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THE EFFECT OF DDAVP ON THE CIRCADIAN RHYTHM IN URINE EXCRETION: A STUDY IN ELDERLY AND YOUNG VOLUNTEERS.

Aims of Study

Impaired ability of the ageing kidney to concentrate urine has been demonstrated in humans. Moreover the circadian rhythm of the 24-hour urine excretion changes considerably with age. Healthy young persons excrete less than 20% of their total during the night whereas healthy elderly persons have a nocturnal urine excretion of 33% or more of the daily output. Desmopressin (dDAVP) is a synthetic analogue (V_2 receptor agonist) to AVP and mimics the anti-diuretic effect of the natural occurring hormone which makes it useful for managing a number of disorders involving regulation of the urine production such as nocturia, enuresis nocturna and diabetes insipidus. The aim of this study was to look further into the changes in the circadian urine excretion in elderly and young healthy volunteers following a single oral dose of dDAVP.

Methods

Healthy elderly (=65 years) and young (aged 20-40 years) volunteers were included in the study. Health was confirmed by a thorough history taking and a physical examination excluding any clinically significant disease. Any kind of lower urinary tract symptom apart from nocturia led to exclusion. The participants were admitted to the hospital for 48 hours. From two days prior to hospitalisation and during the hospital stay the amount of fluid intake was standardized to a daily intake of 25mL/kg BW/24 hours. The participants were asked to empty their bladder at least every 3 hours during daytime in separate bottles. The nighttime was represented by only one collection comprising any voiding during the night and the first morning void. From the individual urine samples urine volume (U_{vol}) was determined. The first 24 hours were spent at baseline conditions. On the second night the participants were given a single oral dose of desmopressin 0.4mg followed by another 24 hours of urine sampling.
Repeated measurement analysis, one way ANOVA and t-tests were used when appropriate. Results were considered significant when $p<0.05$. Pearson's correlation coefficient was calculated to reveal pairwise correlations.

Results

The group of elderly participants were sub-grouped according to the size of nocturnal urine excretion in elderly nocturnal polyurics (> 33% urine excretion during nighttime) and elderly controls. There was a borderline significant difference in the baseline nocturnal urine excretion fraction of the daily total between young and elderly controls (fig. 1).

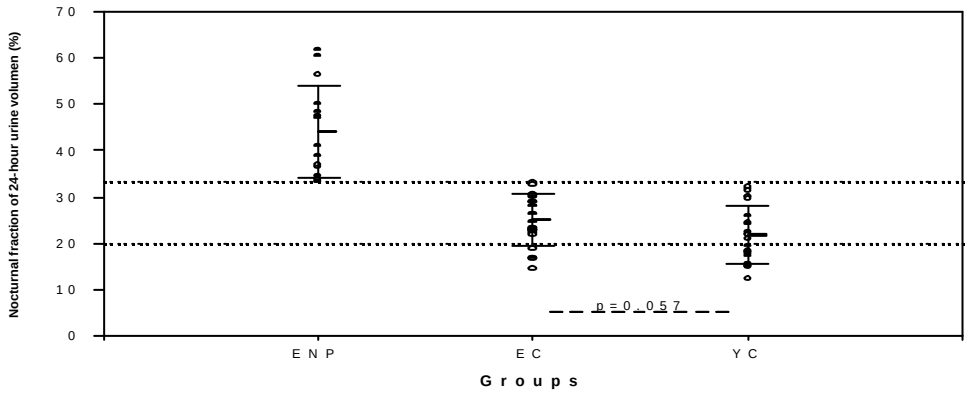

Fig. 1. Baseline nocturnal urine excretion fraction of the daily total. ENP=elderly nocturnal polyurics, EC=elderly controls, YC=young controls.

