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Changes in the urine composition during its passage through the ureter. A concept of urothelial function

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Abstract Studies in our and other laboratories have negated the general assumption that the urothelium functions as a simple conduit and support the concept of a dynamic urothelium. Based on this concept, we investigated the hypothesis that urine undergoes changes during its passage in the ureter. Urine samples were separately collected from the renal pelvis and ureters of 23 volunteers (15 men, eight women, mean age 37.6 years) through cutaneous ureterostomy performed as a treatment for bladder cancer. The pH was determined using a pH electrode, osmolality by means of micro-osmometry and Na and K by flame photometry. The pH and osmolality of ureteric urine showed no significant differences from renal pelvic urine, whereas the Na and K levels of the ureteric urine were significantly increased (both $P < 0.05$). Gender and age differences were not significant. Renal pelvic urine undergoes changes in Na and K concentrations during its passage through the ureter. These findings presumably indicate that the ureteral urothelium is a functioning epithelium and that the renal pelvic and ureteric urine are not identical.

Keywords pH · Osmolality · Sodium · Potassium · Urothelium

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Introduction

It is generally assumed that the urothelium allows the urine to be stored without the reabsorption of urinary waste products [1, 2]. Hence, the composition of urine from the renal pelvis has been claimed to be identical with the voided urine [1, 2]. Studies have revealed, however, that the composition of urine changes during its transport through the urinary vessels, a finding ascribed by researchers to a modifying function of the urothelium [3–5]. The renal pelvis and ureteric urothelia have an absorptive function [3, 4, 6]. The values of pH, osmolality, and sodium and potassium concentrations obtained from vesical urine samples were shown to differ significantly from those obtained from urine in the renal pelvis [7]. This change in urine composition in the lower urinary tract supports the concept of a dynamic urothelium [7]. Based on this assumption, it is postulated that, as the composition of urine changes on its way through the urinary tract, urine sampled after voiding differs in composition from urine obtained from the bladder. A recent study [5] has determined that voided urine shows significant increases in pH, osmolality, and sodium and potassium concentration compared to urine contained in the bladder. In view of these results, we hypothesized that urine may also undergo changes during its passage through the ureter from the renal pelvis. This hypothesis is investigated in the current communication.

Materials and methods

Subjects

The subjects were recruited from patients who had undergone cystectomy and bilateral cutaneous ureterostomy as a treatment for bladder cancer at hospitals of the Cairo University Faculty of Medicine. Cystectomy and cutaneous ureterostomy were performed 4–8 years (mean 5.2 ± 1.2) prior to enrollment in the study. Study exclusion criteria included obstruction between the renal pelvis and urinary bladder or urinary tract infection. A total of 23 subjects (15 men and eight women, mean age 37.6 ± 10.2SD years, range 28–49) were enrolled. The subjects had a normal urinary tract, and the urine cultures were sterile. They gave informed consent and the study was approved by the Cairo University Faculty of Medicine Review Board and Ethics Committee.

Physical examination and neurologic assessment were normal. Laboratory work-up, including blood count, renal and hepatic function tests, and electrocardiography, was within normal limits. Serum creatinine ranged from 0.9–1.0 mg/dl. Renal pelvic and ureteric samples were collected from one ureter: the right in 13 subjects and left in ten; ureteric selection was random.

Methods

All subjects fasted for 8 h prior to testing and then were allowed free access to fluids. After 4 h, a 5-ml sample of renal pelvic urine was collected using a 6 F catheter introduced into the renal pelvis through the cutaneous ureterostomy. Catheter lubrication was not performed to avoid urine contamination. The catheter was then removed and another similar catheter was introduced into the ureter such that its tip lay at approximately 1 cm proximal to the cutaneous ureterostomy, and 5 ml of urine was collected. All samples were frozen in liquid nitrogen and stored at −70°C prior to analysis.

The renal pelvic and ureteric samples were thawed at room temperature and centrifuged separately. Urine pH was measured using a pH electrode which was pre-calibrated at pH 4 and 7. Urine osmolality was measured by an automatic micro-osmometer, and sodium and potassium concentrations by means of flame photometry.

Reproducibility was ensured by repeating the measurements at least twice for each subject, and the mean value was calculated. The results were analyzed statistically using the paired t-test. Values are given as the mean ± SD, and differences assumed significant at $P < 0.05$.

Results

All of the samples from the subjects studied were available for assessment. The values of urine pH, osmolality and sodium and potassium concentrations for the samples of urine obtained from the renal pelvis and ureter are shown in Table 1. The pH and osmolality of ureteric urine showed no significant differences from those of the renal pelvic urine. The pH of both urine sample types was within the normal physiologic range of 4.8–7.4. Higher alkalinity and osmolality were noted in men than in women and in the young than in the elderly, although the difference was not significant.

The Na and K of renal pelvic and ureteric urine were within the established normal reference ranges for random urine samples (25–200 mM for Na, and 12–80 mM for K). However, the ureteric urine exhibited a significant increase in the Na and K levels over those of the renal pelvic urine (both $P < 0.05$, Table 1). There were no significant differences between men and women or the young and elderly.

These results were reproducible with no significant differences when the tests were repeated for the same subject.

