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EFFECTIVENESS OF TAMSULOSIN HYDROCHLORIDE AND ITS MECHANISM IN IMPROVING NOCTURIA ASSOCIATED WITH LOWER URINARY TRACT SYMPTOMS/BENIGN PROSTATIC HYPERPLASIA

Hypothesis / aims of study

The incidence of benign prostatic hyperplasia (BPH) among elderly men is high. BPH involves lower urinary tract symptoms (LUTS), and these symptoms sometimes greatly reduce the patient's quality of life (QOL). The LUTS associated with BPH (LUTS/BPH) include storage symptoms as well as voiding symptoms; although the incidence of voiding symptoms is higher than that of storage symptoms. A previous epidemiological investigation revealed that nocturia was the most bothersome of the storage symptoms.

The main approaches for improving LUTS/BPH are the treatment of symptoms and improvement of the patient's QOL. Drug therapy, especially α_1-receptor blockers, is widely used as the first-line therapy.

We performed a prospective study on the effectiveness of tamsulosin hydrochloride (TAM) to improve the nocturia associated with LUTS/BPH. We evaluated the International Prostate Symptom Score (I-PSS) and frequency volume charts (FVCs) of the patients and discussed the mechanism by which TAM improves nocturia.

Study design, materials and methods

We selected LUTS/BPH patients with a mean nocturnal frequency of 2 or more times per day, as indicated by the FVC data for 3 days. Patients who had taken an α_1-receptor blocker in the previous 2 weeks and those with prostate cancer, inflammation of the prostate and the bladder, and with a lower urinary tract stone were excluded from the study. TAM was administered at a dosage of 0.2 mg/d for 8 weeks.

The FVC, I-PSS, QOL index, post-void residual, and uroflowmetry were determined before therapy and at 8 weeks after the TAM administration. On the basis of the FVCs of the patients, we divided them into 2 groups: a responder group that showed improved nocturnal frequency (1 or more times per day) and a non-responder group that showed no improvement (less than once a day). These 2 groups were then compared by statistical analysis via the Mann-Whitney *U* test and signed-rank test.

Results

160 LUTS/BPH patients were finally analyzed: The responder group, in which the nocturnal voiding frequency improved, finally comprised 97 patients, and the non-responder group, in which no improvement was observed, comprised 63 patients.

In the background data of the patients in the 2 groups, the values of nocturnal frequency and post-void residual were significantly higher in patients of the responder group than in those of the non-responder group. There was no significant difference between the 2 groups with regard to the other parameters.

Although there were no significant differences between the 2 groups with regard to the total I-PSS of the storage symptoms, voiding symptoms, and QOL score, after TAM administration, a significant improvement was observed in each of these parameters in both the groups. The I-PSS of both groups improved after TAM administration; however, in the non-responder group, the score for straining showed no significant improvement. No significant differences were observed between the 2 groups with regard to the other parameters.

The FVCs of the patients in the responder group revealed a significant increase in the hours of undisturbed sleep (HUS) and volume of urine in the first nocturnal voiding episode. The daytime frequency and the mean daytime urine volume per void for patients in both groups improved significantly after TAM administration. In the responder group, the 24-hour production decreased significantly after TAM administration. Further, the nocturnal urine volume and the nocturnal polyuria index also decreased significantly. Although there was no difference in the mean nocturnal urine volume per void between the groups, we observed that the mean daytime urine volume per void in the responder group increased significantly after TAM administration.The post-void residual of the responder group decreased significantly, and the maximum and mean urinary flow rates showed an improvement after TAM administration.

