Assessment of renal concentrating ability

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Summary and conclusions

Maximum urine osmolality was measured during a 24-hour control period in normal ambulant and working subjects and hospital inpatients and compared with that achieved after intramuscular injection of 4 μg desamino-cys-1-8-D-arginine vasopressin (DDAVP). Most of the normal subjects passed maximally concentrated urine at some time during the control period. The results suggest that in less active subjects or hospital inpatients the DDAVP test is a suitable method of assessing renal concentrating ability.

Introduction

Renal concentrating ability has usually been determined by measuring the maximum urine osmolality achieved after variable periods of dehydration, during the administration of vasopressin tannate in oil, or during a combination of both manoeuvres. Now that vasopressin tannate in oil is no longer available a synthetic analogue of arginine vasopressin, desamino-cys-1-8-D-arginine vasopressin (DDAVP), has been employed.[1-3] Little attention has been given to the observations of Jones and de Wardener[4] that some people habitually consume so little fluid that the concentration of the urine on a control day might be the same as that achieved after 48 hours of dehydration, and in many reports control observations have not been made. We have measured urine osmolality in a group of normal ambulant active subjects and a group of hospital inpatients during a control period of 24 hours and again after 4 μg DDAVP given by intramuscular injection.

Subjects and methods

The normal subjects comprised 16 male doctors and medical technicians aged 22-57 years (mean 33 ± SD 9 years), who volunteered for the tests. They remained ambulant and carried out their normal duties throughout. Thirteen hospital inpatients—eight men and five women aged 22-58 years (mean 38 ± 12 years)—who gave fully informed consent, were also studied.

During a 24-hour control period the subjects continued with their normal diet and fluid intake, and aliquots of all urine samples passed during the period were saved for determination of urine osmolality. At the end of the control period (about 7 am in the case of the inpatients, and 10 am in the case of the normal subjects) an intramuscular injection of 4 μg DDAVP was given. Over the next 24 hours aliquots of all urine specimens passed were again saved for determination of urine osmolality. The maximum urine osmolality achieved during the control period was compared with that achieved after the DDAVP. In 13 of the normal subjects venous blood was taken for determination of plasma osmolality just before and 24 hours after the administration of DDAVP. Urine and plasma osmolalities were determined on an Advanced osmometer. Endogenous creatinine clearances were measured in all subjects. Creatinine was determined on an auto-analyser.

The significance of differences between mean values was assessed with Wilcoxon's matched pairs signed ranks test.

Results

In the normal subjects (table I) there was no significant difference in maximum urine osmolality between the control and DDAVP periods. The mean maximum urine osmolality in the control period was 991 ± SD 140 mmol(mosmol)/kg, while the mean maximum value after DDAVP was 1042 ± 108 mmol/kg. During the control observations only two normal subjects failed to achieve a maximum urine osmolality exceeding 800 mmol/kg. After DDAVP all 16 subjects achieved a maximum urine osmolality exceeding 800 mmol/kg. The mean plasma osmolality before DDAVP in the 13 normal subjects in whom it was measured was 289 ± 5·5 mmol/kg, and 24 hours after DDAVP it was 286 ± 5 mmol/kg (table I). The tendency for the plasma osmolality to fall slightly after DDAVP was significant ($P = 0{\cdot}02$). None of the normal subjects, or patients, complained of any side effects, and in particular there were no symptoms of water intoxication.

In the inpatients (table II) there was a significant difference between the maximum urine osmolality during the control period and that achieved after DDAVP. The mean maximum value in the control period was 755 ± 181 mmol/kg, and after DDAVP 836 ± 117 mmol/kg ($P = 0{\cdot}02$). During the control period eight of the 13 patients had a maximum urine osmolality below 800 mmol/kg, but only three failed to achieve this value after DDAVP. Two of these three patients (cases 4 and 5) were studied shortly after an episode of acute pyelonephritis, and the third patient (case 8) had chronic pyelonephritis with renal calculi and hypertension. In cases 5 and 8 there was also reduced creatinine clearance.

Discussion

Jones and de Wardener[4] studied urine osmolality in a group of 17 normal subjects and obtained a mean maximum value of 1118 mmol/kg (range 1009-1301 mmol/kg) after 48 hours of dehydration. They compared the results obtained with this unpleasant test with the maximum urine osmolality achieved after 5 units of vasopressin tannate in oil and recorded a mean maximum urine osmolality of 972 mmol/kg (range 813-1135 mmol/kg). Jones and de Wardener pointed out that some people habitually drink very little and described two women who had urine osmolalities on a control day similar to those found after 48 hours of dehydration.

