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The effectiveness of terazosin, an α1-blocker, on bladder neck obstruction as assessed by urodynamic hydraulic energy

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Objective To investigate the effectiveness of terazosin, an α1-adrenoceptor blocking agent, on bladder neck obstruction (BNO), by assessing the urodynamic hydraulic energy profile.

Patients, subjects and methods The study included 17 men (mean age 60.1 years, range 24–84), comprising 11 patients with BNO (mean age 66.5 years) and six normal volunteers (mean age 48.1 years). A five-transducer microtip catheter was used to measure the pressure in the bladder and at the bladder neck, and in the membranous and bulbous urethra during voiding. All the subjects then received terazosin, 1 mg/day orally for 2 weeks, and were re-assessed.

Results The bladder neck diameter at maximum flow significantly ($P<0.02$) increased in the 11 patients with BNO after treatment with terazosin. The relative hydraulic energy profiles before terazosin treatment showed the greatest hydraulic energy loss between the membranous and the bulbous urethra in the normal subjects, and between the bladder neck and the membranous urethra in the men with BNO. After terazosin treatment, the greatest energy loss was between the membranous and the bulbous urethra in men with BNO, similar to that in the normal controls, i.e. the whole profile of relative hydraulic energy became normal.

Conclusion Terazosin was effective in opening the bladder neck and improving the hydraulic energy profile in men with BNO.

Keywords Bladder neck obstruction, α-blocker, hydraulic energy, urodynamic study, microtip transducer catheter

Introduction

Bladder neck obstruction (BNO) is a cause of urinary disturbance that occurs by the narrowing or obstruction of the bladder neck during voiding [1]. The bladder neck is considered to be governed by the sympathetic system; the smooth muscle around the bladder neck is rich in α-receptors and, at least in the male, is richly innervated with noradrenaline-containing nerves [2]. Hedlund and Anderson [3] reported that prazosin, an α-blocker, was effective in treating BNO, but there have been few reports of the effects of α-blockers on BNO, and the effect has not been assessed by a full urodynamic study. Terazosin is a highly selective α1-blocker [4] and has been reported to be effective in treating the symptoms of BPH [5–8].

Rossier and Fam [9] and Schurch *et al.* [10] directly measured the bladder neck and detrusor pressure in patients with a neurogenic bladder, using video pressure-flow studies with a five-microtransducer catheter. With the same technique, Tojo *et al.* [11] studied the relationship between bladder neck diameter and hydraulic energy at maximum urinary flow rate (Q_{max}). They found that the greatest energy loss corresponding to a 'hydraulic jump', or 'elastic jump' [12] occurred between the membranous and the bulbous urethra in normal men, and between the bladder neck and the membranous urethra in men with BNO. They also reported that the 'flow rate controlling zone', so termed by Shäfer [13], lay at the membranous urethra in men with bladder neck diameters of $\geqslant 0.73$ cm and at the bladder neck in those with diameters of $\leqslant 0.60$ cm [11]. In the present study, BNO was defined as a symptomatic condition of BOO localized at the bladder neck on voiding cysto-urethrography (a bladder neck diameter of $\leqslant 0.6$ cm), with obstructed voiding values on pressure-flow study, and with no prostatic hypertrophy or nervous disorders causing any voiding dysfunction, as judged by neurological examinations. The aim of the study was to determine whether terazosin improved the opening of the bladder neck and influenced the urodynamic hydraulic energy profile in patients with BNO.

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Patients, subjects and methods

The study included 17 men (mean age 60.1 years, range 24–84) comprising 11 patients with BNO (mean age 66.5 years) and six normal volunteers (mean age 48.1 years). A prostate volume of <15 mL, as measured by TRUS, was defined as normal; the mean (SD, range) prostate volume in patients with BNO was 7.9 (3.0, 5–15) mL, their Q_{max} was 7.5 (3.8) mL/s and their detrusor pressure at Q_{max} was 88.3 (12.9) cmH_2O. All these patients had obstructed voiding values on a video-urodynamic study. Six volunteers with no LUTS (one doctor, two paramedical staff and three volunteers) were recruited exclusively for the study. In all men urine samples were cultured and any men with a UTI, e.g. cystitis, prostatitis or prostatodynia, were excluded. None of the men were receiving drugs that might affect voiding function (anticholinergics, other α-blockers, β-agonists or antagonists) during the study. Local ethical committee approval and written informed consent from each subject were obtained before entry into the study.

A video-urodynamic study was performed according to the methods reported by Rossier and Fam [9]. An 8 F, five-transducer microtip catheter (Millar Instruments Inc., Houston, TX) was inserted into the urethra of each subject while he was supine with 15° of pelvic rotation. The transducers were located 0.3 cm (no. 1), 4.3 cm (no. 2), 7.3 cm (no. 3 and 4) and 10.3 cm (no. 5) from the distal tip of the catheter, allowing the simultaneous measurement of pressures in the bladder neck and membranous urethra. A three-transducer catheter was inserted in the anus to measure the rectal pressure and anal sphincter pressure [9–11]. Both catheters were electrically connected to a polygraph system (RM 6000, Nihon Kohden, Japan) to simultaneously record intravesical pressure, pressures at the listed levels of the urethra, rectal pressure, EMG of the external urethral sphincter and the urinary flow rate. Radiocontrast solution (60% urographine) diluted with distilled water (1 : 5) was injected into the bladder through the five-transducer catheter until maximum desire to void; the pressure/flow study was then commenced.

