Kidney International, Vol. 60 (2001), pp. 748–756

Level of hydration and renal function in healthy humans

Pietro Anastasio, Massimo Cirillo, Lucia Spitali, Annamaria Frangiosa, Rosa Maria Pollastro, and Natale G. De Santo

Department of Pediatrics, Division of Adult and Pediatric Nephrology, Medical School, Second Naples University, Naples, Italy

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Background. High hydration is commonly used in renal studies to improve the completeness of urine collection. The renal effects of hydration are not well defined.

Methods. Renal function was studied under fasting conditions (baseline) and after a meat meal (2 g of protein/kg body weight) in 12 healthy adults on a low and high hydration regimen of 0.5 and 4 mL of oral water per kg body weight/30 min, respectively.

Results. Urine flow, urinary and plasma Na, K, urea, and osmolality were stably different on low and high hydration regimens. At baseline, there were significant or borderline significant correlations of plasma and urine osmolality with glomerular filtration rate (GFR; inulin clearance) only in the low hydration regimen. GFR was higher in the low than the high hydration regimen at all time points. The difference was significant at baseline (19.2%) and at 90 to 180 minutes after the meal (14.4%). After the meal, GFR increased significantly over baseline values only in the high hydration regimen (30.0% at peak time). Urinary excretion of Na, urea, and osmoles was lower in the low than the high hydration regimen at all time points: The difference was significant for Na (at baseline) and osmoles (all time points). Urinary K excretion was not different in the two regimens. After the meal, there were significant increases in urinary excretion of Na (in the low hydration regimen) and urea (90 to 180 min after the meal).

Conclusions. In fasting adults, high hydration lowered GFR and increased natriuresis. After a meat meal, GFR increased only in the high hydration regimen and natriuresis only in the low hydration regimen. Hydration affects GFR and natriuresis under fasting conditions and after a meat meal.

The level of hydration is commonly increased to enhance the urine flow rate and completeness of urine collections in studies of renal function. Except for changes in the urine flow rate and urine concentration, the effects of hydration on renal function are not well defined. In animals, evidence of an inverse association between hydration and glomerular filtration rate is considered a hemodynamic adaptation to changes in the intrarenal urea recycling secondary to differences in urine concentration [1–3]. In humans, conflicting data on the effects of hydration on urinary excretion of main osmoles and glomerular filtration rate are reported. In a study on renal lithium clearance in healthy men, Boer et al found that high hydration reduces urinary sodium excretion under fasting conditions and does not affect GFR [4]. In a study on the renal responses to a protein-rich meal, Hadj-Aissa et al reported that in healthy volunteers, high hydration increases urinary sodium excretion under fasting conditions and blunts the transient GFR increase secondary to the meat meal [5]. In those two studies, urine collections were based on spontaneous voiding without use of a bladder catheter. In the study of Hadj-Aissa et al, the protocol also included the use of an osmotic diuretic, which might have affected renal function. Thus, the discrepancies between the conclusions of the two previous studies might reflect limitations in the precision of urine collection and/or confounding due to the use of an osmotic diuretic.

The present study further investigated the influence of hydration on indices of renal function by using bladder catheterization for urine collections. Two different levels of hydration were studied in healthy individuals who were on their habitual diet in the days before the experiments. Renal function was studied under fasting conditions and after a meat meal, which is a standard method to induce renal hyperfiltration in healthy individuals and in patients with renal or non-renal diseases [6–10].

METHODS

Healthy volunteers were selected to participate in the study. Selection criteria included a negative personal and family history of renal diseases and other medical disorders, a body mass index (weight/height^2) <28 kg/m^2, diastolic blood pressure <90 mm Hg, normal routine laboratory investigations, and no treatment with drugs. A total

Key words: urine flow, glomerular filtration rate, sodium, osmolality, fluid management, water hemodynamics.

Received for publication May 26, 2000
and in revised form February 23, 2001
Accepted for publication March 1, 2001

of 12 individuals (5 men and 7 women) participated in the study and their mean age ± SD was 30.2 ± 4.6 years. Written informed consent was given by all participants. The study consisted of two identical tests—one on low hydration and one on high hydration—done with a randomized sequence in a three- to four-week interval (N = 6, low/high; N = 6, high/low). Habitual fluid intake and habitual diet were not modified prior to the tests. On the day before the low and high hydration tests, a morning blood sample collected under fasting conditions and a 24-hour urine collection were obtained for measurements of plasma creatinine, 24-hour urinary volume, and 24-hour urinary excretion of creatinine, urea, sodium (Na), and potassium (K). Morning plasma creatinine and 24-hour urinary creatinine excretion were used to calculate creatinine clearance. Weight and height were used to calculate body surface area ($71.84 \times \text{height}_{cm}^{0.725} \times \text{weight}_{kg}^{0.425}$).

