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NOCTURNAL POLYURIA AND NOCTURNAL ARGININE VASOPRESSIN (AVP): A KEY FACTOR IN THE PATHO-PHYSIOLOGY OF MONOSYMPTOMATIC NOCTURNAL ENURESIS

Hypothesis / aims of study

The lack of circadian rhythm of plasma arginine vasopressin (AVP) in primary nocturnal enuresis is still a mater of debate by some authors. The goal of the presented study is to identify the relationship between AVP deficiency, nocturnal polyuria and low urinary osmolality in children suffering of primary monosymptomatic nocturnal enuresis (NE).

Study design, materials and methods

The study was carried out on two groups. Group A: 50 children (28 males and 22 females) with primary monosymptomatic nocturnal enuresis of age 7-15 years old and group B: 30 non enuretic children of the same age group. Enuretic children are chosen to be bed wetting 2 or more times per week and stopped any medication for the treatment of enuresis 2 weeks prior to the study. A 24 hour frequency volume chart was obtained for group A in a day of average fluid intake. Nocturnal polyuria (NP), which was defined as nocturnal urine production during the period of sleep which equals to or more than 130% of estimated bladder volume for age(1). The last voiding volume before sleep is excluded while the first volume voided in the morning is included. Twenty four hour urine volume and frequency were recorded by the mother and she was instructed to let the child void before sleep then at 12 am, 4 am and 8 am. The voided urine volume before sleep considered to be a part of diurnal urine production. If an enuretic episode occurred, the diary was repeated in another day and the mother was instructed to wake the child to void more frequently by night and collect the volumes and record it. For the estimation of nocturnal plasma level of AVP in both groups A and B we used Correlate-EIA™ which is an Arg^8-Vasopressin enzyme immunoassay, Samples were withdrawn at 2 am in a day of average water intake with 4 hours fluid restriction before sampling. Samples were withdrawn on EDTA 1 mg/ml blood and centrifuged at 18,000 rpm for 15 minutes. Plasma is then separated and stored in a temperature of -70 ^oC until time of usage. At the same time a sample was withdrawn for blood osmolality. For the estimation of nocturnal urinary osmolality in both groups, the children voided at 8 pm then 3 urine samples were obtained at 12 am, 4 am and 8 am, the mathematical mean was calculated for the three samples and the result was considered to be the urine osmolality ,(U osm). The results of AVP level and nocturnal urine osmolality were compared in both groups. Comparison between the two groups was done by Student t test. *P* value of 0.05 or less was considered statistically significant. When more than 2 groups were compared, ANOVA test with post Hoc analysis was used to compare means. All numbers in the text are mean ± standard deviation (SD).

Results:

Of the 50 enuretic children included in the study we found that 29 (58%) children were considered to have nocturnal polyurea and 21 children did not. Table (1)

Table(1)

	number of children	children with nocturnal polyuria
Males	28	17(60.7%)
Females	22	12(54.54%)
Total	50	29

Mean AVP level was 32.49 ± 18.251 pg/ml in enuretic group and was 44.80 ± 18.194 pg/ml in control group with p value 0.005 which indicated significant difference between both groups.

Mean urine osmolality for enuretics and controls respectively was 690.46 ± 159.61 mOsm/L and 865.06 ± 158.658 mOsm/L, this difference was highly significant ($p<0.001$). When the enuretic group was subdivided according to the presence or absence of nocturnal polyuea, no significant difference was found between the controls and enuretics without NP. On the other hand, significant difference was found between the controls and NE patients with NP. Furthermore, significant difference was found between patients with and without nocturnal polyuria within the NE group. Similar findings were found when the means of urine and blood osmolality were compared. (Table 2).

(Table 2).

	Blood osmolality		Urine osmolality		AVP	
	mean	SD	mean	SD	mean	SD
control	850.46*	123.07	865.06*	158.65	44.80*	18.19
Enuretics without NP	881.54#	115.02	814.68#	137.64	46.98#	16.68
Enuretics with NP	781.03*#	124.21	610.00*#	166.94	21.10*#	9.06

* Statistical significance between controls and enuretics with NP

\# Statistical significance between enuretics with NP and enuretics without NP

Interpretation of results

In our study, enuretics showed decreased mean nocturnal AVP level as compared to non enuretics, and this difference was statistically significant. Furthermore, measuring the mean nocturnal urinary osmolality in both groups showed that it was much lower in enuretics. Also the presence of nocturnal polyuria in the enuretic group in 58% supports the theory that deficiency of AVP and production of large amounts of hypo-osmolar urine during night is a significant cause of mono symptomatic nocturnal enuresis. However, it is not clear whether the low blood osmolarity of these patients is the trigger for decreased production of AVP. The normal levels of AVP in NE patients without NP refutes this factor as a causative agent for NE in this subtype of patients

Concluding message

We conclude that monosymptomatic enuresis in children is frequently associated with a decreased nocturnal AVP excretion, together with an increased nocturnal urine production. Nocturnal enuresis pathopysiology apparently include different subtypes of patients. We have shown that urine and blood osmolality, and nocturnal AVP in patients suffering monosymptomatic nocturnal

enuresis with nocturnal polyuria are lower than those of both enuretic patients without nocturnal polyuria and normal individuals. This may have a future impact on the treatment offered to these subtypes of patients.

References

1- J Urol 2006; 176:314

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Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Ain shams university ethics committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**