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ORIGINAL PAPER

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Ureterovesical junction inhibitory reflex and vesicoureteral junction excitatory reflex: description of two reflexes and their role in the ureteric antireflux mechanism

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Abstract The purpose of this study was to investigate the response of the ureterovesical junction (UVJ) to ureteric distension and to bladder filling with the aim of elucidating the mechanism of UVJ antireflux. The study was performed on 13 healthy volunteers [age 41.4 ± 10.2 (SD) years; nine men, four women]. A ureteric catheter connected to a pressure transducer was introduced into the ureter proper. After recording the ureteric pressure, the catheter was withdrawn to the bladder, and the resting pressures in the UVJ and bladder were registered. The catheter was positioned in the UVJ and a 3F balloon-tipped ureteric catheter was introduced into the ureter proper and filled with saline in increments of 1 ml. The pressure response of the ureter and UVJ to ureteric distension was recorded. The bladder was then filled with 400 ml saline at two rates, slow (10 ml/min) and rapid (150 ml/min), and UVJ pressure response was registered. The aforementioned tests were repeated after anesthetizing the UVJ, the bladder musculature surrounding the UVJ and the ureteric wall at the site of the ureteric distension, respectively.

Ureteric distension of the lower 2–3 cm effected ureteric pressure elevation ($P < 0.05$) and a UVJ pressure drop ($P < 0.05$); no pressure response of the UVJ occurred upon ureteric distension above this level. Slow bladder filling induced an increase in the UVJ ($P < 0.01$) and vesical ($P < 0.01$) pressures only when vesical filling reached a mean of 219.6 ± 79.4 ml and above. Upon rapid vesical filling, the pressure response occurred at a smaller volume (136.6 ± 52.3 ml). The pressure response did not occur when the UVJ was anesthetized.

The study showed that lower ureteric distension was associated with a UVJ pressure drop. This reflex relationship, which we call the "ureterovesical junction inhibitory reflex," was reproducible and disappeared on anesthetizing the UVJ or ureter. Vesical filling above a certain volume induced a UVJ pressure increase which was reproducible and disappeared on anesthetizing the UVJ; we call this reflex relationship the "vesicoureteral junction excitatory reflex." These two reflexes seem to regulate the entry of urine from the ureters to the bladder and prevent ureteric reflux during bladder filling.

In conclusion, two reflexes are identified that might contribute to the mechanism of UVJ antireflux.

Key words Ureter · Urinary bladder · Reflexes · Ureterovesical junction · Reflux

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Introduction

The ureterovesical junction (UVJ) plays an important role in preventing reflux of urine into the ureters during bladder filling and voiding. It is also the site that controls the entry of urine from the ureters into the urinary bladder. Tanagho and Hutch [7] and Tanagho et al. [8, 9] related the antireflux mechanism of the UVJ to the trigone. As the bladder fills the trigone is stretched and this increases the resistance at the intravesical ureter with firmer closure of the UVJ. During voiding, trigonal contraction seals the intravesical ureter against both reflux and efflux [7–9]. The interrelationship between the trigone and the intravesical ureter was demonstrated radiologically [9] and by electrical and pharmacologic stimulation of the trigone, resulting in increased resistance and degree of closure of the UVJ [10]. However, other investigators [3] deny the presence of active trigonal contraction and assume that the trigone only conforms to various changes in the underlying detrusor. The valvular mechanism has been put forward as an efficient way of allowing a free flow of urine across the UVJ [6].

In view of this controversy and the incomplete understanding of the antireflux mechanism of the UVJ, this study was initiated to investigate the response of the UVJ to ureteric distension and to bladder filling, with the aim of elucidating the precise antireflux mechanism. The study was approved by our Faculty Review Board.

Materials and methods

Subjects

The study was performed on 13 healthy volunteers, with a mean age of 41.4 ± 10.2 (SD) years (range 28–48 years). There were nine men and four women. They gave their written informed consent before entering the study. They had had no previous history of urinary troubles or at the time of presentation. Urinalysis and sonography of the urinary tract were normal. Physical examination, including neurologic assessment, was also normal.

