600

hirayama A[1], fujimoto K[1], tannbo M[1], momose H[1], hirao Y[1]
1. Nara medical university

THE CIRCADIAN RHYTHM DISORDER OF AVP COULD BE PREDICTED BY A SIMPLE AND NON-INVASIVE TEST VIA MEASURING URINE CONCENTRATIONS OF AVP

Hypothesis / aims of study

The increase in the nocturnal urine volume is one of the important factors that cause nocturia in elderly men. The circadian rhythm deficiency of arginine vasopressin (AVP) was strongly suggested to be responsible for this increase in the nocturnal urine volume. To determine whether the nocturnal voided volume is associated with the endocrine status of AVP and to evaluate the correlation between the plasma and urine concentrations of AVP (P_{AVP} and U_{AVP}), we measured P_{AVP} and U_{AVP} of in-patients with various urological diseases**.**

Study design, materials and methods

A total of 36 in-patients without heart failure, diabetes mellitus, diabetes inspidus or renal failure (31 men and 5 women older than 50 years of age) were enrolled in this study. All patients underwent the following test after explanation of the aim and methods of this study, and informed consent was obtained. Their water intake was restricted to 25 ml/kg/day for at least one day before taking sample materials. The blood and urine samples were taken every 6 hours (at 6:00 am, 12:00 am, 6:00 pm and, 12:00 pm)(fig1). To eliminate the posture influence on P_{AVP} by the cardiovascular and hormonal dynamics at the time of blood sampling, all patients were placed at rest in the supine position for 30 min before sampling. The blood and urine samples were submitted for the measurement of concentrations (P_{AVP} and U_{AVP}) and the osmolality. The urine samples were also submitted for creatinine (Cr) measurement for adjusting U_{AVP} by the urine creatinine level to $U_{AVP/Cr}$. The nocturnal voided volume was defined as the total amount of urine volume recorded on the frequency volume chart (FVC) between 10:00 pm (lights-out) and 6:00 am (lights-on), including the first voided volume after arising.

Results

The patients' characteristics are shown in Table 1. Nocturnal voided volume greater than 35% of the 24-hour production was defined as nocturnal polyuria (NP). Nineteen and 17 patients were classified into the group with NP and the group without NP, respectively. There was no significant difference in the age and Cr clearance between the two groups. On the FVC, a significant difference was seen in the nocturnal voided volume between the two groups whereas there was no difference in 24-hour production and the 24-hour frequency between them. There was no significant difference in P_{AVP} at each sampling time between the two groups, but $U_{AVP/Cr}$ at 12:00 pm and 6:00 am in the group with NP were significantly smaller than those in the group without NP. The nocturnal voided volume showed a correlation with P_{AVP} at 12:00 pm and $U_{AVP/Cr}$ at 6:00 am. The coefficient of correlation showed that U_{AVP} at 6:00 am seemed to have a mildly stronger correlation with the nocturnal voided volume than P_{AVP} at 12:00pm (P_{AVP} at 12:00 pm: r=0.33, p=0.047, $U_{AVP/Cr}$ at 6:00 am: r=0.46, p=0.005). There were positive correlations between P_{AVP} and $U_{AVP/Cr}$ at the same sampling time, as well as between P_{AVP} at 12:00 pm and $U_{AVP/Cr}$ at 6:00 am as shown in Table 2.

Interpretation of results

The correlation between the nocturnal voided volume and U_{AVP} at 6:00 am, with a stronger correlation coefficient than P_{AVP} at 12:00 pm, suggested that the nocturnal decrease in AVP secretion was an important factor, which increased the nocturnal voided volume as a representative cause of nocturia.

Concluding message

The present data clearly demonstrated that the significant decrease in $U_{AVP/Cr}$ at 6:00 am led to nocturia due to increased nocturnal voided volume, and that the circadian rhythm disorder of AVP could be predicted by a simple and non-invasive test via measuring $U_{AVP/Cr}$ at 6:00 am.

Fig1 **Time schedule of this study**

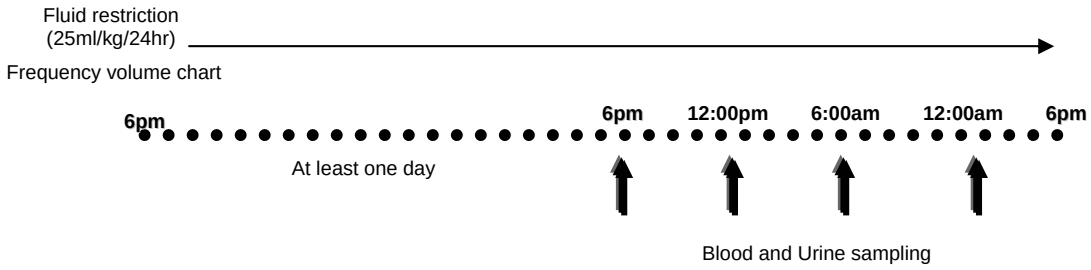

Table.1
Patients characteristics compared between the 2 groups with or whithout nocturnal polyuria

	no NP(n=17)			NP(n=19)			p value
Age (yrs)	67.4	±	8.5	72.8	±	7.3	n.s.
Ccr(ml/mim)	74	±	18	80	±	25	n.s.
men/women	14	/	3	17	/	2	n.s.
24-hour production(ml)	1479	±	384	1527	±	397	n.s.
24-hour frequency	10.2	±	2.5	10.4	±	2.7	n.s.
Nocturnal urine volume(ml)	351	±	156	698	±	198	p<0.0001
P_{AVP} 6:00pm (pg/ml)	1.8	±	1.8	1.1	±	1.3	n.s.
P_{AVP}12:00pm	1.5	±	1.5	1	±	1	n.s.
P_{AVP} 6:00am	1.2	±	0.9	1	±	0.8	n.s.
P_{AVP}12:00am	1.5	±	0.9	1.2	±	1	n.s.
U_{AVP}/Cr 6:00pm (pg/ml/Urine Cr)	20.1	±	26.3	12.7	±	9.3	n.s.
U_{AVP}/Cr12:00pm	18.6	±	18.9	8.8	±	5.8	p<0.03
U_{AVP}/Cr 6:00am	22.7	±	18.1	12	±	7.6	p<0.04
U_{AVP}/Cr12:00am	28.2	±	23.4	17.8	±	12.5	n.s.

Table2

Correlation between P_{AVP} and U_{AVP} of each sampling time

		P_{AVP}							
		6:00pm		12:00pm		6:00am		12:00am	
		p=	r=	*p*=	r=	*p*=	r=	*p*=	r=
U_{AVP}	6:00pm	0.056	0.33						
	12:00pm	0.06	0.32	0.039	0.34				
	6:00am			0.0048	0.46	<0.0001	70		
	12:00pm					0.054	0.33	0.036	0.5