well tolerated without orthostatic defect symptomatology. The age and weight differences were of no significance. Immediately after the onset of tamsulosin treatment a rapid decrease of storage and voiding symptoms is registered and the quality in life improves.

Discussion

McClung et al. (2000), Frishman et al. (1999) claim that beside the relaxing effect on the smooth muscles of the lower urinary tract, alpha$_1$-blockers have a positive effect on the molecular metabolism, plasma lipids, and apoptosis of the prostatic cells. Based on the understanding of molecular and pharmacological differences in their activity, Hancock et al. (2000) proposed to differentiate alpha$_1$-blockers into subtypes. Subtype alpha$_1$-A as selective blockers affecting adrenoceptors in the prostate, alpha$_1$-B blockers affecting blood vessels and alpha$_1$-D blockers affecting the detrusor muscle. At the EAU congress in Stockholm, Hoffner (1999) stated, that according to the data published by WHO, due to phytotherapeutic medications but mainly due to the broad choice of alpha$_1$-blockers the conservative treatment of BPH has increased twofold within the last 9 years. In the USA by in 1998 50 % less TURPs were carried out in 1990.

Bush et al. (1999) state that in the period from 1989 to 1995 the number of performed TURP and PE open operations has decreased by 52 % in Great Britain. Breza et al. (2000) stated that TURP and PE open decreased in Slovakia. Brooks (1999) has assessed more than 1150 pts and this author has found, that there is practically no difference in the symptomatic difficulties of patients given the dose of 0.4 or 0.8 mg of tamsulosin. Lowe (1999) has studied the effectiveness of tamsulosin in patients below and over 65 years of age. No evident difference was registered in the two numerous groups of patients studied. According to Rolan (1999) tamsulosin is an alpha$_1$1-blocker with a clinically irrelevant vasodilatory effect, which does not interact with anticoagulatory medications. According to DeMey et al. (2000), Tewari et al. (1999), Michel et al. (1998) tamsulosin is a medication which does not cause orthostatic symptomatological difficulties even in patients older than 60 years. Marks et al. (2000) have established that 4—6 hours after the administration of a single capsule of tamsulosin, a signifficant improvement of the Q_{max} value by 3.7 ml/s takes place when compared with placebo. Goepel et al. (1999) and Naryan (1998) have not found any signifficant difference in the tolerance to tamsulosin administered in the morning or in the evening.

Conclusion

Due to fytotherapeutic medications and due to the broad choice of alpha$_1$-blockers, conservative treatment has replaced almost 50 % of surgical interventions in the treatment of BPH. The beneficial effect of medication is given by its potentially highest prostatoselectivity, its lowest daily dosage, high tolerance and the possibly lowest level of interaction side effects (Schulman et al., 1999; Lee, 2000; Horiuchi et al., 1999) with no overall negative impact on the sexual function (Hoffner et al., 1999). One capsule of tamsulosin daily causes a fast decrease in voiding and storage difficulties, and no relevant vasodilatation effect or adverse orthostatic symptoms were registered (Cooper et al., 1999; Maruenda et al., 1999). It is not necessary to test this medication. We did not have to discontinue the treatment in any of our 72 pts. Within a short period after the onset of treatment, tamsulosin causes an improvement of the Q_{max} value, as well as an improvement in the QOL.

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