Multichannel impedance monitoring for evaluation of alpha-adrenoblocker effect on the ureteral function in patients with stone disease

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Abstract. The study of distal ureter function was carried out on patients with stones in the upper urinary tract, who underwent ureteroscopy and lithotripsy procedures. The parameters of ureteral peristalsis such as peristalsis amplitude, peristalsis rate, ureteral wall tone, contractile wave duration, and its direction obtained by multichannel impedance ureterography were assessed and compared from two groups of patients. The group I patients received tamsulosin in addition to standard regimen, while the group II patients matched according to the stone size and location were managed without tamsulosin medical therapy. In comparison with group II, the group I patients demonstrated smaller average peristalsis amplitude (0.60±0.08 vs 0.81±0.06 Ohm), shorter contractions (7.1±0.3 vs 7.7±0.3 s), greater peristalsis rate (3.3±0.3 vs 2.8±0.2 per minute), and diminished ureteral tone (4.0±0.5 vs 4.7±0.2 Ohm$^{-1}$). Incidence of the retrograde contractile waves was two-fold greater in the group II, while normal antegrade regular contractions were 30% more frequent in the group I. In addition, our results showed that the effect of tamsulosin on ureteral function was manifested in the patients with different stone size and location in the upper urinary tract, and it depended pronouncedly on individual ureteral tone and contractility parameters.

1. Introduction
Alpha-1 adrenoblocking agents are increasingly used in the treatment of distal ureteral stones. Their beneficial effects include promoting spontaneous stone passage, shortening of the stone expulsion time, and analgesia [1, 2, 3]. These effects are explained by ability of these agents to block specific receptors situated mainly in the distal ureter resulting in moderation of ureteral contractility [2] and by relaxation of smooth muscles in the ureteral wall [4]. However, stone disease management with tamsulosin is characterized with varying rate of success [1-4]. The stone size and location are considered as the most important factors in stone passage [4], while little objective data is available on the ureteral function after alpha-blocker treatment in clinical trials. In our previous studies, the peristalsis of ureter in patients with upper urinary tract stones evaluated by multichannel impedance monitoring significantly differed from the peristalsis of stone-free ureter. We distinguished four types of peristaltic disorders based on quantitative (amplitude and tone) as well as qualitative (shape and direction of the waves) attributes. Those data allowed us to suppose that tamsulosin effect would depend on initially different ureteral conditions in individual patients.

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The purpose of this study was to evaluate the peculiarities of ureteral function in patients with stones in the upper urinary tract after alpha-blocking treatment with tamsulosin.

2. Material and methods

The study of distal ureter peristaltic function was carried out on patients with stones in kidney and proximal (n=24) or distal (n=14) ureter, who were subjected to ureteroscopy and lithotripsy procedures. Patients were divided into two groups: the “tamsulosin” group I patients (n=15) treated with tamsulosin (0.4 mg daily) in addition to the standard regimen, and the control group II patients managed without tamsulosin matched according to the stone size and location (n=25).

Ureteral function was assessed by multichannel impedance ureterography with the help of special probe inserted into ureter coupled with RPKA2-01 impedance converter. The following parameters were evaluated: the peristalsis amplitude and rate, ureteral wall tone, and the number of contractile wave characteristics including velocity, duration, shape, and direction of their propagation in the ureter. The measurements of the renal pelvic pressure (RPP) were made electromanometrically in patients with indwelled nephrostomy tube.

3. Results

The average data on peristaltic function after tamsulosin treatment in patients with stone disease compared to the controls are shown in table 1. The average magnitude of peristalsis amplitude was higher by 0.22±0.10 Ohm (27%, p<0.02) in patients treated with tamsulosin compared to the control group. In the group I (tamsulosin), the following trends were observed: contractions were shorter (by 9%, p<0.1), frequency was greater (by 18%, p<0.1), and the wall tone was smaller (by 14%, p<0.5) compared to the group II. The retrograde contractile waves occurred twice more often in the control group, while the normal antegrade regular contractions were more frequently observed in the tamsulosin group (by 30%). The contractile wave velocity of antegrade ureteral contractions did not differ.

Table 1. Effect of tamsulosin on the parameters of ureteral function in stone disease patients.

| Parameter                        | Tamsulosin group | Control group |
|----------------------------------|------------------|--------------|
| Amplitude (Ohm)                  | 0.81±0.06        | 0.60±0.08    |
| Contractile wave velocity (cm/s) | 1.83±0.30        | 2.12±0.06    |
| Contraction rate (min^-1)        | 2.81±0.18        | 3.32±0.28    |
| Contractile wave duration (s)    | 7.75±0.26        | 7.09±0.26    |
| Ureteral wall tone (Ohm^-1)      | 4.66±0.25        | 4.00±0.54    |

These peristalsis changes in distal ureter were evaluated together with RPP, which is an important urodynamic parameter characterizing the upper urinary tract. Initially, the average mean values of RPP were elevated in patients with stone disease compared to its normal values (10 cm H2O) reported in literature [5]. In patients treated with tamsulosin, the average RPP values were smaller by 15-28% compared to that in the control group (table 2). These data can be an indicator of improved urine transport along the ureter in patients of the “tamsulosin” group I, because diuresis via the nephrostomy tube was similar in both groups (1.1±0.1 and 0.9±0.1 ml/min).

The obtained average results agree with literature on the mechanisms of alpha-blocker effects including ureter spasm relief and decrement of the contractile amplitude [2, 4]. These factors are proved to be important to promote successful stone passage down the ureter. Another factors postulated as significant for stone elimination are the stone size and location [4]. As the stone size was similar in both groups for proximal (1.14±0.17 vs 0.93±0.15 cm) and distal (1.02±0.16 vs 0.93±0.11...
cm) stones, we analyzed whether there was an interrelation between the ureteral function and stone location.