Interpretation of results

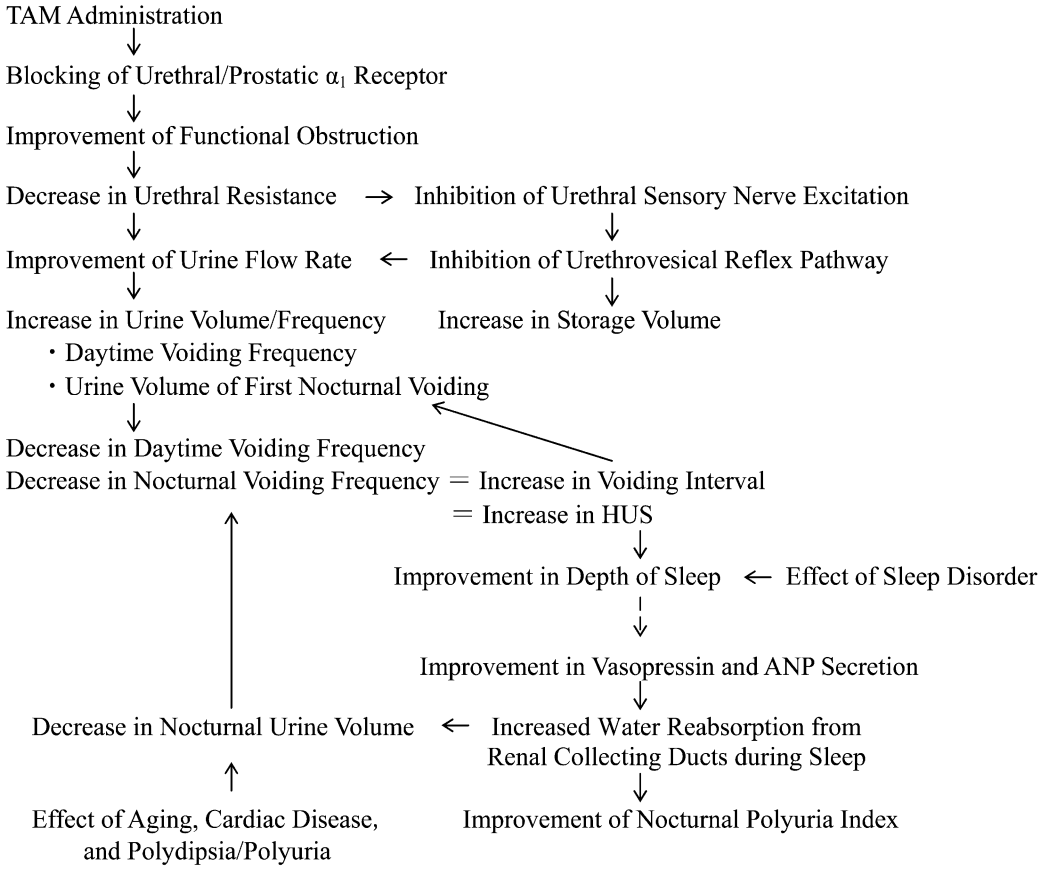
The mechanism by which TAM improves nocturia has not been elucidated yet. However, from a comparison of the data for both groups, the following mechanism was hypothesized (Figure). TAM improves functional obstruction and decreases urethral resistance by blocking the urethral/prostatic α_1 receptor, as indicated by the significant improvement in the urinary flow rates in the responder group. Further, it has recently been reported that in rats, TAM inhibits the excitation of the urethral sensory nerve by decreasing urethral resistance. Inhibition of the urethra-vesical reflex pathway may effect an increase in bladder compliance and contribute to the improvement of storage symptoms. An increase in functional voiding capacity combined with an improvement in the urinary flow rates could increase the mean urine volume per void, resulting in a decrease in the nocturnal and daytime frequencies.

A notable observation was that the nocturnal urine volume and the nocturnal polyuria index decreased significantly in the responder group, which probably contributed to the improvement of nocturia. Some studies suggest that a relationship exists between nocturnal polyuria and high blood pressure, disturbance of the circadian rhythm of arginine vasopressin, and atrial natriuretic peptide. In the case of the responder group in this study, it is speculated that the improvement of sleep quality might improve the circadian rhythm of hormone secretion. Such improvement in the endocrine milieu is thought to increase water reabsorption from the renal collecting ducts during sleep and lead to a decrease in the nocturnal urine volume.

Concluding message

TAM improves the bladder compliance by decreasing nocturnal urine volume, and thereby improves the QOL by reducing frequency and increasing HUS for patients suffering from nocturia associated LUTS / BPH.

Figure



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