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Atrial natriuretic peptide is only a minor diuretic factor in dehydrated subjects immersed to the neck in water

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Summary. To determine if the atrial natriuretic peptide (ANP) is an important factor for inducing diuresis during head-out water immersion even in dehydrated subjects, six healthy volunteers were immersed up to the neck in water at 34.5° C for three hrs. Significant diuresis and natriuresis occurred, but urine osmolality decreased and negative C_{H_2O} was restored in a positive direction toward zero, even though subjects were still in a state of considerable dehydration. Plasma renin activity and plasma angiotensin I and II concentrations decreased but that of plasma aldosterone remained unchanged during water immersion, and plasma ANP did not increase thoughout the examination. On the basis of the data of the present study, the factor inducing diuresis during head-out water immersion in hydrated subjects appears to differ from that in dehydrated subjects, and the main factor inducing diuresis during water immersion in dehydrated subjects may be the suppression of vasopressin release and not ANP.

Key words: Atrial natriuretic peptide — Head-out water immersion — Diuresis - Free water clearance — Vasopressin — Renin — Aldosterone

Introduction

In a number of studies, the redistribution of blood volume due to head-out water immersion has been reported to result in significant and reproducible natriuresis in hydrated subjects (Graveline and Jackson 1962; Arborelius et al. 1972). Recently, increased atrial natriuretic peptide (ANP) concentration in the plasma has also been reported to occur during such immersion, and this is assumed to be one of the causes of diuresis in hydrated subjects (Ogihara et al. 1986; Berbes et al. 1986; Epstein et al. 1986).

Except in a few reports (Epstein et al. 1975; Norsk et al. 1986; Shiraki et al. 1986), examination of the hydrated condition was preceded by the administration of liquids and food before and during head-out water immersion. The present study was conducted to determine whether ANP is a main factor inducing diuresis even in water immersed dehydrated subjects.

Subjects and methods

Six healthy male volunteers between the ages of 19 and 24 years were used for the present study. The mean body weight was 58.9 ± 1.2 kg. None of the subjects had a past history of hyertension, diabetes, cardiovascular, renal or liver disease. Informed consent was obtained from each subject.

Following 14 h overnight dehydration, the subjects sat for a 60 min control period. Following this, they emptied their bladders and were then immersed up to the neck in water. All the subjects were seated in a study tank in this condition for 3 h. Before and during the examination, there was no administration of food or liquid. The temperature of the water was kept at 34.5 ± 0.5° C.

Blood samples were taken −60, 0, 30, 60, 120 and 180 min from the start of the examination, and urine samples were obtained at the same times as for blood except at 30 min. Circulating plasma volume (CPV) was measured using 1.0% Evans blue at 0 and 60 min after starting the examination. Plasma and urine ANP concentrations were measured by radioimmunoassay as previously reported (Marumo et al. 1986). Plasma renin activity (PRA) and plasma aldosterone concentration (PAC) were measured by radioimmunoassay (RIA). Plasma angiotensin I and II concentrations were also measured by RIA. Free water clearance (C_{H_2O}) was calculated by conventional formulae. Plasma Evans blue was measured by the method of Gregerson (1944). The data obtained were expressed as means ± SEM. For determination of statistical significance, Wilcoxon's paired test was used.

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Results

Blood chemistry and hormone concentration

Both prior to and during the experiments, subjects were permitted neither liquid nor food. The data obtained from the blood samples are shown in Table 1. Total protein concentration (TP) and hematocrit (Ht) significantly increased, and plasma osmolality (Posm) remained essentially the same, though its mean value increased during the immersion. PRA and angiotensin I and II concentrations decreased while PAC stayed the same. From these data, it appears that dehydration became more extensive during water immersion. However, circulation plasma volume did not significantly change during the first 60 min of the experiment. The plasma ANP concentration significantly decreased 3 h after the start of the experiment.

Urinary examinations

As shown in Table 2, urine volume significantly increased, while urine osmolality decreased. The

Table 1. The data obtained from the blood samples

	0	30	60	120	180 min
Posm ($mosmol \cdot h^{-1}$)	287 ± 2	289 ± 1	287 ± 1	289 ± 1	290 ± 1
PRA ($ng \cdot ml^{-1} \cdot h^{-1}$)	2.63 ± 0.75	1.75 ± 0.30	1.43 ± 0.28	1.28 ± 0.24*	1.07 ± 0.18*
Angiotensin I ($pg \cdot ml^{-1}$)	126.0 ± 47.2	45.0 ± 5.9	45.5 ± 4.8	57.7 ± 20.5	56.3 ± 21.6*
Angiotensin II ($pg \cdot ml^{-1}$)	64.7 ± 5.0	44.5 ± 5.2*	44.7 ± 4.6*	32.7 ± 4.0***	38.2 ± 3.0***
PAC ($ng \cdot ml^{-1}$)	10.7 ± 0.61	10.5 ± 1.36	9.83 ± 1.33	8.67 ± 1.15	10.3 ± 1.31
ANP ($pg \cdot ml^{-1}$)	84.7 ± 18.2	80.9 ± 19.7	79.7 ± 14.4	69.8 ± 11.7	69.8 ± 15.4**
CPV (ml)	3635 ± 395		3143 ± 269		
TP ($g \cdot dl^{-1}$)	6.8 ± 0.1	6.9 ± 0.2	7.0 ± 0.2	6.9 ± 0.1	7.1 ± 0.1*
Ht (%)	45.2 ± 0.9	45.3 ± 0.8	44.8 ± 1.0	45.7 ± 1.0	46.4 ± 0.6*