For each test, participants were instructed to come to the clinic early in the morning under fasting conditions, defined as after an overnight fast. After measurements of body weight, height, and blood pressure, participants were placed in the recumbent position with a bladder catheter for urine collection, and with a venous cannula in each arm, for intravenous infusion and collection of blood samples, respectively. An intravenous infusion of inulin and paraaminohippuric acid was initiated as a bolus (0.42 mL per kg body weight) and continued throughout the test at a constant rate of infusion (0.012 mL/min per kg body weight) to maintain plasma inulin at approximately 20 mg/100 mL and paraaminohippuric acid at approximately 2 mg/100 mL. Hydration protocols were based on the administration per os of tap water: 0.5 mL per kg body weight every 30 minutes in the low hydration test, and 4 mL per kg body weight every 30 minutes in the high hydration test. After initiating a constant rate of intravenous infusion, the low and high hydration tests included the following: first, an equilibration (90 min); second, measurements under fasting conditions (90 min); third, a meat meal with 2 g of protein per kg body weight as a lean beefsteak cooked without the addition of salt or other seasoning [7–10]; and finally, after-meal measurements (180 min). After equilibration (not used for analysis), six consecutive and separate urine samples of 45 minutes each were collected as follows: two samples in the 90 minutes under fasting conditions and four samples in the 180 minutes after the meal. Venous blood samples were withdrawn at the initiation and completion of each urine collection. For a given substance, the urinary excretion rate was calculated as the urinary concentration times the urine flow rate, and renal clearance as the urinary excretion rate divided by the average plasma concentration between initiation and completion of urine collection; fractional excretion was calculated as the percent ratio of renal clearance to GFR.

Table 1. Descriptive statistics in 12 healthy volunteers on the day before the test and morning of the low and high hydration test

	Low hydration	High hydration
Day before the test		
24-hour urinary volume *mL*	1286 ± 133	1216 ± 131
24-hour urinary sodium *mmol*	155.3 ± 8.3	156.3 ± 10.9
24-hour urinary potassium *mmol*	53.5 ± 3.2	50.3 ± 2.1
24-hour urinary urea *mmol*	351.4 ± 18.0	330.8 ± 13.8
Plasma creatinine *μmol/L*	75.8 ± 5.4	77.1 ± 5.6
Creatinine clearance *mL/min*	109.5 ± 4.9	108.8 ± 5.9
Morning of the test		
Weight *kg*	70.1 ± 3.6	70.9 ± 3.4
Body surface area m^2	1.79 ± 0.05	1.79 ± 0.05
Systolic blood pressure *mm Hg*	111.7 ± 3.9	114.8 ± 4.4
Diastolic blood pressure *mm Hg*	71.9 ± 2.6	74.8 ± 2.8

Differences between the low and high hydration were not significant by the Student t test for paired data.

Inulin clearance was used as an index of GFR and paraaminohippuric acid clearance as an index of renal plasma flow. Filtration fraction was calculated as the percent ratio of GFR to renal plasma flow. Urea, creatinine, Na, and K were measured by automated biochemistry; inulin and paraaminohippuric acid by a colorimetric technique [7–10]; osmolality by automated osmometer.

Statistics

For statistical analyses, the baseline value was calculated as the average of two 45-minute measurements under fasting conditions; the 0 to 90-minute value was calculated as the average of two 45-minute measurements in the interval of 0 to 90 minutes after the initiation of the meal; the 90- to 180-minute value was calculated as the average of two 45-minute measurements in the interval of 90 to 180 minutes after the initiation of the meal. Because of interindividual variability in the temporal pattern of the response of GFR to the meal, peak GFR was defined as the highest GFR in any of the 45-minute collections after the meal [6, 7]. Renal reserve was calculated as peak minus baseline GFR values [6, 7]. Statistical procedures included the Student t test for paired observations and simple correlation analysis.

RESULTS

Descriptive statistics

Table 1 shows mean ± SE values for the 24-hour urine collections and related variables in the day before the low and high hydration tests and for anthropometry and blood pressure in the morning at the initiation of the tests. Consistent with differences in the level of hydration, large differences were maintained between the low and high hydration tests in urine flow rate (Fig. 1) and in the concentration of urinary and plasma variables (Fig. 2).

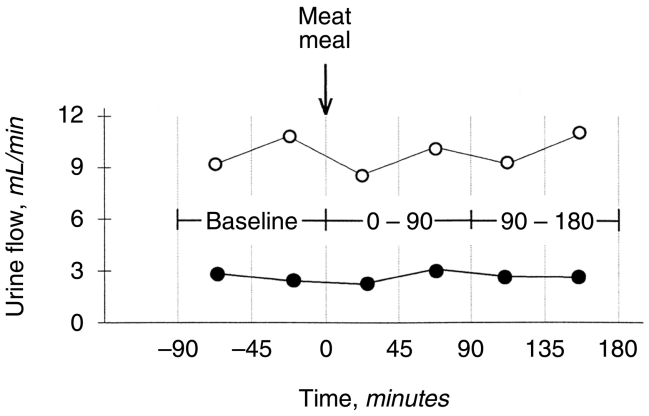

Fig. 1. Mean urine flow rate in 12 healthy individuals on low hydration (●) and high hydration regimens (○).

