

A PROSPECTIVE, SIX-YEAR FOLLOWUP OF SILODOSIN MONOTHERAPY FOR THE TREATMENT OF LUTS/BPH: WHAT ARE THE FACTORS FOR CONTINUATION OR WITHDRAWAL?

Hypothesis / aims of study

The efficacy and safety of silodosin, a relatively new Alpha1A-adrenoceptor (AR) selective antagonist, was reported in randomized, double-blind, placebo-controlled Phase III studies performed in Japan, the United States and Europe, silodosin has been shown to be significantly more effective than placebo in improving storage, voiding, and quality of life (QOL) subscores [1-3]. Similarly, silodosin was more effective than placebo in improving Qmax. Although alpha1-AR antagonists (alpha1-blockers) have been reported to be effective, there is a relative paucity of long-term data on the maintenance of this drug. A high drop-out rate has been reported in the previous long-term followup study of alpha1-blockers. However, the reason of the withdrawal has not been fully investigated. The objective of the present study is to prospectively evaluate the long-term efficacy of silodosin for the treatment of male LUTS/BPH for more than six years.

Study design, materials and methods

The inclusion criteria were: 1) a total IPSS of 8 or more, 2) Qmax of 15 mL per second or less as evaluated by uroflowmetry, and 3) prostate volume (PV) of 15 mL or more as measured by ultrasonography. Silodosin with a daily dose of 8 mg (4 mg b.i.d.) was administered. The IPSS and QOL index were determined. Free urinary flow rate and post-void residual urine volume (PVR; mL) were evaluated at the end of the observation period and after the therapy. These parameters were compared at baseline and at 1 mo, 3 mo, 6 mo, 12 mo, 24 mo, 36 mo, 48 mo, 52 mo, 60 mo, and 72 mo after the treatment.

Results

A total of 104 male patients with LUTS/BPH, aged 71.5±8.2 years old, were enrolled. Adverse events (grade I) were 22 events in 14 patients (13.5%). Most frequent adverse event was abnormal ejaculation in 6 (5.8%), followed by dizziness in 4 (3.8%), thirst in 4 (3.8%), diarrhea or loose stool in 3 (2.9%), skin rash in 2 (1.9%), and then nasal congestion, abnormal liver function and decreased serum platelet in 1 patient each (grade I). However, the number of adverse events in patients who discontinued treatment was 11 (10.6%).

Withdrawal was noted in 5 patients (4.8%) after the initial treatment, 5 (4.8%) after 1-2 mo, 17 (16.3%) after 3-5 mo, 8 (7.7%) after 6-8 mo, one after 9-11 mo, 16 (15.3%) after 12-23 mo, nine (8.7%) after 24-35 mo, 10 (9.6%) after 36-47 mo, two (1.9%) after 48-59 mo, and 5 patients (4.8%) after 60-72 mo. Overall, 78 patients (75.0%) had withdrawn at 72 months of treatment. Baseline PV and serum PSA level were 44.1±23.9 mL and 3.4±3.6 ng/mL, respectively. PV did not change significantly up to 60 months (45.5±22.8mL at 12mo, 44.3±22.1mL at 24mo, 42.9±22.0mL at 36mo, 45.2±18.8mL at 48mo, and 45.2±22.4mL at 60mo). The reasons for withdrawals were; lost to followup for unknown reasons in 27 patients (26.0%), side effects in 9 patients (8.7%), insufficient or unsatisfactory efficacies in 31 patients (30.0%), satisfied with the current condition and wished no further treatments in 6 (5.8%), and other reasons in 5. In 31 patients who withdrew because of insufficient or unsatisfactory effects, surgery was performed in 21 patients (surgery group; 20.2%). Therefore 26 patients (25.0%) were still on silodosin monotherapy (continuing group). The baseline total IPSS as well as total voiding and storage subscores and the post-micturition score did not differ between the continuing group and the surgery group, but baseline QOL index was significantly lower in the continuing group than in the surgery group.

Baseline PV was significantly smaller in the continuing group than in the surgery group ($p=0.016$). PV at 12 months (76.5±34.9 mL) did not increase significantly compared with the baseline value (69.7±32.4 mL) in the surgery group ($n=9$, $P=0.129$): PV was increased in 4 patients at the time of surgery compared with the baseline levels (56→88 mL, 94→116 mL, 33→59 mL, 33→57 mL), and did not change in 5 patients.

In patients who were taking silodosin monotherapy, the mean total IPSS, the total storage symptom subscores, the total voiding symptom subscores, the post-micturition score, and the QOL score decreased significantly (all $p<0.0001$) at 1 month after the treatment initiation and remained stable (significantly improved) up to 72 months. Qmax increased significantly ($p<0.0001$) and PVR decreased significantly ($p<0.001$) at one month after the therapy, and these changes were sustained for up to 72 months.

Interpretation of results

The most common reasons for withdrawal during 6-year followup were unknown (26%), insufficient efficacy (29%) and side effects (9%). Four patients (19%) with large prostate (PV of 56-113.5 mL) underwent surgery due to acute urinary retention. Therefore, a patient with large prostate (probably more than 55 mL) might be considered for adding dutasteride or surgery from the initiation of treatment. In the present study, adverse events were noted in 21%, including 10.6% of patients who withdrew. The withdrawal due to side effects may occur within 3 months in most of the patients.

Concluding message

At 72 months after silodosin monotherapy, the withdrawal rate was 75% in patients with LUTS/BPH. The characteristics of patients with stable condition up to 72 months seem to be relatively small baseline PV, low PSA, and low QOL index (mean, <4.1), but age, baseline IPSS, Qmax, and PVR did not seem to be related. Effects of silodosin for LUTS were immediate (within one month) and these effects were stable up to 72 months if patients continue treatment.

Table. Baseline characteristics of patients who were taking silodosin for more than 72 months (continuing group), patients who withdrew because of insufficient effects and underwent surgery (surgery group), and patients who withdrew because of insufficient effects and dutasteride was added (dutasteride group)

	Age (yrs)	PV (mL) ^d	PSA (ng/mL)	IPSS	QOL index (mL/sec)	Qmax (mL)	PVR
Continuing group ^a (n=26)	69.5±6.3	42.3±22.7	2.5±2.5	18.0±6.6	4.0±1.1	7.7±3.4	196.3±137.9
Withdrawal group							
Surgery group ^b (n=21)	70.4±6.0	62.2±30.7*	4.5±3.2*	19.6±6.7	5.4±0.8*	6.4±2.7	132.1±106.8
Dutasteride group ^c (n=6)	79.0±7.3	44.6±22.7	3.5±2.8	21.4±12.7	5.4±0.9	9.3±2.5	82.7±47.3

^apatients who were taking silodosin for more than 72 months

^bpatients who withdrew because of insufficient effects and underwent surgery

^cpatients who withdrew because of insufficient effects and dutasteride was added

^dPV=prostatic volume

*P<0.05

References

1. Int J Urol 2008;15: 193–9.
2. BJU Int 2006; 98:1019-24
3. J Urol 2013;189 (1 Suppl):S122-8

Disclosures

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