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IMIDAFENACIN REDUCES NOCTURIA IN BPH/OAB PATIENTS WITH OR WITHOUT HYPERTENSION: A SUB-ANALYSIS OF THE GOOD-NIGHT STUDY

Hypothesis / aims of study

There is increasing evidence that nocturia is associated with lifestyle diseases. Among these diseases, hypertension is a risk factor for increased frequency and severity of storage symptoms [1], and these conditions cause sleep disturbance and nocturnal polyuria. Nocturia with hypertension is refractory to treatment with alpha-blockers alone in patients with benign prostatic hyperplasia/overactive bladder (BPH/OAB). We have previously shown the efficacy and safety of combination therapy with an anticholinergic agent (imidafenacin) and an alpha-blocker as second-line therapy after failed alpha-blocker monotherapy for BPH/OAB with nocturia [2]. In this post-hoc analysis, we examine changes in nocturia in BPH/OAB patients with hypertension using data from the GOOD-NIGHT study.

Study design, materials and methods

Stratified analyses were conducted on data from a randomized, open-labelled, controlled trial of imidafenacin: the GOOD-NIGHT study in Japan. Eligible men for the GOOD-NIGHT study were aged >50 years old, had nocturia more than twice per night, and did not respond to treatment with an alpha-blocker alone for more than 4 weeks. Patients were randomised into 3 groups: alpha-blocker alone (group 1), and alpha-blocker plus imidafenacin 0.1 mg twice daily (group 2a) or 0.1 mg nightly (group 2b). In the post-hoc analysis, nocturia with or without hypertension for 8 weeks was compared between patients treated with combined therapy of imidafenacin and an alpha-blocker (groups 2a + 2b) and those treated with an alpha-blocker alone (group 1). Hypertension was defined as use of hypotensive drugs or diagnosis based on an interview. The relative contributions of night time urine production and bladder capacity were determined by analysis of a 3-day voiding diary. The primary endpoints were improvements in night time frequency and N-QOL score. Changes from baseline in nocturnal urine volume and post-void residual volume, and hours of undisturbed sleep (HUS) were assessed as secondary efficacy measures. Nocturnal polyuria was defined as a nocturnal polyuria index (NPi) of >33% of the 24-hour urine volume and low bladder capacity was defined as a nocturnal bladder capacity index (NBCi) >1.3 [3]. The NBCi was derived from the voiding diary and is a quantitative method for comparing nocturnal bladder capacity with 24-hour bladder capacity (maximum voided volume) [3]. A higher NBCi indicates a lower bladder capacity. A paired t-test or unpaired t-test was used for statistical analysis, with $p<0.05$ considered significant.

Results

A total of 152 patients were enrolled in the study and 130 (46 in group 1, 43 in group 2a, and 41 in group 2b) were assessed for efficacy at 8 weeks. The 130 patients included 35 (26.9%) with hypertension and 95 (73.1%) without hypertension. There was a trend for patients with hypertension to have a higher nocturnal urine volume than those without hypertension ($p=0.1399$). Nocturia episodes in group 1 did not change significantly from baseline after 8 weeks of treatment regardless of hypertension (0.05±0.16 episodes in non-hypertension cases, N.S.; 0.15±0.15 episodes in hypertension cases, N.S.). In contrast, there were significant decreases in nocturia episodes in patients treated with imidafenacin regardless of hypertension (-0.42±0.14 episodes in non-hypertension cases, $p<0.0010$; -0.67±0.13 episodes in hypertension cases, $p=0.0053$, $p<0.0001$). Changes of N-QOL scores showed a similar trend: N-QOL scores significantly increased from baseline with imidafenacin treatment (8.86±2.04 in non-hypertension cases, $p<0.0001$; 13.26±2.10 in hypertension cases, $p<0.0001$), but not with alpha-blocker treatment alone (4.02±2.67 in non-hypertension cases, N.S.; 5.61±3.97 in hypertension cases, N.S.). HUS, NPi, and NBCi improved only in patients with hypertension who were treated with imidafenacin (52±17 min, $p<0.01$; -4.13±-1.59, $p<0.01$; -0.31±0.09, $p<0.01$; respectively). Residual urine volume was unchanged in the study period.

Interpretation of results

In this post-hoc analysis, we provide the first evidence that an anticholinergic agent, imidafenacin, is effective for nocturia in BPH/OAB patients with hypertension. Nocturia has multifactorial symptoms and is associated with lifestyle diseases. Hypertension induces increased levels of circulating catecholamines. In the daytime, these high levels of catecholamines decrease renal blood flow, decrease daytime urinary production, and increase daytime intravascular volume expansion. The excess circulating volume in the daytime then induces night time diuresis. Thus, OAB with hypertension is related to nocturia and nocturnal polyuria. The most important findings in this study are that imidafenacin decreased nocturia and increased bladder capacity, and also improved nocturnal polyuria and decreased NPi. These clinical findings are supported by results from an animal model showing that imidafenacin decreased urine production through C-fiber afferent nerves in the rat bladder. The suppression of urine production by imidafenacin is not dependent on antidiuretic or diuretic hormones [3]. In the current study, 78% of the patients had nocturnal polyuria and 38% had low bladder capacity, and imidafenacin was effective in both of these subgroups (data not shown). A detailed explanation of the mechanism of action is yet to be established, but imidafenacin may have a potential to improve nocturia with a reduction in nocturnal polyuria. It is also noteworthy that there were no clinically important or statistically significant changes in the incidences of acute urinary retention and increased residual urine volume.

Thus, imidafenacin was effective and well tolerated in BPH patients with nocturia and OAB. The limitations of the study include its performance as a retrospective post-hoc subgroup analysis, the small number of patients, and the lack of clarity regarding the degree of hypertension at baseline. However, we suggest that a large-scale prospective study in patients with hypertension and nocturnal polyuria, and including other anticholinergic drugs, is warranted based on the results.

Concluding message

Imidafenacin is effective for nocturia in BPH/OAB patients with or without hypertension and could reduce nocturnal polyuria.

References

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