Influence of hydration on GFR and renal hemodynamics

At baseline, the mean values of GFR (+19.2%) and renal plasma flow (+13.4%) were higher in the low than high hydration regimen (Table 2). For filtration fraction, the difference between the low and high hydration regimens was not significant (+4.5%). For GFR, the difference between the two groups was consistent in all individuals (Fig. 3). In correlation analyses for baseline GFR, the coefficients were significant or borderline significant with plasma and urinary osmolality in the low hydration, but not the high hydration regimen (Fig. 4). The coefficient with urine osmolality was significant only for urine osmolality above 300 mOsm/kg as previously found in rats [11]. In the low and high hydration regimens, the correlation coefficients of baseline GFR values were not significant with the urinary and plasma concentration of Na, K, and urea, and with their urinary to plasma ratios (data not shown).

After the meal, the mean values of GFR and renal plasma flow were higher in the low than the high hydration regimens, but to a lesser degree than under fasting conditions (Table 2). The difference between low and high hydration was significant only in the 90- to 180-minute period for GFR (+14.4%), but not significant for renal plasma flow. For filtration fraction, mean values in the low and high hydration regimens were not significantly different under fasting conditions (Table 2). Compared with baseline, the meal induced transient changes in GFR and renal plasma flow, but not in filtration fraction. In the low hydrated regimen, the after-meal GFR and renal plasma flow values were reduced below baseline values, but not significantly. However, in the high hydrated group the after-meal GFR and renal plasma flow were increased over baseline values, but this was significant only in the 0 to 90-minute period. For the 0 to 90-minute period, the GFR change over baseline was significantly different between the low and high hydration regimens with expression of data as an absolute change (-5.12 ± 3.10 and 7.84 ± 3.47 mL/min, $P = 0.027$) and percent change of baseline GFR (-4.23 ± 2.49 and $8.47 \pm 3.86\%$, $P = 0.023$). For the 90- to 180-minute period, the GFR changes were not significantly different between the two regimens. The peak of after-meal GFR was not significantly different between the low and high hydration regimens (130.4 ± 6.5 and 124.0 ± 5.9 mL/min, P = NS). Renal reserve was lower in the low than the high hydration regimen; the difference was borderline significant with expression of the data as absolute change (15.2 ± 3.7 and 27.5 ± 4.3 mL/min, $P = 0.057$), and significant with the data as percent change of baseline GFR (13.7 ± 3.6 and $30.0 \pm 5.5\%$, $P = 0.031$).

Influence of hydration on urinary excretion of Na, K, urea, and total osmoles

Urinary sodium. In all periods, urinary Na excretion was lower in the low than the high hydration regimens (Table 3). The differences between the low and high hydration regimens were significant only for the baseline period. After the meal, urinary Na excretion increased over baseline values in both regimens. The after-meal increase over the baseline value was large and significant in the low hydration regimen (+35.5% in the 0 to 90-minute period, 42.2% in the 90- to 180-minute period), and modest but not significant in the high hydrated regimen (+18.7% in the 0 to 90-minute period and +7.5% in the 90- to 180-minute period). Because of larger increases in the after-meal urinary Na excretion in the low hydration regimen, the difference in urinary Na excretion between the two regimens progressively reduced from baseline values to the 90- to 180-minute period. The findings were similar in the analyses of data expressed as renal clearance. For the baseline period, Na clearance was significantly lower in the low than high hydration regimen (data not shown) due to a lower urinary Na excretion in the presence of higher plasma Na (Fig. 2). Fractional Na excretion rates are shown in Table 4. At baseline, fractional Na excretion was significantly lower in the low than high hydration regimen due to a lower renal Na clearance in the presence of higher GFR. After the meal, fractional Na excretion increased over baseline values, significantly in the low hydration regimen (+42.2% in the 0 to 90-minute period, +45.1% in the 90- to 180-minute period), but not significantly in the high hydration regimens (+16.3% in the 0 to 90-minute period, +12.1% in the 90- to 180-minute period).