Methods

With the subject lying supine, a 3F ureteral catheter with a side port was introduced into the ureter. A metallic clip was applied to the catheter end for the purpose of fluoroscopic control. The catheter was introduced into the ureter so that its tip lay in the ureter proper approximately at its middle. It was perfused with 37 °C sterile saline at a rate of 1.6 ml/min using a Harvard model 600.910/20 continuous perfusion pump and connected to a strain gauge pressure transducer (Statham 230B, Oxnard, CA, USA). Pressure measurements started with the gauge at zero level. The zero point was chosen at the level of the anterior abdominal wall and the gauge was kept at this level when later measurements were done. After measuring the pressure in the ureter, the catheter was withdrawn from the ureter to the urinary bladder using a mechanical device for automatic catheter withdrawal (9021H, Disa, Copenhagen). The pressure during withdrawal was recorded. The catheter positioning was under fluoroscopic control when it was found necessary.

After recording the resting pressures in the ureter, bladder and UVJ, the catheter was positioned in the UVJ, and a 3F balloon-tipped ureteric catheter was introduced into the ureter proper to lie above the UVJ. The balloon was 1/2 cm in diameter. It was connected to a Statham pressure transducer and filled with saline in increments of 1 ml. The balloon response to filling when it was not in the ureter (i.e., in air) showed no transient pressure rise similar to the one obtained when the balloon was filled in the ureter; this indicates that the response was ureteric and not from the balloon. The pressure response of the ureter and UVJ to ureteric distension by the balloon placed in the upper, middle and lower parts of the ureter was recorded. The balloon catheter was then withdrawn from the ureter to lie in the urinary bladder while the catheter at the UVJ was left in place. The bladder was filled with 400 ml saline at two rates, slow (10 ml/min) and rapid (150 ml/min), and the pressure response of the UVJ during vesical filling was recorded.

The part of the urinary bladder surrounding the UVJ was anesthetized. Through the cystoscope, 2–3 ml 2% xylocaine was injected into the bladder musculature; the needle was introduced 1–1.5 cm away from the ureteric orifice and injections made at multiple points in the bladder wall. The aforementioned tests of ureteric distension and slow and rapid bladder filling were performed after 10 min and 2 h when the anesthetic effect had waned. On another day, the test was repeated after injecting the intramural segment of the UVJ with 2–3 ml 2% xylocaine. The injections were performed in the UVJ at multiple points. The test was also performed after injecting the ureteric wall at the site of balloon distension with 2 ml 2% xylocaine to anesthetize the ureteric segment to be distended. Two to three milliliters of saline was injected into the periureteric musculature, UVJ and the ureter at the site of distension, respectively, and the aforementioned tests were repeated. These injections were done on separate days. After injection of xylocaine or saline, the response of the UVJ to ureteric distension and bladder filling was determined after 10 min and 2 h of injection. To ensure reproducibility of the results, the pressure measurements were repeated at least twice in the same subject and the mean value was taken.

Statistical analysis

The results of the study were analyzed statistically using Student's t-test. Values were taken to be significant at $P < 0.05$. Values are given as means ± standard deviation (SD).

Results

No complications were encountered during or after the tests. All the subjects completed the study and were evaluated. The mean resting (basal) pressure was 6.3 ± 2.2 cmH_2O (range 2–8 cmH_2O) in the ureter proper, 10.4 ± 2.1 cmH_2O (range 8–12 cmH_2O) in the UVJ and 8.2 ± 3.2 cmH_2O (range 6–14 cmH_2O) in the urinary bladder.

Response of the UVJ to ureteric and bladder distension

Upon ureteric distension with a 1 ml-filled balloon, the ureteric pressure increased to a mean of 18.4 ± 4.2 cm H_2O (range 14–26 cmH_2O, $P < 0.05$) while the UVJ pressure dropped to a mean of 4.3 ± 1.1 cmH_2O (range 3–7 cmH_2O, $P < 0.05$, Fig. 1). This pressure response of the UVJ occurred only upon distension of the lower 2–3 cm of the ureter proper: Ureteric distension above this level effected elevation of ureteric pressure (mean 17.9 ± 3.9 cmH_2O, range 13–24 cmH_2O, $P < 0.05$) but did not induce a pressure response of the UVJ.

