

FACTORS AFFECTING NOCTURNAL POLYURIA IN THE ELDERLY PATIENTS

Hypothesis / aims of study

The increase in nocturnal voided volume plays an important role in nocturia. Although many pathologic conditions leading to nocturnal polyuria (NP) exist, NP can be attributed to water diuresis or solute diuresis as diuresis takes place in the kidney. It was reported that the urinary AVP/urinary Cr (uAVP/uCr) in the early morning can substitute for the

secretion of AVP during nighttime.

The aims of study were to investigate the risk factors affecting NP and to fix cut off a value of uAVP/uCr in the early morning for NP.

Study design, materials and methods

A total 197 patients above 50 years of age were enrolled in this study. The exclusion criteria were those who had past history of heart disease or were treated for heart disease, diabetes mellitus with fasting blood glucose of 200 mg/dl or greater, renal failure (creatinine: Cr > 1.5), those who had hydronephrosis on ultrasound examination, PVR (> 50 ml), those with urinary incontinence frequent enough to interfere with urinary output measurement, those with active urinary tract infection, those taking diuretics or medications including lithium, and those whose 24-hour production exceeded 40 ml x weight. After the objective and method of this study, approved by our Institutional Reviewer Board, were fully explained, informed consent was obtained from all patients. The nocturnal urine volume (NUV) was conveniently defined as the total amount of urine recorded on the frequent volume chart between 22:00 and 6:00 including the first voided volume after arising from bed. All patients submitted single voided urine sample at 6:00. AVP, osmolarity, sodium and Cr in the urine were measured. We selected three definitions of NP as follows: nocturnal urine volume/24-hour production (NPI) > 0.33, nocturnal urine volume (NUV) > 0.9 ml/min x sleeping time, and NUV/weight > 10 ml/kg. Logistic regression was used for analysis of the associated factors correlating with NP. The variables were considered for the multivariate models if their univariate P value was less than 0.1.

Results

The data of 160 eligible patients (138 men and 22 women) were finally evaluated. The mean age of all patients was 71.5 ± 8.0 years. The biologically plausible factors (age, sex, weight, plasma electrolytes (Na, Cl, K, Ca), Ccr, uAVP/uCr, uNa/uCr, 24-hour production, and blood pressure (systolic and diastolic) were included. In the multivariate logistic model, uAVP/uCr and age were independent affectors for nocturia in each definition of NP. The 24-hour production was significant in the NP definitions except for NPI > 0.33 (table 1). Although there was no correlation between age and NUV, there were a significant correlation between NUV and 24-hour production as well as uAVP/uCr (24-hour production: p < 0.0001, r = 0.60, uAVP/uCr: p < 0.0001, r = -0.48). The cut off value of uAVP/uCr for NP in each definition that yielded the highest combined sensitivity and specificity was 22.9 pg/ml (NPI > 0.33), 28.7 pg/ml (0.9 ml/min x sleeping time < NUV), and 23.2 pg/ml (NUV/weight > 10 ml/kg). At these cut off values, the sensitivity was 63%, 80%, and 81%, and the specificity was 66%, 61%, and 68 %.

Interpretation of results

Water diuretics mainly contributed to NP in elderly people, because uAVP/uCr, not uNa/uCr, was an independent affector for NP in each definition of NP.

Although Age was an independent affector for NP in each definition of NP, it did not correlate with NUV. This phenomenon may imply that aging may contribute to the increase in the number of patients who have some NUV. Indeed, it was reported that aging led to an increase in NPI and the number of patients who had nocturia due to NP.

Any increasing in the 24-hour production; i.e., over hydration, brings about decrease not only in the secretion of AVP but also in the corticopapillary osmotic gradient. This phenomenon explains why the 24-hour production may be an independent affector for NP.

Concluding message

The decision making in treatment of nocturia may become easier by making use of the cut off value of uAVP/uCr in the early morning. Nevertheless, we must take into consideration that the 24-hour production is an independent affector for NP when we treat nocturia in patients with NP. When uAVP/uCr does not exceed the cut off value, the standard treatment for nocturia in the patients with NP is proper fluid intake in the first place and secondly prescribing medications such as ADH replacement therapy for the patients who can restrict their fluid intake safely.

Table1.Multivariate analysis on associated variables correcting with nocturnal polyuria

| | Univariate analysis | | | | | | Multivariate analysis | | | | | |
|-----------------------|---------------------|-------------|----------------------------------|-------------|------------------------|-------------|-----------------------|-------------|----------------------------------|-------------|------------------------|-------------|
| | NPI>0.33 | | NUV>0.9ml/min x sleeping time | | NUV/weight> 10ml/kg | | NPI>0.33 | | NUV>0.9ml/min x sleeping time | | NUV/weight> 10ml/kg | |
| | Odds ratio | p- value | Odds ratio | p- value | Odds ratio | p- value | Odds ratio | p- value | Odds ratio | p- value | Odds ratio | p- value |
| Age(y.o.) | 1.06 | 0.0043 | 1.04 | 0.043 | 1.04 | 0.06 | 1.07 | 0.0045 | 1.12 | 0.0002 | 1.10 | 0.002 |
| Sex | 1.06 | 0.34 | 1.6 | 0.31 | 0.66 | 0.37 | | | | | | |
| Weight(kg) | 0.99 | 0.54 | 1.03 | 0.15 | 0.97 | 0.11 | | | | | | |
| Na(meq/l) | 0.86 | 0.06 | 0.91 | 0.23 | 0.89 | 0.19 | 0.92 | 0.36 | | | | |
| Cl(meq/l) | 1 | 0.79 | 1 | 0.89 | 0.99 | 0.51 | | | | | | |
| K(meq/l) | 1 | 0.88 | 1 | 0.77 | 1.01 | 0.73 | | | | | | |
| Ca(mg/dl) | 1.48 | 0.38 | 1.96 | 0.14 | 0.89 | 0.81 | | | | | | |
| CCr(mg/dl/min) | 0.99 | 0.13 | 0.99 | 0.11 | 0.99 | 0.13 | | | | | | |
| uAVP/uCr(pg/ml/Cr) | 0.98 | 0.009 | 0.96 | <0.0001 | 0.94 | <0.0001 | 0.98 | 0.0027 | 0.96 | 0.0003 | 0.93 | <0.0001 |
| uNa/uCr(meq/l/Cr) | 1.07 | 0.43 | 1.01 | 0.93 | 0.98 | 0.82 | | | | | | |
| 24hour production(ml) | 1 | 0.87 | 1.003 | <0.0001 | 1.003 | <0.0001 | | | 1.003 | <0.0001 | 1.003 | <0.0001 |
| Systolic(mmHg) | 1 | 0.91 | 0.99 | 0.47 | 0.99 | 0.36 | | | | | | |
| Diastolic(mmHg) | 0.98 | 0.19 | 0.97 | 0.15 | 0.99 | 0.47 | | | | | | |

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CLINICAL TRIAL REGISTRATION: This clinical trial has not yet been registered in a public clinical trials registry.

HUMAN SUBJECTS: This study was approved by the nara medical university and followed the Declaration of Helsinki Informed consent was obtained from the patients.