Urinary potassium. In all periods, urinary K excretion was not significantly different between the two regimens (Table 3). After the meal, urinary K excretion did not change significantly over baseline values in the low and high hydration regimens. These findings were similar in

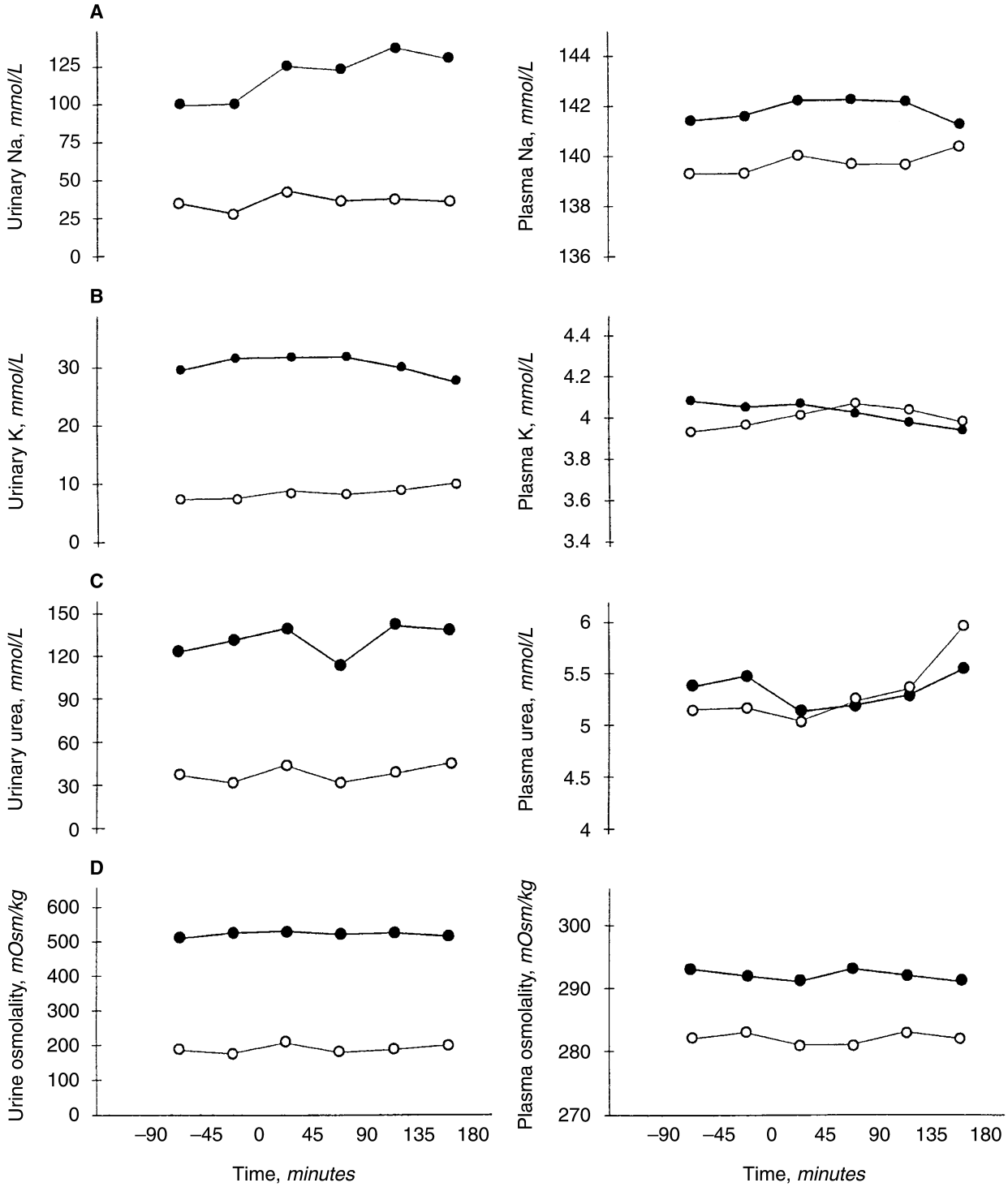

Fig. 2. Urinary and plasma levels of sodium (Na) (*A*), potassium (K) (*B*), urea (*C*), and osmolality (*D*) in 12 healthy individuals on low hydration (●) and high hydration regimens (○). For plasma variables, each point represents the average of measurements done at the initiation and completion of 45-minute urine collection.

analyses with data expressed as renal clearance (data not shown) or as fractional excretion (Table 4).

Urinary urea. In all periods, urinary urea excretion was lower in the low than high hydration regimens (Table 3), but the differences were not significant. After the meal, urinary urea excretion increased over baseline values in both regimens, but was significant only for the 90- to 180-minute period. These findings were similar in

Table 2. Renal hemodynamics under fasting conditions (baseline) and after the meat meal in 12 healthy volunteers on low and high hydration