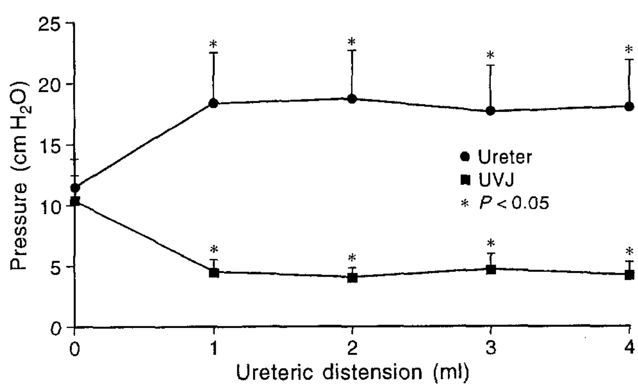

Fig. 1 Pressure response of the ureter and ureterovesical junction to ureteric distension

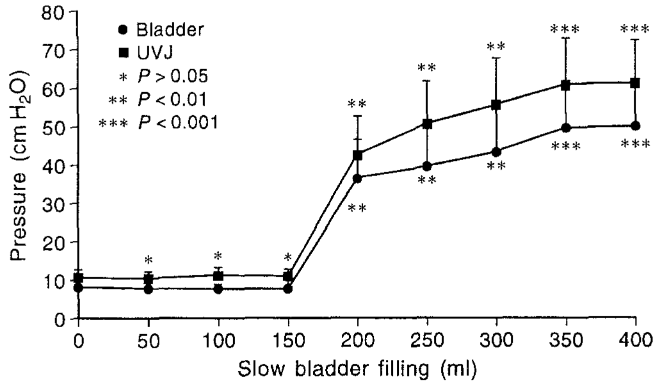

Fig. 2 Pressure response of the urinary bladder and ureterovesical junction to slow vesical filling

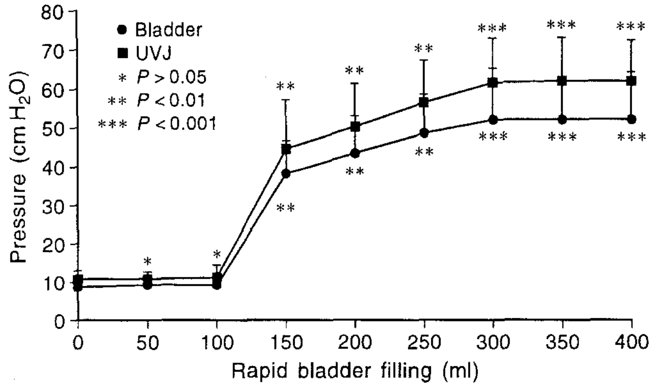

Fig. 3 Pressure response of the urinary bladder and ureterovesical junction to rapid vesical filling

The pressure response in the ureter and UVJ was momentary; it returned to the pre-distension level even when the balloon continued to distend the ureter. Ureteric distension with 2 and 3 ml effected the same ureteric pressure rise and UVJ pressure drop as that with 1 ml, with an insignificant difference ($P > 0.05$, Fig. 1).

Slow bladder filling with saline did not effect a pressure change in either the UVJ or the bladder until the instilled volume reached a mean of 219.6 ± 79.4 ml (range 190–260 ml) when the UVJ pressure rose to a mean of 42.8 ± 10.2 cmH_2O (range 36–55, $P < 0.01$) and the bladder pressure to a mean of 36.4 ± 10.2 cmH_2O (range 29–48, $P < 0.01$, Fig. 2). The UVJ and vesical pressures increased as the bladder instillation increased, to reach their maximum at an instillation volume of mean 358 ± 32.6 ml (range 312–419 ml) when the UVJ pressure registered a mean of 60.9 ± 12.4 cmH_2O (range 48–72 cmH_2O, $P < 0.001$) and the vesical pressure a mean of 49.6 ± 10.4 cmH_2O (range 32–54 cmH_2O, $P < 0.001$, Fig. 2). The vesical and UVJ pressures remained constant at this level even with continued bladder instillation ($P > 0.05$, Fig. 2) until the subject felt the urge to urinate and voided. The vesical pressure represented both the detrusor and abdominal pressures. The abdominal pressure was constant in all measurements; thus the vesical pressure increase was related to the detrusor.

