Urol Res (2006) 34: 261–264
DOI 10.1007/s00240-006-0058-0

ORIGINAL PAPER

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Does the composition of voided urine reflect that of the renal pelvis?

Received: 23 February 2006 / Accepted: 12 April 2006 / Published online: 5 May 2006

Abstract Studies have shown that the urothelium has a transport function and that urine composition changes on its way through the urinary tract. In this study, we investigated the hypothesis that the composition of voided urine differs from and does not reflect that of the renal pelvis. Urine samples were obtained from the renal pelvis and voided urine of 18 healthy volunteers (mean age 36.2 ± 5.1 SD years, 10 men, 8 women). The pH was determined using a pH electrode, osmolality by means of micro-osmometry and Na and K using flame photometry. In comparison to the urine of the renal pelvis, voided urine showed significant increases in pH, osmolality and Na and K concentrations ($P < 0.05$ for each). There were no significant differences in gender and age. This study has demonstrated that the pH, osmolality, Na and K of voided urine differ significantly from the values in the renal pelvis. Urine composition is thus modified as it passes through the urinary tract, which would support the concept of a dynamic urothelium. The composition of voided urine does not seem to compare to renal pelvic urine. This concept needs to be considered in urine analysis evaluation and its relation to renal function.

Keywords Acidity · Alkalinity · pH · Osmolality · Bladder · Kidney

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Introduction

It is generally assumed that urine composition undergoes little or no change along the urinary tract so that the composition of voided urine reflects that produced by the kidney. Based upon this assumption, urinalysis is a vital component of analytical procedures used to assess many normal and pathologic urologic conditions. The hypothesis of an impermeable urothelium is supported by the evidence of its high electrical resistance, low ionic permeability and hydrophobicity [1, 2]. The urothelial impermeability seems necessary to maintain a blood–urine barrier, which allows urine storage without recirculation of renal waste [3]. However, previous studies have demonstrated that the urothelium has a transport function and that urine composition changes as it passes along the urinary tract [4–8]. These studies could prove that the renal pelvis and ureteric urothelia have an absorptive function [6, 9, 10]. It has been recently demonstrated that values of pH, osmolality and Na and K concentrations obtained from vesical urine samples differ significantly from those obtained from urine in the renal pelvis [5] and from the voided urine [7]. Also, it has been shown that the concentration of some of the aforementioned urine parameters obtained from the renal pelvis differed significantly from those of the ureteric urine [8]. In view of these findings, we hypothesized that the composition of voided urine differs from and does not reflect that of the renal pelvis. This hypothesis was investigated in the current study.

Subjects and methods

Subjects

Eighteen healthy subjects volunteered for these tests. They were ten men and eight women with a mean age of 36.2 ± 5.1 SD years (range 28–40). The subjects had normal urinary tracts and the urine cultures were sterile. They gave informed consent after being fully informed

about the nature of the study and their role in the tests to be carried out in the course of the study. The study was approved by the Review Board and Ethics Committee of the Cairo University Faculty of Medicine.

Physical examination and neurologic assessment were normal. Laboratory work-up including renal and hepatic function tests, electrocardiography, uroflowmetry and post-voiding residual urine measurements revealed results within normal limits.

Methods

The subjects fasted during the night and were then asked to empty the urinary bladder. They were allowed free access to fluids. After 3 h, urine samples were obtained from the renal pelvis and voided urine. The subject was asked to void into a graduated flask. Immediately after collection of the voided urine, renal pelvic urine samples were collected from the right kidney. To standardize the technique in the subjects all the urine samples were collected from the right kidney. Under short-acting general anesthesia, a 22-Fr cystoscope was introduced into the bladder without lubricant so as not to contaminate the urine. Under fluoroscopic control, a 6-Fr ureteral catheter was passed up the ureter to the renal pelvis and the first 8–10 drops representing the dead space of the catheter were discarded. Subsequently 3–5 ml of renal pelvic urine was collected; the ureteral catheter was then removed. All urine samples were snap frozen in liquid N_2 and stored at −70°C until analysis.

Stored samples were thawed at room temperature and centrifuged for 3 min at 7,000 rpm to remove particulate matter. Urine pH was measured using an ultra-thin, ultra-long combination glass pH electrode which was calibrated before each measurement with standard buffers at pH 4.0 and 7.0. Urine osmolality was measured using an automatic micro-osmometer, while urine Na and K were measured by means of a flame photometer.

Reproducibility of the results was ensured by repeating the measurements at least twice in each subject, and the mean value was calculated. The results were analyzed statistically using the paired *t*-test and values were given as the mean ± SD. Differences assumed significance at $P < 0.05$.

Results

No adverse side effects were encountered during or after performing the tests and all the volunteers were evaluated. Ureteral catheterization did not induce urothelial traumatization since examination of the urine samples showed them to be free from red blood cell contamination. The urine pH, osmolality, Na and K in samples obtained from the renal pelvis and urinary bladder are shown in Table 1. The pH mean levels and ranges of renal pelvic and voided urine were within the normal physiologic limits of 4.8–7.4. However, within this range and in all the subjects studied, the voided urine was more alkaline than the renal pelvic urine ($P < 0.05$, Table 1). The results revealed no significant difference between men and women or between young and elderly subjects ($P > 0.05$, $P > 0.05$).

Osmolality of all renal pelvic and voided urine samples was within the normal physiologic range of 50–1,300 mosmol/kg [15]. However, the voided urine had a significantly higher mean osmolality than the renal pelvic urine ($P < 0.05$, Table 1). The osmolality showed an insignificant increase in women over men and in the young over the elderly.