	Low hydration	High hydration	*P* value[a]
Glomerular filtration rate *mL/min*			
Baseline	115.1 ± 5.6	96.6 ± 5.0	<0.001
After meal 0–90 min	110.0 ± 5.7	104.4 ± 6.4[c]	NS
After meal 90–180 min	114.4 ± 5.4	100.0 ± 6.2	0.017
Renal plasma flow *mL/min*			
Baseline	501.9 ± 26.6	442.5 ± 25.6	0.019
After meal 0–90 min	481.1 ± 29.8	474.8 ± 25.9[c]	NS
After meal 90–180 min	500.3 ± 28.4	455.8 ± 26.4	NS
Filtration fraction[b] %			
Baseline	23.1 ± 0.7	22.1 ± 0.7	NS
After meal 0–90 min	23.1 ± 0.7	22.2 ± 0.7	NS
After meal 90–180 min	23.1 ± 0.7	22.2 ± 0.7	NS

Data are mean ± SE. NS is not significant.
[a] Low vs. high hydration by the paired Student *t* test
[b] Calculated as the percent ratio of glomerular filtration rate to renal plasma flow
[c] $P \leq 0.05$ vs. baseline on same hydration

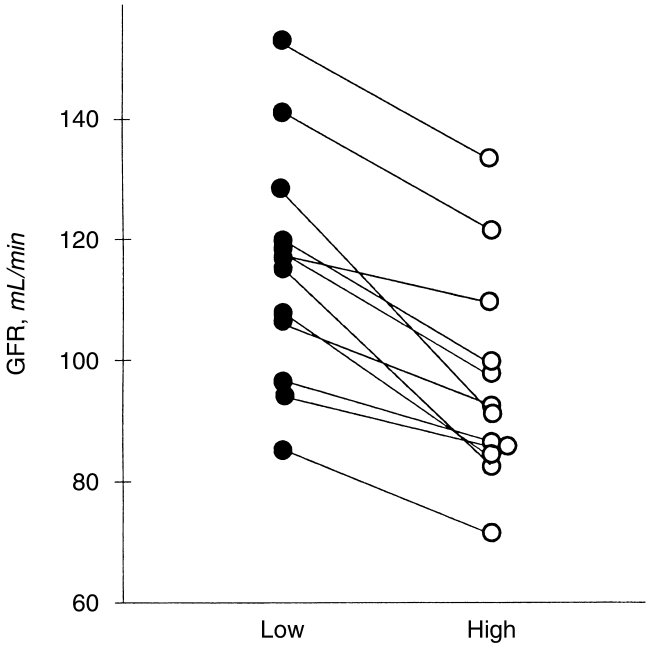

Fig. 3. Individual values of the glomerular filtration rate (GFR, inulin clearance) in the baseline period in the low hydration (●) and high hydration (○) regimens. Each circle represents the average of two consecutive 45-minute measurements.

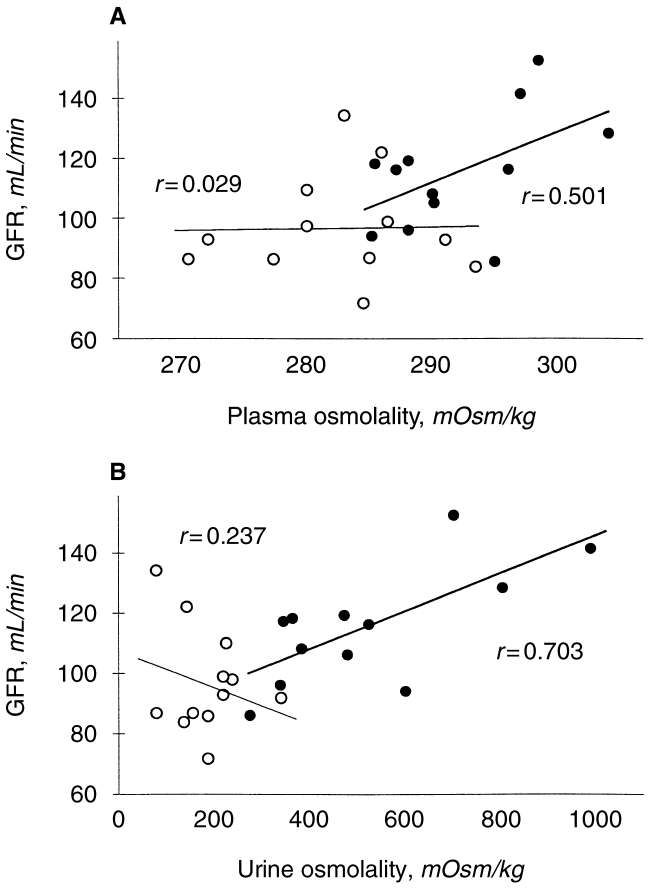

Fig. 4. Correlation analyses of glomerular filtration rate (GFR, inulin clearance) with plasma osmolality (*A*) and urinary osmolality (*B*) in the baseline period in the low hydration (●) and high hydration (○) regimens. Each circle represents the average of two consecutive 45-minute measurements. Correlation coefficients (*r*) were significant or borderline significant in the low hydration regimen (for plasma $P = 0.079$, for urine $P = 0.011$) but were not significant in the high hydration regimen.