Upon rapid saline instillation of the bladder, the UVJ and bladder pressures showed insignificant changes from the basal values ($P > 0.05$) until the instilled volume reached a mean of 136.6 ± 52.3 ml (range 108–186 ml), when the UVJ and vesical pressures increased, registering means of 44.6 ± 12.4 cmH_2O (range 38–59 cmH_2O, $P < 0.01$, Fig. 3) and 38.2 ± 8.2 cmH_2O (range 29–49 cmH_2O, $P < 0.01$), respectively. The UVJ and vesical pressures continued to rise as the instilled saline increased until they registered means of 61.4 ± 11.4 cmH_2O (range 52–74 cmH_2O, $P < 0.001$, Fig. 3) and 52.9 ± 12.3 cmH_2O (range 38–63 cmH_2O, $P < 0.001$), respectively, at 300 ml

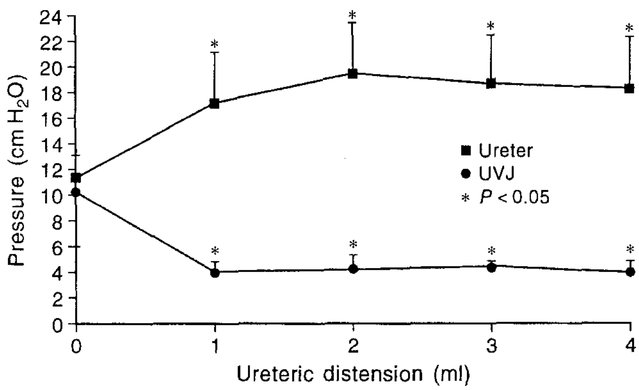

Fig. 4 Pressure response of the ureterovesical junction and ureter to ureteric distension 10 min after anesthetizing the periureteric bladder musculature

instillation. They showed an insignificant elevation with a further increase of the instilled volume ($P > 0.05$, Fig. 3) until the subjects felt the urge to urinate and voided.

Response of the UVJ to the anesthetized bladder or UVJ

When the periureteric bladder musculature was anesthetized and the ureter was distended or the bladder filled with saline, the UVJ after 10 min and 2 h of xylocaine injection showed a pressure response similar to that before injection (Figs. 4–6). The response of the anesthetized UVJ was different. The UVJ did not respond to ureteric or bladder distension after 10 min of injection while the ureteral and vesical pressures rose as mentioned above (Figs. 7–9); the UVJ response returned 2 h later when the anesthetic effect had waned. The UVJ did not respond to distension of the anesthetized ureteric segment. Saline injection of the UVJ, periureteric bladder musculature or the distended ureteric segment did not affect the UVJ pressure response to ureteric or vesical distension ($P > 0.05$).

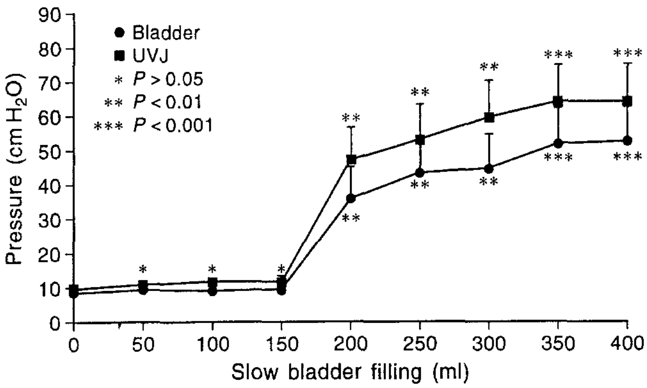

Fig. 5 Pressure response of the ureterovesical junction and urinary bladder to slow vesical filling 10 min after anesthetizing the periureteric bladder musculature

