

DISCONTINUATION OF DRUG TREATMENT IN MEN WITH LOWER URINARY TRACT SYMPTOMS SUGGESTIVE OF BENIGN PROSTATIC HYPERPLASIA

Hypothesis / aims of study

Drug treatment, especially alpha 1-blockers has been considered a safe and effective first-line treatment option for lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH), or LUTS/BPH. However, treatment with alpha 1-blockers is limited when the treatment is not effective or when adverse reaction occurs, which may result in poor compliance or even discontinuation of the treatment. In fact, there may be not few patients who discontinue drug treatment because of the non-response to the treatment or the adverse reaction, or at patients' discretion. Because LUTS/BPH, uncommonly, causes acute urinary retention (AUR), discontinuation of drug treatment may promote the risk of AUR or the need for invasive therapy. However, the incidence of treatment interruption because of the non-response, adverse event, cure of LUTS/BPH symptoms and also the incidence of discontinuation at patients' discretion have remained unknown. Aims of this retrospective study were 1) to elucidate the discontinuation rate of drug treatment in patients with LUTS/BPH, 2) to investigate the predictors of patients who discontinue the treatment and 3) to evaluate the relationship between the discontinuation of drug treatment, AUR and prostate surgery.

Study design, materials and methods

A total of 1036 male patients (age; 70 ± 9.1 years old) newly diagnosed as having LUTS/BPH at our outpatient clinic during January 2004 to December 2005 were enrolled to this retrospective study. Inclusion criteria were patients who had evidence of LUTS/BPH with no proven infections, no neurogenic bladder disease or other obvious pathology. Patients younger than 45 years old and older than 85 years old were excluded. As a screening test, serum prostate-specific antigen (PSA) level was evaluated and the prostate volume was assessed by transabdominal ultrasonography. Patients were divided into 8 groups; 1) follow-up group who followed-up without drug treatment, 2) drug treatment group who continued to receive drug treatment, 3) surgery group who underwent prostate surgery during the study, 4) cure group who adjourned drug treatment by gaining cure or improvement of LUTS/BPH, 5) non-responder group who interrupted drug treatment because of the non-response to the treatment or deterioration of LUTS/BPH, 6) adverse reaction group who interrupted drug treatment because of adverse reaction, 7) discontinuation group who discontinued drug treatment at patients' discretion and 8) others (urethral strictures, interstitial cystitis and so on). Discontinuation was defined as interruption of drug treatment more than 4 months. Discontinued patients were not followed-up after discontinuation. The incidents of each group were retrospectively evaluated and the characteristics of each group were also investigated. Statistical analyses were undertaken using the non-parametric Mann-Whitney U-test, with $p < 0.05$ considered to indicate statistical significance.

Results

1) Of the 1036 patients, 66 (6.4%) followed-up regularly without pharmacological treatment and other 970 received pharmacological treatment, mainly with alpha 1-blocker (0.2 mg tamsulosin or 75-50 mg naftopidil). Among the 970 patients who chose drug treatment first, 96 patients underwent prostate surgery for LUTS/BPH (9.9%; transurethral resection of the prostate in 85 patients, suprapubic prostatectomy in 8 and transurethral ethanol injection for prostatic obstruction in 3). Internal urethrotomy for urethral stricture was done in 8 patients and hydrodistention of the bladder for interstitial cystitis in 3. During this study, 340 cases of the patients who chose drug treatment first (35.1%) discontinued the treatment. The reasons of discontinuation were cure or improvement of LUTS/BPH by drug treatment in 83 (24.4%), non-response to the treatment or deterioration of LUTS/BPH in 30 (8.8%), adverse reaction in 26 (7.6%) and at patients' discretion in 201 (59.1%).

2) Table shows the mean age, serum PSA level and prostate volume of each group. The mean PSA level and prostate volume in surgery group were statistically higher than those in other groups, respectively. The mean age, PSA level and prostate volume in discontinuation group were significantly lower than those in drug treatment group, respectively. The mean age, PSA level and prostate volume in cure group were also significantly lower than those in drug treatment group, respectively. There were no significant difference in age, PSA and prostate volume between discontinuation group and cure group.

3) AUR occurred in 11 patients during the study (1.1%; followed-up group in 0 patient, cure group in 0, non-responder group in 1 and discontinuation group in 1). In our study, there was no significant difference in PSA level and prostate volume between the patients who suffered AUR and those who did not (PSA (ng/ml) $p = 0.0991$; 2.8 ± 1.6 v.s. 2.3 ± 2.6 , prostate volume (ml) $p = 0.259$; 28 ± 9 v.s. 26 ± 16 , respectively).

Interpretation of results

Our data demonstrated that the probability of both discontinuation of drug treatment at patients' discretion and interruption due to cure may be high in patients who are younger, who have lower PSA level and who have small prostate volume. Misdiagnosis and placebo effect should be considered in those patients. However, discontinuation at patients' discretion and interruption due to cure would not cause AUR and prostate surgery, because the risk of AUR and the need for prostate surgery are generally attributed to the serum PSA level and prostate size in patients with LUTS/BPH.

Concluding message

Our result demonstrated that more than 90% of patients newly diagnosed as LUTS/BPH received pharmacological treatment and a third of them discontinued the treatment. Discontinuation at patients' discretion and interruption due to cure may be more frequent among younger persons, lower PSA level and smaller prostate size. Whereas discontinuation at patients' discretion and interruption due to cure are not rare, those events would not cause AUR and prostate surgery. Whereas the non-response to alpha 1-blocker and the adverse reaction of alpha 1-blocker

uncommonly, 5.8% in our study, limit the drug treatment, just for those cases a careful follow-up should be necessary after discontinuation.

Table

Plus-minus values are means±SD.

| | Follow-up | Drug treatment | Surgery | Cure | Non-responders | Adverse reactions | Discontinuation at patients' discretion |
|----------------------|-----------|----------------|----------|----------|----------------|-------------------|---|
| n (%) | 66 (6.4) | 521 (50.3) | 96 (9.3) | 83 (8.0) | 30 (2.9) | 26 (2.5) | 201 (19.4) |
| Age (yr) | 69±9.8 | 71±8.7 | 73±6.8 | 65±9.2 | 69±8.8 | 72±7.2 | 67±9.8 |
| PSA (ng/ml) | 2.1±1.9 | 2.2±2.1 | 5.1±4.9 | 1.4±1.4 | 1.4±2.2 | 2.7±3.7 | 1.7±1.8 |
| Prostate volume (ml) | 23±10 | 26±14 | 50±17 | 21±13 | 24±15 | 23±9.1 | 21±11 |

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DISCLOSURES: NONE

HUMAN SUBJECTS: This study did not need ethical approval because this study was retrospective and no appropriate ethics committee approval was there in our hospital but followed the Declaration of Helsinki Informed consent was not obtained from the patients.