The Na and K levels in both the renal pelvis and bladder urine were within the established normal reference ranges for random urine samples (25–200 and 12–80, respectively). However, the voided urine Na and K levels exhibited a significant increase ($P < 0.05$, $P < 0.05$, respectively) compared to those of the renal pelvis (Table 1). There was no significant difference between men and women or between young and elderly ($P > 0.05$, $P > 0.05$, respectively).

The aforementioned results were reproducible with no significant differences when the tests were repeated in the same subject.

Discussion

The current study provides evidence that the composition of the voided urine differs from that of the renal pelvis in humans. The voided urine is more alkaline and contains a greater Na and K concentration than the renal pelvic urine. Urine acidification relative to that of

Table 1 The urine pH, osmolality, Na and K in urine samples from the renal pelvis and voided urine

Parameters	Renal pelvic urine		Voided urine	
	Mean	Range	Mean	Range
pH	6.04 ± 0.3	5.72–6.64	6.82 ± 0.08*	6.68–7.06
Osmolality (mosmol/kg)	341.6 ± 58.2	278–416	486.4 ± 60.3*	438–566
Na (mM)	92.3 ± 7.4	82–106	151.6 ± 32.5*	146–158
K (mM)	24.3 ± 5.8	16–32	49.6 ± 9.8*	40–59

Values are given as mean ± standard deviation
P values of the voided urine were compared to those of the renal pelvic urine, *$P < 0.05$

the arterial blood occurs as urine passes through the kidney nephron so that the renal pelvic urine is more acidic than that of the proximal tubule [5]. Recent studies have shown that the acidity of the renal pelvic urine does not undergo significant changes during urine passage through the ureter [8]. Meanwhile, more urine alkalization occurs in the bladder [5] and reaches its maximum in the urethra so that the voided urine is highly alkalinized compared to the urine from the rest of the urinary tract [7]. These pH modifications are suggested to depend on several factors such as changes in carbon dioxide tension, the buffering capacity of excreted bicarbonate, phosphate and ammonium or the transport of H^+ equivalents [11]. Changes in the urine pH within the urinary tract may constitute a medium for infections and stone formation [12]. Thus, urine sample alkalization decreases Ca^{2+} solubility in solution with a resulting precipitate formation [12]. Urine within the urinary tract having an above-normal acidic content might play a role in stone formation.

In the current study, the period of time between sampling of the voided and the renal pelvic urine was short enough to exclude influences such as, for example, the circadian rhythm on urinary composition. The source of the increased pH, osmolality, Na and K levels in voided urine compared to renal pelvic urine needs to be clarified. A recent study [8] has shown a significant increase of Na and K in the ureteric over the renal pelvic urine, while the pH and osmolality were similar. These parameters were significantly higher in the bladder urine than in the renal pelvis [5], signifying that the bladder appears to add to the pH and osmolality levels of the renal pelvic urine. The increase of pH, osmolality, Na and K in the voided urine compared to the urine contained in the bladder is most likely a urethral function [7].

The increase of osmolality is suggested to denote either a shift of water from the lumen or transport of solutes into the urine as the latter travels through the urinary passages. It appears that the mucus secreted by the urethral mucus glands, which is alkaline [13], is responsible for the increased osmolality and alkalinity of the voided urine [7]. Also, the secretions of the prostate and seminal vesicles which may drain into the urethra during voiding may cause an increase of osmolality and alkalinity in the voided urine. The rapid flow of urine into the hollow urethral tube during micturition seems to create a negative pressure at the prostatic and vesicular ductal orifices which open into the urethra [14]. This negative pressure apparently sucks the secretions of the seminal vesicles and the prostate into the urethra and presumably functions to clear the prostatic and seminal vesicles from their stored secretions. It appears that these secretions would explain the significant increase of the alkalinity and osmolality in the voided against the vesical urine. Likewise, the significantly increased Na and K levels in the voided urine may be produced by the urethral, prostatic and vesicular secretions which presumably contain Na and K.

One might presuppose that the presence of secretions from the seminal vesicles and prostate in the male urine produces a difference in the voided urine of men against women. The results of our examination have, however, shown that this difference was of no statistical significance.

The increased alkalinity and osmolality of voided urine may be advantageous. We suggest that these changes in the urine characteristics protect the urethra from the possibly injurious effect of the acidic urine on the urethral epithelium, especially as the rapid flow of the urinary stream may cause friction and traumatization of the urethra. This potentially traumatizing effect of the urinary flow on the urethral epithelium appears to be minimized not only by the increased urine alkalinization, but also by the lubricant effect of the mucus priming the urethral wall. After termination of urination the urethra probably remains wet from voiding, and it is worth mentioning that the acidic urine may injure the urethral urothelium if they stay in contact over a long period. Meanwhile, we do not know the effect of increased Na and K in the voided urine. Is it just a derivation from the urethral mucous glands and the secretions of prostate and the seminal vesicles? Further studies may clarify this point.

It may be argued that urothelial irritation by the ureteric catheter could cause a biochemical response which leads to the reported changes in urine pH, osmolality, Na and K. However the presence of the catheter in the ureter was but momentary because it was instantly withdrawn following renal pelvic urine collection of 3–5 ml as already mentioned.

In conclusion, this study has shown that the pH, osmolality, Na and K levels in voided urine differ significantly from the relevant values in the renal pelvis. The urine composition is thus modified as it passes through the urinary tract, supporting the concept of a dynamic urothelium. The composition of the voided urine does not seem to reflect that of the renal pelvis. This concept needs to be considered in urine analysis evaluation and its relation to renal function.

Acknowledgment Margot Yehia assisted in preparing the manuscript.

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