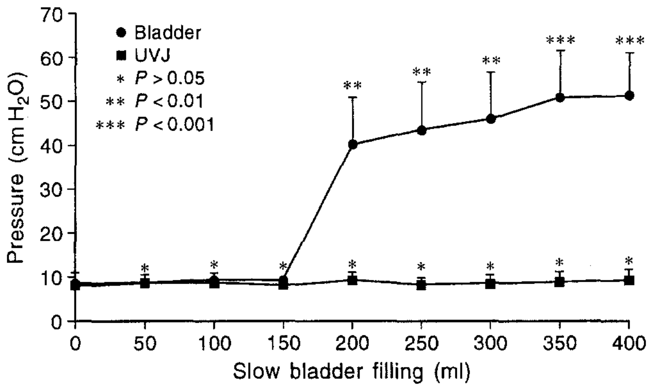

Fig. 8 Pressure response of the ureterovesical junction and bladder to slow vesical filling 10 min after anesthetizing the ureterovesical junction

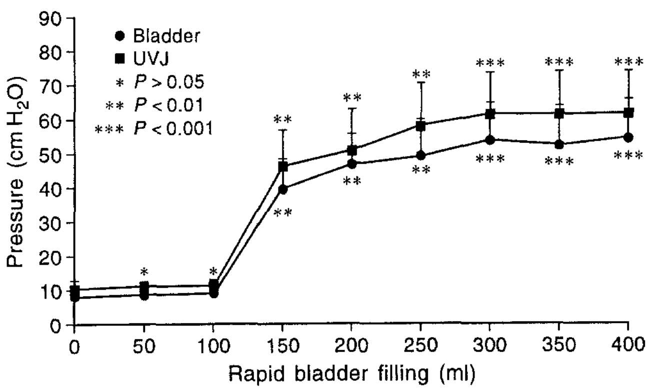

Fig. 6 Pressure response of the ureterovesical junction and urinary bladder to rapid vesical filling 10 min after anesthetizing the periureteric bladder musculature

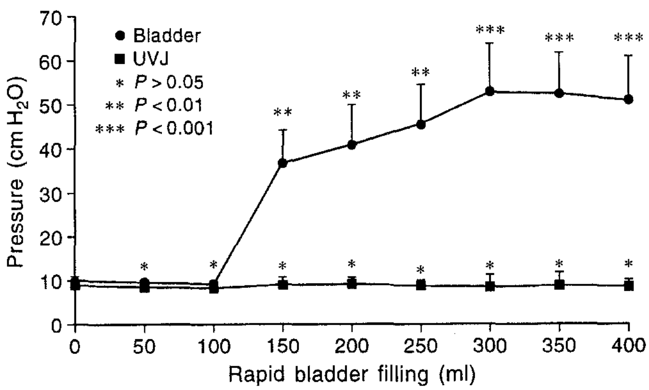

Fig. 9 Pressure response of the ureterovesical junction and bladder to rapid vesical filling 10 min after anesthetizing the ureterovesical junction

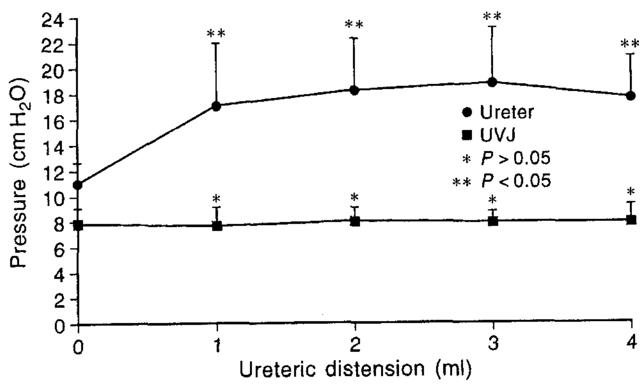

Fig. 7 Pressure response of the ureterovesical junction and ureter to ureteric distension 10 min after anesthetizing the ureterovesical junction

The aforementioned pressure measurements were reproducible with no significant difference ($P > 0.05$) when they were repeated in the same subject.