At baseline the circadian rhythm of the diuresis differed significantly between groups ($p<0.001$), the most notable differences being between the elderly nocturnal polyurics and the control groups during nighttime and mid-afternoon (fig.2). After dDAVP the differences between the two groups of elderly levelled out (fig.2), but between the age groups the peak diuresis of the day varied; the young controls peaked in the middle of the afternoon followed by a decrease to baseline levels, whereas the elderly peaked at the end of the 24-hour registration period. There was no difference in 24-hour diuresis between groups but the young controls had a significantly higher 24-hour diuresis after dDAVP (0.97±0.04mL/h/kg) compared to baseline (1.18±0.06mL/h/kg).
In all 3 groups there was a significantly change in diuresis over time after a single dose of dDAVP ($p<0.001$) with a shift in urine excretion from nighttime to late afternoon and evening the following day (fig. 3).
There was a positive correlation between baseline nocturnal diuresis and the change in nocturnal diuresis from baseline to dDAVP ($?_{Pearson}=0.84$, $p<0.001$).

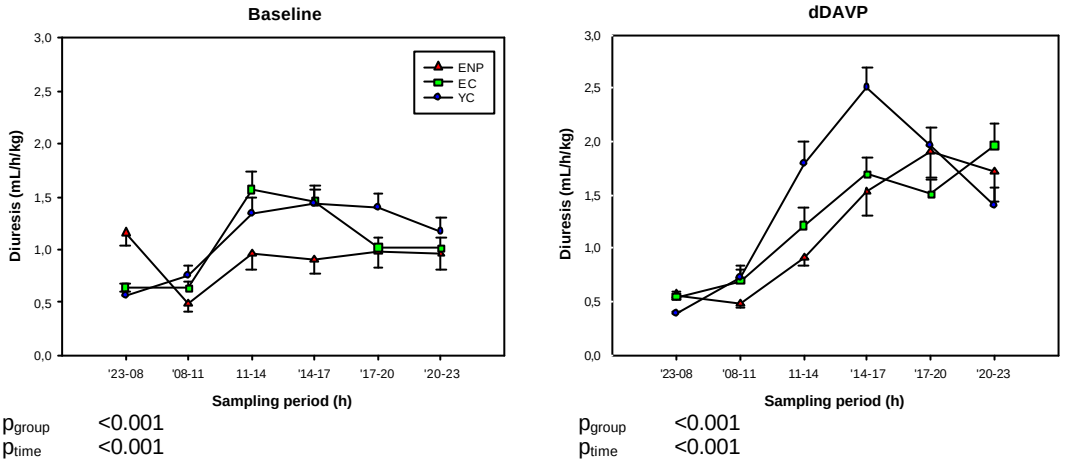

Fig. 2. The circadian variation in urine excretion during baseline and after a single oral dose of dDAVP.

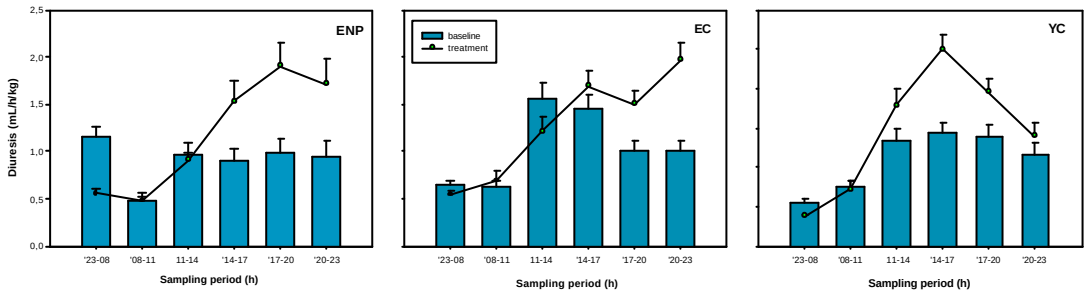

Fig. 3. Within groups changes in urine excretion after dDAVP.

Conclusions

The baseline nocturnal diuresis is a good predictor of the response to dDAVP in terms of reduction in nocturnal urine excretion. A single dose of dDAVP restores the circadian rhythm of the diuresis in nocturnal polyurics and even further decreases the nocturnal diuresis in controls. Furthermore dDAVP postpones the peak diuresis of the day in elderly persons. The postponed diuresis seen in the elderly participants indicate a longer duration of antidiuresis compared to the young controls.