analyses with the data expressed as renal clearance. In all periods, urea clearance was not significantly lower in the low versus high hydration regimen (data not shown) because of the lower urinary urea excretion in the presence of similar or higher plasma urea (Fig. 2). With data expressed as fractional excretion (Table 4), the urea excretion rate at baseline was significantly lower in the low than high hydration regimen due to a lower renal urea clearance in the presence of higher GFR. After the meal, the fractional urea excretion rate increased significantly over baseline values in the low hydration regimen (+25.0% in the 0 to 90-minute period, +26.5% in the 90- to 180-minute period). In the high hydration regimen, the changes over baseline values in the fractional urea excretion rates were not consistent and not significant (−2.6% in the 0 to 90-minute period, +5.1% in the 90- to 180-minute period).

Urinary osmoles. In all periods, urinary osmole excretion was significantly lower in the low than high hydration regimens (Table 3). After the meal, urinary osmole excretion increased over baseline values in both regimens, but the differences between the baseline and after-meal period values were not significant. These findings were similar in analyses with the data expressed as renal clearance (data not shown) or fractional excretion (Table 4).

Table 3. Urinary absolute excretion of sodium, potassium, urea, and total osmoles under fasting conditions (baseline) and after the meat meal in 12 healthy volunteers on low and high hydration

	Low hydration	High hydration	*P* value[a]
Sodium *mmol/min*			
Baseline	0.225 ± 0.025	0.305 ± 0.044	0.040
After meal 0–90 min	0.305 ± 0.043[b]	0.362 ± 0.036	NS
After meal 90–180 min	0.320 ± 0.028[c]	0.328 ± 0.032	NS
Potassium *mmol/min*			
Baseline	0.070 ± 0.015	0.074 ± 0.010	NS
After meal 0–90 min	0.079 ± 0.016	0.077 ± 0.008	NS
After meal 90–180 min	0.068 ± 0.008	0.083 ± 0.009	NS
Urea *mmol/min*			
Baseline	0.276 ± 0.029	0.313 ± 0.026	NS
After meal 0–90 min	0.300 ± 0.040	0.321 ± 0.022	NS
After meal 90–180 min	0.342 ± 0.035[b]	0.371 ± 0.040[b]	NS
Osmole *mOsm/min*			
Baseline	1.216 ± 0.110	1.783 ± 0.301	0.047
After meal 0–90 min	1.296 ± 0.142	1.837 ± 0.254	0.048
After meal 90–180 min	1.282 ± 0.092	1.883 ± 0.334	0.042

Data are mean ± SE. NS is not significant.
[a] Low vs. high hydration by the paired Student *t* test
[b] $P \leq 0.05$, [c] $P < 0.001$ vs. baseline on same hydration

Table 4. Fractional excretion[a] of sodium, potassium, urea, and total osmoles under fasting conditions (baseline) and after the meat meal in 12 healthy volunteers on low and high hydration

	Low hydration	High hydration	*P* value[b]
Sodium % Baseline	1.42 ± 0.16	2.14 ± 0.28	0.027
After-meal 0-90 min	2.02 ± 0.33[c]	2.49 ± 0.19	NS
After-meal 90-180 min	2.06 ± 0.21[d]	2.40 ± 0.22	NS
Potassium %			
Baseline	15.7 ± 3.7	19.3 ± 2.2	NS
After-meal 0-90 min	19.3 ± 4.6	18.6 ± 1.6	NS
After-meal 90-180 min	15.9 ± 2.0	22.2 ± 3.1	NS
Urea %			
Baseline	46.4 ± 4.8	64.5 ± 5.9	0.012
After-meal 0-90 min	58.0 ± 7.7[c]	62.8 ± 4.8	NS
After-meal 90-180 min	58.7 ± 5.7[c]	67.8 ± 6.1	NS
Osmole %			
Baseline	3.67 ± 0.33	6.66 ± 1.11	0.019
After-meal 0-90 min	4.12 ± 0.48	6.48 ± 0.89	0.024
After-meal 90-180 min	3.91 ± 0.30	6.94 ± 1.18	0.020

Data are mean ± SE. NS is not significant.
[a] Calculated as the percent ratio of renal clearance to glomerular filtration rate
[b] Low versus high by paired Student *t* test
[c] $P \leq 0.05$, [d] $P < 0.001$ vs. baseline on same hydration

DISCUSSION

The present study shows that short-term changes in the level of hydration of healthy adults influence not only urine concentration, but also GFR and urinary Na excretion.

