180

Cho M C[1], Ku J H[1], Kim S W[1], Paick J[1]
1. Department of Urology, Seoul National University Hospital

Hypothesis / aims of study

Nocturia is considered to be the main cause of disturbance of sleep maintenance and the quality of life for elderly men. In the previous study, we suggested that treatment with terazosin can reduce patients' episodes of nocturia both subjectively and objectively in some men with lower urinary tract symptoms (LUTS) [1]. This study was performed to determine the efficacy of a diuretic agent, hydrochlorothiazide, as second-line therapy after failed alpha-blocker therapy.

Study design, materials and methods

The study inclusion criteria were: (i) no response or <25% reduction in subjective nocturia on International Prostate Symptom Score (IPSS no. 7), or (ii) no response or <25% reduction in objective nocturia on frequency-volume chart (FVC) after 4-week terazosin therapy, or (iii) nocturia on average twice or more per night (according to the FVC) after 4-week terazosin therapy. In all, 63 patients were entered into this prospective study and treated with 25mg of hydrochlorothiazide and 4 mg of terazosin once daily for 4 weeks. Of the 63 eligible men, 45(71.4%) completed the study. The effectiveness was assessed by analyzing the IPSS and FVC at baseline (the end of 4-week terazosin treatment) and at the end of 4-week hydrochlorothiazide treatment.

Results

There were no serious side effects in all patients. On the IPSS, a reduction of ≥50%, 49~25%, 0~24%, increase in nocturia was seen in 6, 6, 0, 33 patients, respectively. On the FVC, 14 patients reported that the treatment reduced their nocturia by more than half; 4 reported a reduction of 25~49% and 27 reported no response to treatment or increase in nocturia. Like the result of 4-week terazosin treatment, multivariate regression analysis showed that the actual number of nightly voids was the only independent risk factor. The actual number of nightly voids was associated with 3.4-times greater chance of an objective improvement in nocturia of ≥25% (P = 0.045). In a comparable model, there was a significant association between the baseline nocturnal frequency on IPSS and improvements in subjective nocturia. Contrary to 4-week terazosin treatment, greater subjective nocturnal frequency was associated with 0.97-times lesser likelihood of improvements in subjective nocturia (P = 0.004).

Interpretation of results

Recently published guidelines have attributed nocturia to urine overproduction, decreased functional bladder capacity, or a combination of both factors [2]. Physicians treating patients with bladder function abnormalities can choose to administer one of the highly effective antimuscarinic agents. However, when attempting to treat nocturnal polyuria, the physician is presented with a far more limited choice, and is compelled to administer an antidiuretic agent (i.e., desmopressin). However, the therapeutic use of each of these agents may be relatively contraindicated in older adults, or in men suffering from BOO. Desmopressin has been associated with an increased risk of hyponatremia and water retention, and so care must be taken when using desmopressin in the treatment of older patients [3]. Also, anticholinergics may be relatively contraindicated in men with BOO. Nocturia remains a difficult problem, for which many therapies have been proposed in the past.

In the present study, hydrochlorothiazide resulted in a subjective or objective reduction in nocturia episodes when given to some men with LUTS. These results suggest that the combined use of an alpha-blocker and hydrochlorothiazide in the treatment of nocturia in men with LUTS is a reasonable measure. In addition, we noted poor agreement in the responses on the FV charts and the I-PSS question about nocturia. The I-PSS tended to point to a higher prevalence of nocturia than do the FV charts. These findings suggest that the FV chart should be involved in, or included as, an integral part of treatment outcome evaluations in patients suffering from nocturia.

Concluding message

Hydrochlorothiazide treatment is safe and effective in reducing nocturnal frequency for some men with LUTS after failed terazosin therapy. Our findings suggest that the use of a diuretic agent, hydrochlorothiazide–may be a reasonable second-line treatment option in these patients.

References

1. BJU Int (2006) 97; 1017-1023.
2. Neurourol Urodyn (2002) 21; 179-183.
3. BJU Int (2002) 90(Suppl 3); 25-27.

FUNDING: none
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 Clinical research Institute Seoul National University Hospital IRB and followed the Declaration of Helsinki Informed consent was obtained from the patients.