* $p<0.05$, ** $p<0.02$, *** $p<0.005$

Table 2. The data obtained from the urine samples

	0	60	120	180 min
Urine volume ($ml \cdot min^{-1}$)	0.92 ± 0.46	3.08 ± 1.10*	2.22 ± 0.66*	2.28 ± 0.38*
$U_{Na} \cdot V$ ($\mu eq \cdot min^{-1}$)	149 ± 21.6	371 ± 153*	271 ± 58*	279 ± 30*
$U_K \cdot V$ ($\mu eq \cdot min^{-1}$)	70 ± 13	107 ± 32	57 ± 8	50 ± 7
Uosm ($mosmol \cdot l^{-1}$)	897 ± 102	634 ± 152*	538 ± 110***	437 ± 64***
C_{H_2O} ($ml \cdot min^{-1}$)	−2.13 ± 0.49	−1.81 ± 1.15	−1.07 ± 0.58***	−0.88 ± 0.27***
Ccr ($ml \cdot min^{-1}$)	203 ± 22.8	177 ± 7.1*	125 ± 15**	114 ± 8**
U_{ANP} ($pg \cdot min^{-1}$)	36.5 ± 14.1	28.8 ± 16.8	16.7 ± 9.5**	13.0 ± 5.7**
FE_{Na} (%)	0.77 ± 0.21	1.08 ± 0.19**	1.37 ± 0.19**	1.75 ± 0.21**
FE_{ANP} (%)	0.27 ± 0.08	0.21 ± 0.05	0.24 ± 0.09	0.26 ± 0.13

* $p<0.05$, ** $p<0.01$, *** $p<0.005$

urinary excretion of sodium (U_{Na}) significantly increased, while change in that of potassium (U_K) was without significance. C_{H_2O} was restored in a positive direction towards zero. Creatinine clearance (Ccr) decreased. The fractional excretion of sodium (FE_{Na}) increased that of ANP (FE_{ANP}), but not significantly.

Figure 1 shows the changes in urine volume, Uosm, Posm and C_{H_2O}. Urine volume and C_{H_2O} significantly increased while Uosm decreased. Posm also increased but this could be detected after 1 h following the start of the experiment. It thus appears that diuresis occurred as a result of water reabsorption in the kidney.

Figure 2 shows changes in PRA, plasma angiotensin I and II concentrations and PAC. All hormone concentrations except that of aldosterone significantly decreased during water immersion.

Plasma ANP concentration was noted to change only after 2 hrs following the start of the experiment, and underwent statistically significant decrease near the termination of the experiment, as evident from Fig. 3.

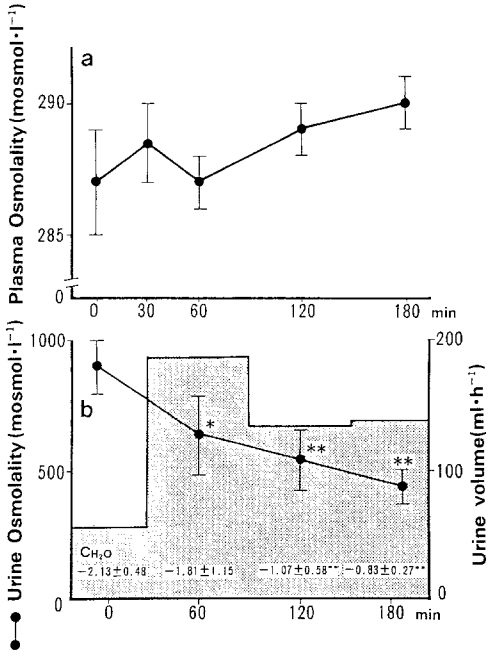

Fig. 1. The changes in urine volume, Uosm, Posm and C_{H_2O} during water immersion. **a** change in plasma osmolality *(Posm)*. The mean increased, but not statistically significantly. **b** changes in urine volume, urine osmolality *(Uosm)* and free water clearance (C_{H_2O}). Closed circles connected by solid line indicate Uosm. Vertical line indicates mean ±SEM. * $p<0.05$, ** $p<0.005$