Effects on GFR

A difference of about 20 mL/min was found in baseline GFR values between the low and high hydration regimens. The seemingly low baseline GFR values were likely due to the prolonged fast before measurements [6]. The difference between the low and high hydration baseline GFR values indicated an inverse association between the level of hydration and GFR. The existence of an inverse association was supported by the results of correlation analyses of plasma or urine osmolality with GFR under fasting conditions. High osmolality—and hence low hydration—was associated with high GFR. The correlations of plasma or urine osmolality with GFR were evident only for measurements in the low level of hydration group, that is, for values of plasma and urine osmolality close to the normal range. This observation is in keeping with findings of a relationship between the renal concentrating activity and GFR reported in rats [2]. Differences in the level of hydration also were associated with differences in GFR changes after the meat meal, which is a standard test for the analysis of the renal reserve, that is, the renal hemodynamic responses to protein ingestion [6–10]. After-meal GFR changes were significant and positive in the high hydration regimen, but were either not significant or negative in the low hydration regimen. Thus, at variance with fasting conditions, hydration was positively associated with after-meal GFR changes. The different after-meal GFR changes in the low and high hydration regimens attenuated but did not eliminate the inverse association found under fasting conditions between hydration and GFR. In fact, the absolute values of GFR also were higher in the low than the high hydration regimens after the meal. Altogether, the GFR data for the fasting and after-meal periods indicate that (*1*) a difference in the level of hydration induces stable differences in GFR under fasting conditions and after a meat meal, and (*2*) a meat meal induces a normal renal reserve—that is, a 25% increase in GFR over baseline values—only when the fasting baseline GFR is maintained in the low range by a high level of hydration. The lack of a normal renal reserve in the low hydration group and the similarity of peak GFR values in both groups suggest that hydration and protein ingestion act through the same mechanism. According to this interpretation, GFR cannot increase after a meat meal in low hydration conditions, since the renal reserve has been already recruited at baseline.

Effects on urinary sodium excretion

A difference of approximately 35% in urinary Na excretion between the two regimens was found under fasting conditions, indicating a direct association of the level of hydration with urinary Na excretion. The data point to an effect at the renal tubular level. In fact, the level of hydration was inversely associated with plasma Na and GFR. The positive association between the level of hydration and urinary Na excretion also was maintained after the meat meal, but the difference in urinary Na excretion between the low and high hydration regimens

was not significant. A lack of significant difference between the two hydration regimens in after-meal data reflects the different changes in urinary Na excretion induced by the meal. In both levels of hydration, the after-meal urinary Na excretion value was higher than the fasting baseline value, but the difference was significant only in the low hydration regimen. The absence of a significant increase in after-meal urinary Na excretion in the high hydration regimen does not contrast with previous data from this laboratory; indeed, the change in after-meal urinary Na excretion is similar to our prior study [10] and nonsignificant only for the low sample size of the present series. Altogether, data on urinary Na excretion for fasting and after-meal periods indicate that (*1*) a difference in the level of hydration induces stable differences in urinary Na excretion under fasting conditions and after a protein rich meal; and (*2*) a meat meal induces a prolonged stimulation of urinary Na excretion, which is more evident when the fasting baseline values of urinary Na excretion are maintained in the low range by a low level of hydration.

Effects on urinary excretion of potassium, urea, and osmoles

No significant association was found between the level of hydration and urinary K or urea excretion. For K excretion, differences between the fasting and after-meal periods also were not significant. For urea, the after-meal increase in urinary excretion reflected the after-meal increase in urea generation, since it followed the changes in plasma urea. The effect of hydration on urinary Na excretion was the main determinant of the association between hydration and urinary osmole excretion as the effects on urinary excretion of K and urea were negligible. The lack of effects on K and urea in combination with the effects on Na suggests that the level of hydration influences the excretion of mainly reabsorbed osmoles, such as Na, more than reabsorbed and secreted osmoles, such as urea and K.

Regarding the effects of hydration on GFR under fasting conditions, our present findings are in contrast with data of Boer et al [4] and in agreement with data of Hadj-Aissa et al [5]. In the first study [4], a high level of hydration induced a nonsignificant increase in GFR. This conclusion was biased by the lack of bladder catheterization, and hence by a likely difference in the completeness of urine collection between experiments on low and high hydration. In agreement with present data, Hadj-Aissa et al reported that high hydration was associated with a low GFR, but the difference was not significant. A lack of significance in their study could reflect limitations in the precision of the technique due to lack of bladder catheterization and single measurement of GFR. For the effects of hydration on after-meal GFR changes, the present finding of after-meal GFR increases in the high but not low hydrated regimen is in contrast with data reported by Hadj-Aissa et al on the same issue [5]. As also discussed by Hadj-Aissa et al [5], an increase in GFR after a protein-rich meal in the presence of copious hydration is the standard observation in individuals without and with renal disease [6–8]. In the study of Hadj-Aissa et al, the lack of GFR increases after the protein-rich meal in the high hydration group could be accounted for by several factors. The use of an osmotic diuretic could have affected the results, since the effects of such a drug on the GFR responses to the meal are not described in the literature nor were analyzed in that study. The type of the protein-rich meal also could be a confounder, since participants in that study were given not only red meat but also cheese and milk. Other factors cannot be excluded. The lack in the present study of GFR increases after the protein-rich meal in the low hydration regimen is a novel finding to our knowledge and needs further investigation. It suggests that high hydration, or the reduction in GFR associated with high hydration, plays a role in the GFR rise secondary to protein ingestion. For the effects of hydration on urinary Na excretion, the present finding of a direct association with the level of hydration is in agreement with the conclusion of two previous studies [5, 12] and in contrast with data reported by Boer et al [4]. For findings on urinary Na excretion, in addition to inadequate urine collection, the study of Boer et al might have been biased by the high K intake of the participants, a factor that by itself stimulates renal Na excretion [13]. The present findings also are in agreement with data of Choukroun et al for the lack of effects of hydration on urinary K excretion [12].