In our series seven of the 16 normal subjects achieved a maximum urine osmolality during control observations within the range found by Jones and de Wardener after 48 hours of dehydration, and all but two of the normal subjects achieved a maximum urine osmolality exceeding 850 mmol/kg during control observations—that is, within the range found by Jones and de Wardener in normal people after the administration of vasopressin tannate in oil. Our normal subjects were ambulant and performing their normal daily duties as doctors and medical technicians. Hence apparently a majority of young active people pass maximally concentrated urine at some time during an average working day. The time at which the maximally concentrated urine was passed varied considerably, and in half the subjects it was passed during the afternoon, no doubt reflecting individual patterns of activity, drinking, and insensible losses of fluid. Interestingly the maximally concentrated urine passed

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TABLE I—*Results in normal male ambulant subjects*

Subject	Age (years)	Creatinine clearance (ml/min)	Maximum urine osmolality (mmol/kg)		Plasma osmolality (mmol/kg)	
			Control	DDAVP	Control	DDAVP
1	39	132	899	1084	296	295
2	29	122	1020	1155	292	290
3	35	105	990	1015		
4	36	103	730	993		
5	44	108	1108	988	294	287
6	25	143	1119	1211		
7	57	107	996	1058	290	292
8	32	136	1001	1020	290	285
9	39	115	904	1023	297	294
10	28	90	1054	1037	290	286
11	27	97	773	980	276	280
12	26	113	1039	889	285	283
13	27	132	1215	1157	289	288
14	29	137	917	947	285	280
15	22	126	1229	1254	288	282
16	30	106	877	865	286	284
Mean ± SD	33 ± 9	117 ± 16	991 ± 140	1042 ± 108	289 ± 5·5	286 ± 5

Conversion: SI to traditional units—Urine and plasma osmolality: 1 mmol/kg = 1 mosmol/kg.

TABLE II—*Results in hospital inpatients*

Case No	Age (years)	Sex	Diagnosis	Creatinine clearance (ml/min)	Maximum urine osmolality (mmol/kg)	
					Control	DDAVP
1	30	M	Renal calculi	127	763	807
2	24	F	Renal calculi	91	736	805
3	34	F	Chronic pyelonephritis and calculi	82	631	838
4	28	M	Acute pyelonephritis and calculus	107	379	638
5	22	F	Acute pyelonephritis	64	733	770
6	49	M	Proteinuria and hypertension	144	868	913
7	27	M	Mild hypertension	130	770	885
8	55	F	Chronic pyelonephritis and calculi, and hypertension	58	577	622
9	49	M	Investigation of abnormal liver function values	86	592	804
10	58	M	Recurrent prostatitis	86	933	869
11	36	M	Mild hypertension	92	1073	1017
12	38	F	Right loin pain, normal blood pressure	97	892	994
13	44	M	Focal hyalinosis, normal blood pressure	95	873	901
Mean ± SD	38 ± 12			97 ± 25	755 ± 181	836 ± 117

Conversion: SI to traditional units—Urine osmolality: 1 mmol/kg = 1 mosmol/kg.

during the control period was not always that passed on rising in the morning after a night's sleep.

Of the 13 hospital inpatients, only five achieved a maximum urine osmolality exceeding 800 mmol/kg during the control period, presumably reflecting the reduced activity of such patients, with less insensible loss of fluid and possibly greater fluid intake than the normal ambulant and working subjects.

In active and ambulant subjects it therefore appears to be unnecessary to employ prolonged periods of dehydration or the administration of an antidiuretic to determine renal concentrating ability. If the urine osmolality exceeds 800 mmol/kg in any urine sample passed during a 24-hour control period then renal concentrating ability is normal. Allowance must, of course, be made for the progressive reduction in renal concentrating ability with age.[5] If the maximum urine osmolality is below 800 mmol/kg a test with intramuscular DDAVP should be given. In sedentary subjects or hospital inpatients it seems expedient to omit control observations and to measure the maximum urine osmolality achieved during the 24 hours after an intramuscular injection of 4 μg DDAVP with the subject on a normal fluid and dietary intake.

Intranasal DDAVP has been used in a short test of renal concentrating ability,[1–3] but we used the intramuscular route to ensure greater accuracy in dosage.

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ONE HUNDRED YEARS AGO Interesting further correspondence has, according to *Nature*, appeared in the British Guiana *Royal Gazette*, relative to the qualities assigned to the fruit of the papaw-tree. It has been recently asserted, in an article in the *Pharmaceutical Journal*, "that the most interesting property attributed to it is the power of its juice to render bad flesh tender." Mr Monro of Georgetown furnishes certain facts which, he says, are commonly known to the natives of British Guiana relative to this fruit. A horse tied near one of these trees rapidly loses health, and a stud horse becomes useless. Any pressure on the body of the animal leaves an inelastic indentation. The sap of the tree will soften steel; and, before the process of tempering was known in the colony, the blacksmiths used to drive their brittle chisels and plane vices into the wood, leaving them there for a day or two; and tough meat, wrapped in the leaf for only a few minutes, becomes tender; and the same thing happens if it be suspended against the tree itself. The seed of the ripe fruit is an excellent vermifuge, and children have a great partiality for it. (*British Medical Journal*, 1879.)