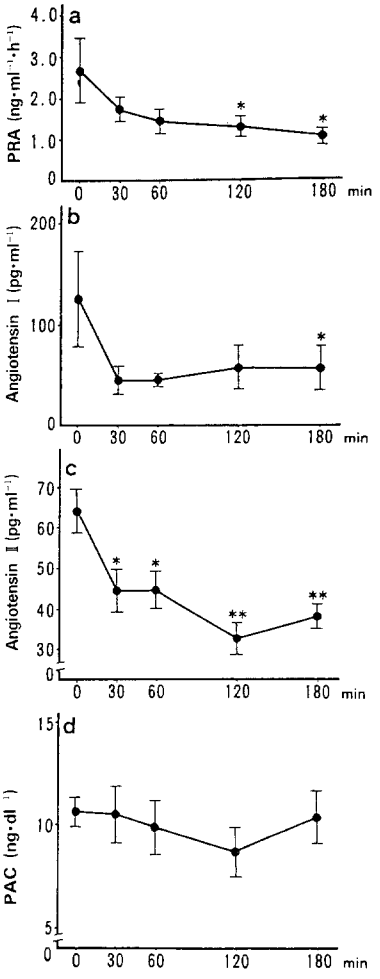

Fig. 2. The changes in PRA, plasma angiotensin I and II and aldosterone concentrations. **a** aldosterone *(PAC)*; **b** angiotensin II; **c** angiotensin I; **d** plasma renin activity (PRA). * $p<0.025$, ** $p<0.005$

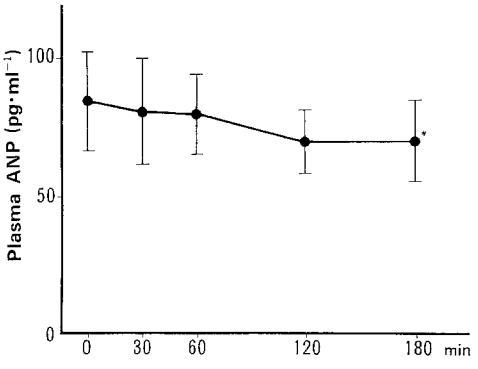

Fig. 3. The change in plasma ANP during water immersion. * $p<0.02$

Discussion

Behn et al. (1969) were among the first to study the effects of head-out water immersion resulting in significant diuresis and increased central blood volume, heart volume and cardiac output and decreased total peripheral resistance. Epstein (1976) confirmed central hypervolemia with increased cardiac output and natriuresis, kaliuresis, and diuresis to be associated with the prompt important suppression of PRA and PAC. Plasma vasopressin concentration (PVC) was found not to change during water immersion (Greenleaf et al. 1983; Kravik et al. 1984; Ogihara et al. 1986); their subjects were hydrated by the intake of drinks and food before and during the experiment.

It would be quite difficult to show conclusively that the rapid decrease reported in PAC (Epstein 1976) is a cause of natriuresis, since change in sodium reabsorption in the kidney requires at least a 90 min time delay after altering PAC (Edelman 1975). Thus diuresis, natriuresis and kaliuresis may be induced mainly by increased plasma ANP concentration due to central hypervolemia in water immersed hydrated subjects (Ogihara et al. 1986; Berbes et al. 1986; Epstein et al. 1986). The data of the above authors using hydrated subjects are valid, in that central hypervolemia may increase left atrial pressure, resulting in increased ANP secretion. Thus, ANP induced diuresis, natriuresis and kaliuresis (Cody et al. 1986).

Several researchers (Epstein et al. 1975; von Ameln et al. 1985; Norsk et al. 1986; Shiraki et al. 1986) reported that PVC was suppressed in water immersed subjects dehydrated by previous liquid deprivation. Unfortunately, they did not examine changes in the renin-angiotensin-aldosterone system or ANP concentration in plasma. Harrison et al. (1986) reported that both PRA and PAC were suppressed independently of hydration status, while PVC was suppressed during dehydrated immersion. We employed essentially the same conditions as those of Epstein (1975), whose subjects were examined following overnight dehydration. PRA and angiotensin I and II concentrations in plasma decreased but PAC remained about the same. There was no increase in plasma ANP concentration during the examination. However, urine osmolality significantly decreased and C_{H_2O} was restored to zero, even though the extent of dehydration was considerable. Central hypervolemia in hydrated subjects occurs in water immersion, causing increased plasma ANP concentration and decreased PRA and PAC. In dehydrated subjects, slight central hypervolemia may occur with progressive dehydration and renal blood flow decreases during water immersion. In a state of dehydration, water immersion was found in this study to suppress vasopressin release and decrease PRA, angiotensin I and II concentrations but to have no effect on PAC. It decreased plasma ANP concentration. These findings, along with other data of the present research, support the hypothesis that suppression of vasopressin release during water immersion in dehydrated subjects is the main factor inducing diuresis. However, natriuresis cannot be explained entirely on the basis of decreased FE_{Na} or suppressed vasopressin release. Other factors inducing natriuresis such as cathecholamines should also be considered.

In conclusion, the main factor inducing diuresis in hydrated water immersed subjects appears conclusively to differ from that in dehydrated subjects, and diuresis induced by water immersion in dehydrated subjects may occur due, not to increased plasma ANP concentration, but mainly to suppressed vasopressin release.

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