Discussion

The drop of the UVJ pressure upon distension of the lower part of the ureter proper as demonstrated in the current study postulates a reflex relationship between the two actions. The reproducibility of this reflex action as well as its absence upon anesthetizing the ureter at the distension site or the UVJ, which seem to represent both arms of the reflex, point to constancy of the reflex action. We call this reflex relationship the "ureterovesical junction inhibitory reflex" (UVJIR). It seems that this reflex facilitates the passage of a bolus of urine through the intravesical segment of the ureter into the bladder. The excreted urine drops are believed to accumulate momentarily above the UVJ until they reach a certain volume that evokes the UVJIR, which allows the bolus to pass to the bladder. This may explain the efflux of urine from the ureteric orifice in jets. Investigators assume that a urine bolus passes through the UVJ as a result of contraction of the musculature of the intravesical ureter, which becomes shortened and widened and reduces the resistance to passage of the bolus into the bladder [1]. This mechanism of passage of a urine bolus through the UVJ does not, however, contradict our results. It explains the anatomical mechanism by which the UVJ opens. The current study could demonstrate that this occurs through the UVJIR. The reflex seems to regulate the passage of urine from the ureter to the bladder. A disorder of this reflex action might disturb the mechanism of urine transport to the bladder.

The study also showed that ureteric distension by the balloon was associated with increased ureteric pressure, which might indicate ureteric contraction that is believed to assist in propelling the urine bolus down the ureter and through the UVJ. This is in accord with other investigators, who state that the ureter has peristaltic activity [2, 11]. However, the local pressure rise which occurs upon ureteric distension does not necessarily represent peristaltic ureteric contraction. It might be related to the viscoelastic properties of the ureter.

The study has demonstrated that the vesical and UVJ pressures increased during bladder filling only when the filling reached a certain volume. The vesical pressure during the early filling did not rise probably due to bladder adaptation to the increasing volume [5]. During this stage, the UVJ did not respond to vesical filling; the vesical pressure was still below the UVJ pressure and the possibility of reflux did not exist. Bladder filling above the aforementioned levels was associated with elevation of both the vesical and UVJ pressures. The latter was higher than the vesical pressure, thus preventing ureteric reflux. The increase of the UVJ pressure upon elevation of the vesical pressure postulates a reflex relationship. The constancy of this relationship was ascertained by reproducibility and its absence on anesthetizing the UVJ. We call this reflex relationship the "vesicoureteral junction excitatory reflex." It seems that this reflex is evoked when the vesical pressure increases to the degree that it endangers the UVJ competence. The UVJ closes and prevents reflux of urine from the urinary bladder. It may be argued that the rise in UVJ pressure parallel to the rise in the intravesical pressure does not necessarily indicate a reflex response but may represent a mechanical transmission of intravesical or detrusor pressure or a direct effect of detrusor muscle contraction. However, the rise in UVJ pressure does not seem to be due to mechanical transmission of the intravesical or detrusor pressure because the subjects in our series had no ureterovesical reflux. It is also highly probable that this pressure rise is not due to a direct effect of detrusor muscle contraction since the UVJ responded to the intravesical pressure rise after anesthetizing the part of the detrusor surrounding the UVJ.

Another point that needs discussion is that the pressure of the anesthetized UVJ was low while the intravesical pressure was high. It may be assumed in such a case that the urine runs back from the bladder into the ureter and the pressure in both equalizes. The explanation might be that this pressure equalization occurred some time after UVJ pressure measurement. Alternatively, there might be another mechanism that prevented such pressure equalization; this point needs further exploration.

Investigators [4] stated that the low pressure normally present in the resting bladder (8–15 mmHg) is sufficient to passively compress the roof of the intravesical ureter against the underlying detrusor to prevent reflux. We believe that the vesical pressure is too small to compress the UVJ and to prevent reflux especially when the bladder is full or contracting. Other investigators claimed that ureteric peristalsis is one of the defensive mechanisms that protects against reflux in humans [1]. However, there is no danger of vesicoureteral reflux at rest or during the early phase of vesical filling as the ureteric pressure pushing the urine bolus down the ureter is higher than the resting vesical pressure. In the late stages of vesical filling, the vesical pressure rises (29–48 cmH_2O) to above that of the contracting ureteric segment (14–26 cmH_2O) with a resulting risk of UVJ reflux. These high levels of vesical pressure evoke the vesicoureteric excitatory reflex that closes the UVJ and prevents reflux.

In conclusion, the study demonstrated that the UVJ reacts to ureteric and vesical distension by reflex relaxation or contraction, respectively. These reflex actions regulate the passage of urine through the UVJ and, at the same time, prevent UVJ reflux.

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