The bladder neck region was defined as the most proximal portion of the urethra at which the recorded pressure exceeded the simultaneously measured bladder pressure during resting conditions. Its location was confirmed fluoroscopically. The membranous urethra, or external sphincter zone, was defined by the area corresponding to maximal urethral pressure during urethral profilometry. Its location was also confirmed fluoroscopically and its position almost invariably coincided with the membranous urethral region [14]. Under X-ray monitoring, transducers no. 3 and 4 were positioned at the level of the membranous urethra (external urethral sphincter zone). While a little urine was voided, voiding cysto-urethrography was carried out and transducers no. 3 and 4 adjusted so that they were just at the level of the external sphincter. Transducer no. 2 was positioned slightly downward away from the bladder neck and transducer no. 5 was placed at the level of the bulbous urethra. The five-transducer catheter was attached to the lower thigh with a tape. If dislodged by the urinary stream, the catheter was repositioned on an image intensifier and spot films taken to obtain a correction between simultaneous pressure measurements at various anatomical locations of the urethro-vesical complex [10]. The time delay between the pressure measurement in the urethra and that when the flow curve was recorded on the chart was 1.2 s and the results were corrected accordingly. The width of the bladder neck, as measured on voiding cysto-urethrography in each man at 15° of pelvic rotation, was regarded as the bladder neck diameter.

The hydraulic energy at the chosen levels of the urethra was calculated using Bernoulli's equation:

$$E = p/w + z + v^2/2\,\boldsymbol{g}$$

where p is the intraurethral flow pressure (cmH_2O), w is the density of water (g/cm^3), z is the elevation head (cm), v is the mean velocity of flow (cm/s), and $\boldsymbol{g}$ the acceleration of gravity (980 cm/s^2); E thus calculated represents energy per unit mass. The equation of continuity is Q = Av, where Q is urinary flow rate (mL/s) and A is the cross-sectional area of flow (cm^2). With the subject in the correct position, the difference in vertical level between the bladder and external meatus was negligible. Therefore, the formula can be expressed as:

$$E = \pi/w + v^2/2\,\boldsymbol{g}$$

The cross-sectional area of flow may be considered circular and is less than that of the urethra because of the indwelling 8 F (0.27 cm external diameter) catheter. The real cross-sectional area (A) should be expressed as:

$$p\ (d^2–0.27^2)/4$$

where d is the urethral diameter. As the flow may be regarded as steady at Q_{max}, the hydraulic energy at a level in the urethra at Q_{max} (E) can be calculated as:

$$E = p/w + [4\ Q_{max}/\pi\ (d^2–0.27^2)]^2/2\,\boldsymbol{g}$$

where p is the intraurethral pressure at the level in the urethra at Q_{max} and d is the urethral diameter at the same level in the urethra. The intravesical energy at Q_{max} (E_0) can be expressed as PQ_{max}/w, where PQ_{max} is the intravesical pressure at Q_{max}, because the value of $v^2/2\,\boldsymbol{g}$ is negligible [11].

All subjects were assessed and then received terazosin hydrochloride orally at a daily dose of 1 mg (0.5 mg twice) for 2 weeks. The effect on bladder neck opening was assessed using voiding cysto-urethrography and the changes in hydraulic energy profile.

There was no information before the study to determine the number of men required for statistical validity and thus we aimed to include at least 10 men per group, assuming that would be sufficient for a stable variance. The results were analysed using paired and unpaired Student's *t*-tests, as applicable, with values expressed as the mean (SD, range) and $P < 0.05$ taken to indicate significance.

Results

The bladder neck diameter at Q_{max} was 0.52 (0.07, 0.38–0.60) cm in the patients with BNO and 0.95 (0.17, 0.75–1.13) cm in the normal controls. After terazosin treatment the bladder neck diameter at Q_{max} was significantly higher ($P < 0.02$) in the 11 men with BNO, at 0.60 (0.10) cm, but in the six normal controls it was 0.97 (0.18) cm and did not increase significantly.

Transducers no. 3 and 4 were positioned at the membranous urethra and therefore transducer no. 2 was located 3.0 cm upstream, or slightly downstream from the bladder neck. The values given for the hydraulic energy at the bladder neck do not represent the actual values at that point, but for convenience, these values were expressed as such. Because the absolute value of hydraulic energy varies depending on the intraurethral pressure and urinary flow rate, the relative value of hydraulic energy (E/E_o, the ratio of hydraulic energy at the particular level of the urethra to the energy generated in the bladder) was calculated. The relative value of hydraulic energy at the membranous urethra (external urethral sphincter zone) at Q_{max} in the normal controls before and after terazosin treatment was 0.79 (0.11) and 0.74 (0.12), respectively; the corresponding values in the men with BNO were 0.58 (0.15) and 0.70 (0.18). The values were significantly ($P < 0.01$) higher in the normal controls than in the men with BNO before terazosin treatment and afterward it significantly ($P < 0.01$) increased in men with BNO to a level close to that in normal controls (Fig. 1). The relative hydraulic energy profiles before terazosin treatment showed the greatest hydraulic energy loss between the membranous and the bulbous urethra in the normal subjects, and between the bladder neck and the membranous urethra in those with BNO. After terazosin treatment, the greatest energy loss was between the membranous and bulbous urethra in men with BNO, similar to that in the normal controls. There were no adverse effects, e.g. orthostatic hypotension, headache or dizziness in any subject.