The mechanisms underlying the effects of hydration were not addressed in our study. In keeping with previous observations [2, 11], the present data report an association of plasma and urine osmolality with GFR, and suggest that the effects of hydration might be mediated by an osmolality-related mechanism. The antidiuretic hormone vasopressin, whose secretion parallels plasma osmolality, is a possible candidate since its administration is capable of increasing GFR [14, 15]. According to the model proposed by Bankir et al, the effect of vasopressin on GFR is explained by the vasopressin-dependent stimulation of intrarenal urea recycling and, therefore, by the increase of the transepithelial osmotic gradient [16]. In the thick ascending limb, the high osmotic gradient could limit the process of fluid dilution and could reduce the tubular concentration of sodium chloride. In turn, the low sodium concentration could increase GFR via inhibition of the tubuloglomerular feedback at the macula densa level. In the past, data about the effects of vasopressin on sodium excretion have been controversial [17–21]. However, a vasopressin-depen-

dent mechanism also could explain the reduced natriuresis in the low hydration regimen found in the present study. As discussed by Choukroun et al, vasopressin per se in fact has an antinatriuretic effect due to the direct stimulation of sodium transport in channels of the collecting duct [12, 22]. The natriuretic effects reported for vasopressin reflect the use of certain unphysiological conditions—volume expansion and/or high doses of vasopressin—that induce the confouding of atrial natriuretic peptide release and/or the binding of vasopressin to oxytocin receptors [12]. It appears unlikely that the findings in the present study could be explained by differences in plasma albumin and oncotic pressure, secondary to the different levels of hydration. Theoretically, plasma albumin could influence GFR via an inhibitory effect of plasma oncotic pressure on GFR [23]. Plasma albumin, not measured in our study, should be somewhat reduced in the high hydration regimen, in the same manner as plasma sodium and osmolality. Unless changes occur in the glomerular ultrafiltration coefficient, a reduction in plasma oncotic pressure due to low plasma albumin must increase GFR [23], in contrast with our findings in the high hydration regimen. Other mechanisms cannot be excluded to explain the relationship between the level of hydration and renal function.

The results of the present study also may have practical implications. In routine diagnostic work-up and in clinical research, one should be aware that acute changes in the level of hydration affect renal function. Thus, data obtained in the presence of intense hydration should not be extrapolated to "normal conditions" when the urine flow rate ranges between 0.5 and 1.5 mL/min for the majority of individuals. The present acute findings should not be extrapolated to the chronic effects of hydration due to possible structural changes at renal level. As far as renal disease is concerned, the available data indicate that high hydration is capable of slowing the progression of renal failure in a rat experimental model [24].

In summary, the present study shows that in healthy humans, acute changes in the level of hydration influence GFR and urinary Na excretion under fasting conditions. Compared with high hydration, individuals on a low hydration regimen have higher GFR and lower urinary Na excretion values. Also, hydration influences the renal responses to a protein-rich meal. The after-meal stimulation of GFR and urinary Na excretion is present only when the fasting baseline is maintained at a low value: for GFR by a high hydration and for urinary Na excretion by a low hydration. In other words, both hydration and protein ingestion appear to be significant determinants of GFR and urinary Na excretion. However, the combination of their stimulatory effects does not induce further increases of GFR and urinary Na excretion above certain values, suggesting that a common mechanism is involved.

ACKNOWLEDGMENTS

The study was made possible thanks to funds from the Ministero Ricerca Scientifica e Tecnologica (MURST) for local (40%) and national (60%) projects. The authors are grateful to Dr. Lise Bankir, Ph.D. (INSERM U. 367, Paris, France) for helpful suggestions in the preparation of the study protocol.

Reprint requests to Prof. Massimo Cirillo, M.D., Nefrologia (Edificio 17), Nuovo Policlinico/via Sergio Pansini, 5, 80131 Naples, Italy.
E-mail: massimo.cirillo@unina2.it

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