Nocturnal Polyuria: Excess of Nocturnal Urine Production, Excess of Definitions—Influence on Renal Function Profile

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Abbreviations and Acronyms

FWC = free water clearance
NI = nocturia index
NP = nocturnal polyuria
NPI = NP index
NUP = nocturnal urine production
RFP = renal function profile

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Purpose: This study aimed to identify important differences in renal function profile, and potential water and sodium diuresis cutoffs among participants with nocturnal polyuria according to nocturnal polyuria definitions.

Materials and Methods: This post hoc analysis was based on a prospective study in which participants completed a bladder diary, collected urine and provided a blood sample. With an age dependent nocturnal polyuria index greater than 20% to 33% as the referent 4 definitions of nocturnal polyuria were compared, including 1) nocturnal polyuria index greater than 33%, 2) nocturnal urine production greater than 90 ml per hour and 3) greater than 10 ml/kg, and 4) nocturia index greater than 1.5.

Results: In 112 male and female participants significant differences in baseline characteristics and bladder diary parameters were found according to definition. Diuresis rate, free water clearance and sodium clearance had similar 24-hour courses in the subgroups with and without polyuria by each definition. The range varied more in the subgroup with vs without polyuria, especially at night for diuresis rate and free water clearance. At night the latter decreased in the polyuria subgroup based on each definition ($p < 0.001$ to 0.045). A significant difference vs the no polyuria subgroups was found only for urine production greater than 90 ml per hour and polyuria index greater than 20% to 33%. For each definition sodium clearance remained high in the polyuria subgroup, which differed significantly from the no polyuria subgroups ($p < 0.001$ to 0.030). Free water and sodium clearance cutoffs ranged from −0.65 to −0.85 ml per minute between 12 and 2 a.m., and 0.65 to 0.77 ml per minute between 3 and 5 a.m., respectively, with large sensitivity and specificity differences according to definition.

Conclusions: There were important differences when comparing participants with vs without nocturnal polyuria by definition. The renal function profile indicating the pathophysiological mechanism of nocturnal polyuria did not seem to be influenced by definition but free water clearance and sodium clearance cutoff sensitivity differed substantially. These results must be confirmed in a larger homogeneous sample.

Key Words: kidney, urinary bladder, polyuria, nocturia, diuresis

Nocturnal polyuria is an underestimated and underreported condition, although it is an important cause of nocturnal enuresis in children and of nocturia and urinary incontinence in adults.[1,2] In children

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NP is defined as NUP greater than 130% of expected bladder capacity for age but in adults the number of proposed definitions of NP seem to be infinite.[3] This large variety of definitions compromises the ability to draw conclusions regarding an unambiguous diagnostic and therapeutic approach. There are different types of definitions, including relative definitions in which NUP is set out against 24-hour urine production, absolute definitions based on urine production per time unit or per kg and functional definitions in which urine output is linked to bladder capacity.[4]

NP can be caused by water diuresis due to an impairment in the circadian rhythm of antidiuretic hormone and/or by sodium diuresis due to an impairment in salt regulating hormones such as aldosterone and atrial natriuretic peptide.[5] RFP with measurement of free water and sodium clearance at different time points during 24 hours can reveal the underlying pathophysiological mechanism. With the definition of NPI above 20% to 33% depending on age FWC at the beginning of the night exceeding −0.85 ml per minute correlates to water diuresis while sodium clearance in the middle of the night exceeding 0.65 ml per minute correlates with sodium diuresis.[6]

The question is whether the definition of NP significantly affects the ability to identify the underlying pathophysiological mechanism. This study aimed to compare RFP results in an adult population based on different NP definitions.

MATERIALS AND METHODS

This is a descriptive post hoc analysis of a prospective observational study performed between October 2011 and May 2013. Participants were recruited via posters, brochures and consultations. Healthy nonhospitalized participants with stable renal function were included in analysis. Exclusion criteria were neurogenic bladder, and/or bladder or urethra surgery, 24-hour polyuria (greater than 40 ml/kg/24 hours) and severe urinary incontinence (more than occasional urine leakage).

Participants were asked to complete a bladder diary, collect a RFP and provide a blood sample. Participants who failed to complete the different study parts were excluded.

A bladder diary was collected for 24 hours on 3 separate days starting from the second micturition in the morning until the first micturition the next morning, comprising nocturnal volume. Micturition and drinking frequency and volumes had to be recorded together with the time of going to bed and getting up in the morning.

RFP was determined in urine samples every 3 hours during 24 hours by analysis of diuresis rate, osmolality and sodium concentration. This was done on a day other than the documentation days for the bladder diary. Micturition volume at the time of sample collection had to be documented as well as the volume of any interim micturition to calculate the correct diuresis rate. This test started in the morning with the first sample obtained 3 hours after the first morning micturition.

Serum osmolality and sodium were analyzed in a blood sample. They were used to calculate the renal clearance of each of these substances using the equations, FWC = urine flow − (urine osmolality × urine flow)/plasma osmolality) and sodium clearance = (urine sodium × urine flow)/plasma sodium.

The definitions used to determine NP were 1) the ratio of nocturnal urine production to 24-hour urine production (NPI) above 33%, 2) NUP higher than 90 ml per hour, 3) NUP higher than 10 ml/kg body weight and 4) the ratio of nocturnal urine volume and maximum single voided volume (NI) above 1.5. The NPI greater than 20% to 33% definition served as a referent for all results.[6]

Statistical analysis was performed with SPSS®, version 21. For population characteristics the median and IQR were calculated. For RFP results median values were calculated and presented. The statistical significance of differences between 2 nonparametric variables was analyzed with the Mann-Whitney U test and among related variables it was analyzed by the Friedman test. A ROC was used to determine cutoff values with the highest sensitivity and specificity, and $p > 0.05$ considered statistically significant. This study was approved by the Ghent University Hospital review board (EC 2011/565). The Declaration of Helsinki was adhered to and written informed consent for study participation was obtained from all participants.

RESULTS

A total of 112 participants with a mean ± SD age of 57 ± 16 years were included in analysis. Of the participants 41% were female.

Population

Table 1 lists the general and bladder diary characteristics of the study sample based on the 4 study definitions. Of the study sample 69% and 43% presented with NP at NPI greater than 20% to 33% and greater than 33%, respectively. Of the sample 30% and 27% presented with NP at NUP greater than 90 ml per hour and greater than 10 ml/kg, respectively, and 45% presented with NP at NI greater than 1.5. The prevalence of NP differed significantly according to the chosen definition ($p < 0.001$). Results based on the NPI greater than 20% to 33% definition served as the referent since NPI showed no significant difference according to age, gender, body mass index or bladder diary parameters except nocturnal voided volume and nocturnal voiding frequency.[6] According to the chosen NP definition significant differences in these characteristics were found in patients with vs without NP (table 1).

Participants with NP based on the referent definition (NPI greater than 20% to 33%) presented with significantly higher nocturnal voided volume ($p > 0.001$) and voiding frequency at night ($p > 0.006$)