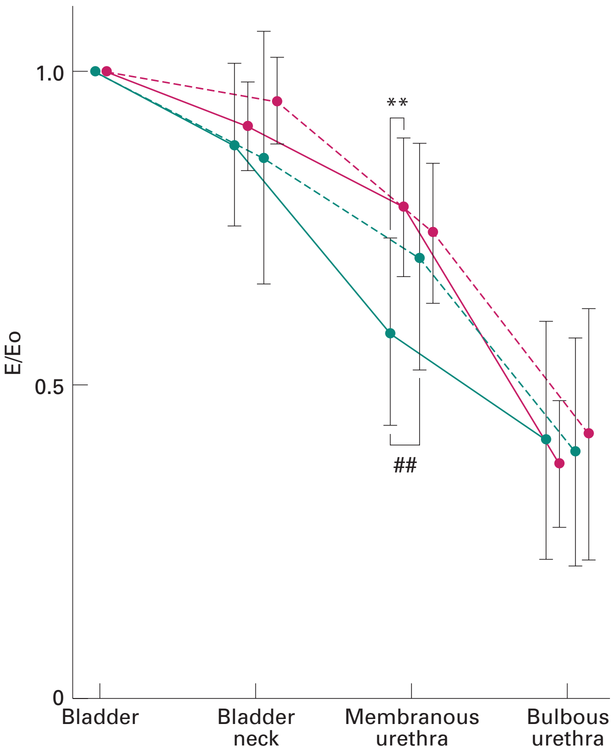

Fig. 1. The mean (SD) relative values of hydraulic energy at Q_{max} (E/E_0) in normal control subjects (red) and men with BNO (green) before (solid line) and after (dotted line) terazosin treatment. The E/E_0 at the level of the membranous urethra in those with BNO was significantly (**$P < 0.01$) lower than that in the normal control before terazosin. After terazosin, it was significantly (##$P < 0.01$) increased to a level close to that in normal controls.

Discussion

BNO has been considered an organic mechanical contracture [15] or a functional detrusor obstruction [16–18]. Urethral pressure profilometry and endoscopy have been used to diagnose the condition, but do not permit a definitive diagnosis [1,16,18–20]. Voiding urethral pressure profilometry [21] has been reported to be useful for diagnosing BNO. Turner-Warwick *et al.* [1,20] defined BNO as a urodynamically obstructive region at the level of the bladder neck, using a video-urodynamic study. In the present study, all patients with BNO fulfilled this definition.

α-Adrenoceptors have been reported to be predominantly present in the bladder base, posterior urethra and prostate [22,23]. Lepor *et al.* [4] reported that the affinity of the α-1 adrenoceptors in the bladder body, bladder base, prostate, and urethra are similar, and that the densities of α-1 adrenoceptors in the bladder base and prostate were statistically significantly greater than in the bladder body and urethra. α-Adrenoceptors abound in the internal sphincter and α-blockers have been reported to relax the internal sphincter or the bladder neck [24,25]. They have also been reported to reduce the urethral resistance and be effective in the treatment of voiding dysfunction in patients with BPH or a neurogenic bladder [26–29].

α-Blockers are reportedly effective in the opening the bladder neck; Cramer *et al.* [30] reported a reduction in urethral pressure and an increase in bladder neck diameter in a bladder-neck opening test using an intravenous α-blocker in patients with spinal cord injury. Kaneko *et al.* [19] reported that patients with BNO could be divided into two groups ('responders' and 'nonresponders') based on the response of urinary flow rate to phentolamine, and that the adrenergic nervous system of the bladder neck had an important effect on the response in 'responders'.

In the present study, LUTS were not assessed because the patients had normal control and were asymptomatic. However, terazosin improved the opening of the bladder neck; the relative hydraulic energy profiles in patients and controls indicated that the 'flow rate controlling zone' of Shäfer [13] lay at the membranous urethra in normal controls and at the bladder neck in those with BNO. After terazosin, the profile in the patients became more like that in the controls, i.e. the whole profile of relative hydraulic energy became normal.

Doses of 1–10 mg of terazosin have been recommended for the treatment of BPH in North American men [6]; however, from clinical results, in Japan the recommended dose is 1–2 mg. Perhaps such a dose-range difference arises from racial differences in body size; therefore, a daily dose of 1 mg was used in the present study. To verify the efficacy of terazosin in treating BNO, a randomized, placebo-controlled, double-blind study is necessary. However, a controlled study would be difficult to conduct because there are fewer patients with BNO than with BPH.

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