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Akino H[1], Maekawa M[1], Nakai M[1], Shioyama R[1], Ishida H[1], Oyama N[1], Miwa Y[1], Yokoyama O[1]

1. University of Fukui

PREDICTIVE FACTORS FOR THE LONG-TERM RISK OF RE-TREATMENT AND PROSTATECTOMY IN PATIENTS USING TAMSULOSIN FOR LOWER URINARY TRACT SYMPTOMS

Hypothesis / aims of study
Alpha-adrenoceptor blockers are now the first-line treatment for patients with benign prostatic hyperplasia (BPH). Tamsulosin, one of the alpha-adrenoceptor blockers with high uroselectivity, has been widely used in Japan for approximately 10 years. However, clinical parameters leading to treatment failure of long-term tamsulosin use have not been studied. Determining these parameters should aid us in identifying the patients who will benefit from tamsulosin. In the present study, we investigated the clinical parameters influencing the long-term risk of re-treatment in patients using tamsulosin for lower urinary tract symptoms (LUTS) suggestive of BPH. The predictive parameters for BPH-related surgery were also investigated, as the decision to perform surgery was thought to be associated with the limit of the effect of relieving bladder outlet obstruction by alpha-adrenoceptor blockers.

Study design, materials and methods
We reviewed the medical files of 135 patients over 50 years of age with LUTS without any obvious pathology other than possible BPE, all of whom were treated at our hospital with tamsulosin between October 1995 and September 2000. The clinical data, including the duration of treatment by tamsulosin alone, additional treatment (use of other drugs or BPH-related surgery), and baseline parameters, e.g., prostate volume, maximum flow rate (Qmax), and voided volume (VV) at free uroflowmetry, post-void residual (PVR), and total score as well as the score for each symptom of the international prostate symptom score (IPSS), were collected in December 2003. All BPH-related surgery was transurethral or open prostatectomy. The re-treatment and prostatectomy percentages were calculated using the Kaplan-Meier method. Predictive value of each baseline parameters for these risks was evaluated with the log-rank test (univariate analysis) and the Cox proportional hazards model (multivariate analysis).

Results
Re-treatment was observed in 66 of the 135 patients studied, and consisted prostatectomy in 45 and use of other drugs in 21 patients. These drugs were propiveline (8), distigmine (6), and naphtopidil (7). The re-treatment and prostatectomy rates were 45.8% and 36.2% at 1 year, 61.3% and 50.1% at 3 years, and, 74.7% and 59.8% at 5 years of follow-up, respectively.
Univariate analysis: Re-treatment rate was found to be related to Qmax, VV, IPSS total score, and score of urgency and straining ($p < 0.05$). Prostatectomy was found to be related to prostate volume, Qmax, VV, IPSS total score, and score of urgency, slow stream, and straining ($p < 0.05$).
Multivariate analysis: Re-treatment and the prostatectomy rates for prostate volume, Qmax, VV, PVR, and IPSS total score, respectively, were evaluated while accounting for all other parameters. Predictive factors for re-treatment were VV of less than 100 ml and IPSS total score of 20 or more, and those for prostatectomy were a prostate volume of 30 ml or more and IPSS total score of 20 or more ($p < 0.05$). In patients with prostate volume of 30 ml or more, the prostatectomy rate increased over the entire period of follow-up.
Re-treatment and the prostatectomy rates for each IPSS symptom were evaluated while accounting for prostate volume, Qmax, VV, and PVR. Urgency, slow stream, and straining were found to be predictive parameters for re-treatment. When excluding patients who underwent prostatectomy from the patients analyzed, urgency was found to be the sole predicting parameter for re-treatment. As predictive parameters for prostatectomy, both slow stream and straining were significant ($p < 0.05$). Straining (score of 3 or more) was found to be associated with a rapid increase in the incidence of prostatectomy (89.9% in 3-year follow-up), whereas the absence and slight degree (score of 0 to 2) of slow stream were associated with a low incidence of prostatectomy (less than 30% over the follow-up duration).

Interpretation of results

Sever LUTS, poor uroflow, decreased voided volume, and an enlarged prostate increased the risk of re-treatment and/or prostatectomy. Urgency was found to be the predictive parameter for re-treatment, which seemed to indicate that the severe urgency could not be relieved enough by tamsulosin alone. Large prostate volume appears to be a substantial risk for prostatectomy, which could be explained by a mechanical prostatic obstruction that could not be relieved by tamsulosin. Voiding symptoms such as slow stream and straining was found to be closely related to the risk for prostatectomy, so we could consider these symptoms to be clinical indicators of the probability of prostatectomy.

Concluding message

Sever LUTS, poor uroflow, decreased voided volume, and enlarged prostate closely related to the risk of re-treatment and/or prostatectomy in BPH patients using tamsulosin. Some special symptoms in IPSS, i.e., urgency, slow stream, and straining, were also found to be associated with these risks. Patients with predictive parameters for these risks should be informed that treatment by tamsulosin alone may not be suitable, and that other treatment such as anti-cholinergic agent and BPH-related surgery will likely be necessary.