### Table 2. Effect of tamsulosin on pressure in renal pelvis in stone disease patients.

|                     | RPP in supine position | RPP in standing position |
|---------------------|------------------------|--------------------------|
|                     | Basal                  | Peristaltic              | Basal                  | Peristaltic              |
| Tamsulosin group    | 13.18±0.64             | 16.57±0.82               | 19.71±1.06             | 24.05±1.08               |
| Control group       | 16.09±0.53             | 19.54±0.57               | 27.20±0.63             | 30.70±0.65               |

3.1. Tamsulosin effects on ureteral peristalsis in patients with various stone location

In patients with stones located in the proximal region of upper urinary tract, there were no significant differences in parameters of ureteral peristalsis between the examined groups except the lower peristalsis amplitude (by 38%, p<0.02) in patients receiving tamsulosin medication. Similar, there was no intergroup difference in renal pelvis pressure.

In the patients with distal stones, no differences were found between the parameters of peristalsis in both groups except RPP, which was significantly lower in the patients of group I (tamsulosin) demonstrating smaller basal and peristaltic pressure components, respectively by 47% and 39% (p<0.01).

### Table 3. Effect of tamsulosin on the functional parameters of ureter and renal pelvis in patients with various stone locations.

|                     | Peristalsis amplitude (Ohm) | Ureteral wall tone (Ohm⁻¹) | Pressure in renal pelvis (cm H₂O) |
|---------------------|-----------------------------|---------------------------|----------------------------------|
|                     | Basal                       | Peristaltic               | Basal                            | Peristaltic               |
| Proximal stones     |                             |                           |                                  |
| Tamsulosin group    | 0.62±0.13                   | 3.86±0.87                 | 14.59±0.87                       | 17.71±1.23               |
| Control group       | 0.99±0.09                   | 3.92±0.25                 | 14.18±0.58                       | 17.43±0.52               |
| Distal stones       |                             |                           |                                  |
| Tamsulosin group    | 0.55±0.19                   | 6.16±2.16                 | 10.0±1.55                        | 14.00±2.23               |
| Control group       | 0.39±0.04                   | 6.1±1.00                  | 18.95±1.71                       | 23.06±2.07               |

Thus, tamsulosin effect on the upper urinary tract urodynamics depended on the stone location. We can hypothesise that renal and proximal ureteral stones can evoke reflex irritation of the excitatory adrenergic fibers in distal ureter that stimulate its contractions and increase the wall tone; therefore, tamsulosin can moderate ureteral function by blocking alpha-adrenergic receptors. Elevated RPP in patients with proximal stones in the upper urinary tract is urodynamic in nature, i.e. it predominantly results from obstruction with a stone hindering urine outflow from kidney. In the case of distal stones, irritation of distal ureter via adrenergic excitatory mechanism can induce reflex elevation of pressure in the kidney; therefore, tamsulosin can induce reduction in RPP by blocking the specific receptors.

3.2. Individual peculiarities of ureteral peristalsis in tamsulosin-treated patients

In both examined groups, there were patients with aberrant peristalsis in distal ureter characterized by very weak chaotic waves (figure 1, A). The tone of ureteral wall in distal ureteral region was high both in the control (6.40±1.64 Ohm⁻¹) and in the tamsulosin (6.96±1.34 Ohm⁻¹) groups. There were no significant differences between other parameters of ureteral peristalsis in both groups and in the values of pressure in renal pelvis (17.59±2.87 vs 17.90±1.79 cm H₂O). We suppose that such aberrant peristalsis can result from previous general inflammatory and fibrotic changes in ureteral wall that cannot be modulated by autonomic neural influences, and therefore would not be affected by
Tamsulosin. These ureters do not actively participate in urine transport, so they should be treated by creating unobstructed low-pressure urine passage.

In patients whose ureters demonstrated evident contractions and moderate ureteral wall tone with preserved antegrade waves (figure 1, B), tamsulosin modified urodynamics in the upper urinary tract. In such patients from the group I compared to group II, the peristalsis amplitude was smaller (0.97±0.25 vs 1.30±0.14 Ohm), the ureteral wall tone was lower (2.30±0.55 vs 3.60±0.56 Ohm-1), the contractions were shorter by 17% and faster by 52%, respectively. Measurements of RPP after tamsulosin treatment revealed significantly smaller values in standing position (13.50±0.69 vs 22.90±5.40 cm H2O) indicating the better urine drainage from the kidney.

**Figure 1.** Pattern of aberrant peristalsis (A) and pronounced contractile function of the ureter (B) in two patients with stone disease. The recording channels from 1 to 6 correspond to impedance measurements from the consecutive (proximal to distal) parts of ureter.

4. Summary

Evaluation of ureteral peristalsis by multichannel impedance monitoring is an important supplementary diagnostic tool both for clinical practice and for understanding the mechanisms of urodynamic disorders in patients with stone disease. Multichannel impedance ureterography yields quantitative and qualitative data on ureteral peristalsis and reveals its individual peculiarities in the patients. This method can be useful when choosing a medical treatment for individual patients, and it can predict the efficacy of treatment.

In the present study of tamsulosin effect on function of distal ureter in patients with stone disease, efficacy of alpha-adrenoblocker treatment can be achieved both for proximal and distal stones in the upper urinary tract, and it largely depends on individual ureter status. In patients with functional peristaltic disorders, especially with those provoked by increased adrenergic stimulation, tamsulosin treatment would be helpful in the terms of contractility normalization and ureteral wall relaxation. Pronounced organic changes in ureteral wall caused by previous inflammatory or fibrosis processes characterized by aberrant peristalsis can be responsible for medication inefficacy.

5. References

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