Discussion

The current study sheds some light on possible changes that occur in urine during its passage through the ureter. It is a general assumption that the ureter is a simple conduit lined by impermeable urothelium, a concept which is evidenced by the high electrical resistance, low ionic permeability and hydrophobicity of the urothelium [2, 8]. Urothelial impermeability has been claimed to be necessary to maintain a blood-urine barrier [1]. However, in the present study we provide evidence that the composition of urine is modified as it passes through the ureter from the renal pelvis. There was no change in the pH values during this passage. This would indicate the absence of pH modifications in the ureter such as changes in CO_2 tension, buffering capacity of excreted bicarbonate, phosphate and ammonium or transport of H^+ equivalents [9]. Changes in pH of ureteric urine may have implications for stone formation.

The unchanging urine osmolality during the passage of urine through the ureter is suggested to stabilize water movement from the ureteric lumen and solute transport into the urine during its passage in the ureter. The increased Na and K levels in the ureteric urine compared to those in the renal pelvic urine appear to result from

Table 1 Urine pH, osmolality, Na and K in samples from the renal pelvis and ureter. Values were given as the mean ± SD. P values of the ureteric urine were compared to those of the renal pelvic urine. N.S. indicates not significant

Parameter	Renal pelvic urine		Ureteric urine	
	Mean	Range	Mean	Range
PH	6.02 ± 0.8	5.66–6.86	6.08 ± 0.9 N.S.	5.72–6.94
Osmolality (mOsm kg)	320.8 ± 60.3	264–408	328 ± 66.8 N.S.	255–428
Na (mM)	90.4 ± 8.6	77–109	136.4 ± 17.4*	112–160
K (mM)	21.8 ± 5.4	14–39	34.8 ± 6.7*	26–46

*$P < 0.05$

the flux of these electrolytes across the ureteric urothelium to the lumen of the ureter. This finding suggests that Na and K move from blood plasma across the ureteric urothelium to the ureteric urine in humans. Previous studies have shown that the mammalian urothelium in the renal pelvis is involved in the modification of urinary concentrations and composition of electrolytes, and the canine and rat ureters reabsorb K, urea and creatinine, and secrete Na [4]. Active Na transport from the luminal space of the urinary tract has been reported in the canine and rabbit bladder urothelium in vitro [3]. It has also been demonstrated that voided urine shows significant increases in pH, osmolality and Na and K concentrations compared to urine contained in the bladder [5]. The current study supports the concept of Na and K transport across the ureteric urothelium. Meanwhile, we cannot refute an electrolyte secretory function of the ureteric urothelium, which may provide an alternative explanation for the increases in these urinary constituents. Another explanation might be that the increase of both Na and K suggests that water was extracted rather than Na or K transported across the ureteric epithelium. However the osmolality of the ureteric urine showed no significant difference against that of the renal pelvis, and this appears to negate such a concept.

The distal ureteral urine showed a Na and K increase without significant change in the osmolality. The cause is not known. However, other solutes, such as urea, may be absorbed from the urine back into the plasma; a point which needs further study. Another point may be raised about the impact of urinary diversion by cutaneous ureterostomy on urine composition compared to the urine in the normal urinary tract. However, when this point is considered, no difference appears to exist. This is because, as the urine in the normal subjects collects in the urinary bladder in drops, the same occurs in the container in patients with cutaneous ureterostomy.

In conclusion, this study has shown that renal pelvic urine undergoes changes in some of its constituents during its passage through the ureter. Na and K in the ureteric urine showed a significant increase compared to that in the renal pelvic urine, while the pH and osmolality did not change significantly. These increases in electrolytes are hypothesized to be due to flux of these electrolytes across the ureteric urothelium to the ureteric lumen. The current study, thus, seems to negate the general assumption that the ureter is a simple conduit, and supports the concept of a dynamic ureteric urothelium.

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References

1. Hohlbrugger G (1995) The vesical blood-urine barrier: a relevant and dynamic interface between renal function and nervous bladder control. J Urol 154: 6
2. Hurst RE, Roy JB, Parson CL (1977) The role of glycosaminoglycans in normal bladder physiology and the pathophysiology of interstitial cystitis. In: Sant GR (ed) Interstitial cystitis. Lippincott-Raven, Philadelphia p 93
3. Wickham JEA (1964) Active transport of sodium ion by mammalian bladder epithelium. Invest Urol 2: 145
4. Levinsky NG, Berliner RW (1959) Changes in composition of the urine in ureter and bladder at low urine flow. Am J Physiol 196: 549
5. Shafik A, El-Sibai, Shafik AA (2004) Do vesical and voided urine have identical composition? Scand J Urol Nephrol 38: 243
6. Schmidt-Nielsen B (1977) Excretion in mammals: role of the renal pelvis in the modification of the urinary concentration and composition. Fed Proc 36: 2493
7. Cahill DJ, Fry CH, Foxall PJD (2003) Variation in urine composition in the human urinary tract: evidence of urothelial function in situ? J Urol 169: 871
8. Lewis SA (2000) Everything you wanted to know about the bladder epithelium but were afraid to ask. Am J Physiol Renal Physiol 278: 867
9. Pitts RF, Ayers JL, Scheiss WA (1948) The renal regulation of acid-base balance in man. III. The reabsorption and excretion of bicarbonate. J Clin Invest 28: 35