625

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CORRECTION OF RENAL FUNCTION BY DESMOPRESSIN AND DICLOFENAC IN INCONTINENT WOMEN WITH NOCTURNAL POLYURIA AND POLYURIA

Hypothesis/aims of study

Urine incontinence seems to include several pathogenetic forms, as efficient therapy is provided by different medications. Commonly used in the treatment of female patients with overactive bladder and nocturnal polyuria is desmopressin which normalizes the water excretion of the kidney, which is disturbed by a presumed inverted rhythm of vasopressin secretion in these patients [1]. Some drugs which eliminate disturbance of urinary bladder function are often used. The kidney may also be involved in the therapeutic effect of diclofenac which blocks prostaglandin synthase, as vasopressin and prostaglandins are known to act competitively in the regulation of renal water reabsorption [2]. The current analysis was undertaken to evaluate the clinical efficiency of desmopressine and diclofenac in incontinent patient with nocturnal polyuria and polyuria.

Study design, materials and methods

A total of 277 patients ≥18 ≤ 55 years of age with complaints of urinary incontinence were included. 143 women had stress incontinence, 43 - urge incontinence and 91 - mixed incontinence. The overall prevalence of nocturia was 34.7±2.9% (96 women): 24.5±3.6% (35 women) in stress incontinence, 46.5±7.6% (20 women) in urge incontinence ($p<0.01$) and 45.1±5.2% (41) in mixed incontinence ($p<0.01$). The frequency of poliuriya (24-urine volume of 40 mL/kg bodyweight or above) was 7±2.1% in stress incontinence , 11.6±4.9% in urge incontinence and 9.9±3.1% in mixed incontinence ($p>0.05$). The frequency of nocturnal polyuria (nocturnal volume / 24-h urine volume of 0.20 or above) was 17.5±3.2% in stress incontinence, 27.9±6.8% in urge incontinence and 25.3±4.6% mixed incontinence ($p>0.05$). All participants performed 24h-urinecollection to determine the voided volumes and the levels of creatinine, osmolality, sodium, magnesium and potassium for each sample. All urine samples collected for 24 h were divided into two 12-h portions: night portion (23:00-07:00) and day portion (07:00 -23:00). A blood sample was taken during the 24- urinecollection to determine the levels of creatinine, osmolality, sodium, magnesium and potassium. Lack of significant differences between the studied parameters in patients with nocturnal polyuria and polyuria and various types of urine incontience has allowed to unite all samples of patients with polyuria (n=24) and nocturnal poluyria (n=60) for the further analysis. The examination of patients with polyuria and nocturnal polyuria was performed twice: in the initial state and 3 weeks after the start of treatment with desmopressin or diclofenac. Patients were randomized to receive either desmopressin or diclofenac in a double –blind fashion. Optimal dose was established through an open-label dose-titration using 0.1 mg, 0.2 mg and 0.4 mg of desmopressin (Minirin) or diclofenac using 25 mg, 50 mg and 75 mg twice a day for one week each. Patients received their optimal dose for three weeks. Safety parameters assessed included incidence of adverse events, vital signs and serum sodium levels.

Results

In patients with polyuria and nocturnal polyuria the glomerular filtration rate was normal, whereas diuresis and solute (sodium, magnesium, potassium) excretion in night samples in nocturnal polyuria and both in night and day samples in polyuria were increased. The higher diuresis and the higher solute excretion observed in nocturnal polyuria and polyuria are accompanied by an increase of free water reabsorption. In nocturnal polyuria and polyuria a high correlation was found between the free water reabsorption and solute excretion. This occurs against the background of the high night and day osmotic concentration.

The statistically significant recovery of renal function occurred in 8 incontinent women with polyuria and 19 with nocturnal polyuria who received diclofenac and in 12 incontinent women with polyuria and 18 with nocturnal polyuria who received desmopressin (Minirin). In these papients there was a statistically significant decrease in diuresis, osmolar clearance and excretion of sodium,potassium and magnesium. Hence, the recovery of renal function was similar after treatment with desmopressin and diclofenac.

Interpritation of results

The thick ascending limb is known to reabsorb up to one-quarter the filtered sodium and about a half the filtered magnesium, while in subsequent parts of the distal tubule and in collecting ducts there is reabsorption of sodium ions but almost no magnesium ions are reabsorbed [3]. These results suggest there is a reduction of ion reabsorption in the thick ascending limb of the Henle loop in incontinent women with nocturnal polyuria and polyuria. Due to this defect, reabsorption of ions and water is decreased; as a result, lager volumes of fluid enter the collecting ducts. These results together with those of desmopressin and diclofenac efficiency in incontinent patients with nocturnal polyuria and polyuria suggest that the increase in diuresis and solute excretion might be due either to reduction of the effect of vasopressin on cells of the thick ascending limb of Henle's loop or to an increase in production of prostaglandins or both.

Concluding message

As both desmopressin and prostaglandin E 2 affect the same cell of the thick ascending limb of Henle's loop, it is likely that nocturnal polyuria and polyuria result from a disturbed regulation of the function of these cells. Normalization can be achieved either by desmopressin administration to stimulate V 2 receptors, wich increase water permeability and water reabsoption in collecting ducts as well as ion reabsorption by cells of the thick ascending limb of Henle's loop, or by decrease in prostaglandin production via declofenac administration.

References

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