

## MANAGEMENT OF NOCTURIA IN PATIENTS WITH BENIGN PROSTATE ENLARGEMENT AND OVERACTIVE BLADDER SYMPTOMS WITH SOLIFENACIN AND TAMSULOSIN COMBINATION TREATMENT VERSUS TAMSULOSIN MONOTHERAPY.

### Hypothesis / aims of study

Nocturia occurs either as part of a spectrum of lower urinary tract dysfunction or as a manifestation of a systemic disease affecting fluid and electrolyte balance. It is the most prevalent of lower urinary tract symptoms (LUTS) in both men and women. In patients with overactive bladder (OAB) syndrome, nocturia affects 48.6% of men and 54.5% of women (EPIC study) (1). Hence, it is expected that treating OAB would positively affect nocturia outcomes. The objective of this study is to assess the effect of combination treatment with tamsulosin and solifenacin versus tamsulosin monotherapy in nocturia parameters in patients with predominately storage LUTS due to benign prostatic hyperplasia (BPH).

### Study design, materials and methods

This is a post-hoc analysis of a prospective, randomized study on the prostate perfusion following tamsulosin monotherapy or combination of solifenacin and tamsulosin. The initial study recruited treatment naïve patients with prostate volume  $\geq 30$ mls and predominantly storage LUTS, who had maximum urine flow rate (Qmax)  $\geq 10$ ml/s, post-void residual (PVR)  $< 100$ ml, scored  $\geq 3$  in the International Prostate Symptom Score (IPSS) urgency question. The recruited patients had at least 3 urgency episodes per 24h, daytime frequency  $\geq 8$  and at least 2 nocturia episodes as documented in a 3-day bladder diary. Patients with neurogenic lower urinary tract dysfunction, PSA  $> 4$ ng/ml, recurrent urinary tract infections or a history of urinary tract malignancy were excluded.

The primary endpoint of this post-hoc analysis was the change in the mean number of nocturia episodes from baseline to week 26 as recorded in the bladder diary. Secondary endpoints were changes in nocturia question of IPSS, storage IPSS subscore, total IPSS score and OABq/V8 questionnaires scores. A subgroup analysis was carried out, comparing mean nocturnal frequency and question 7 of IPSS in different baseline groups. These were: prostate volume ( $\geq 60$ mls), baseline detrusor overactivity, bladder outlet obstruction index ( $\geq 40$ ) and cystometric capacity ( $> 300$ mls).

Patients were randomized into two treatment groups. Group I received Tamsulosin 0.4mg and Group II received Tamsulosin & Solifenacin 5mg, which could be titrated to Solifenacin 10mg at week 4. All patients were submitted to pressure-flow study, transrectal and transabdominal ultrasonography. Paired t-test was used for intragroup variability and Mann-Whitney test for intergroup variability. Sample size calculation was based on previously published data and was found that in order to detect a difference  $\geq 30\%$ , a power sample of 80% is achieved with 60 randomized subjects. The local Ethics Committee approved this study and all recruited patients gave their written informed consent.

### Results

A total of 80 men were enrolled in the study. At baseline, both groups were comparable for bladder diary, questionnaire scores, prostate parameters and demographics. Sixty-three men completed the study (Group I: n=31, Group II n=32). Mean (SD) nocturia frequency at baseline was 3.48 (1.24) in the tamsulosin group and 3.56 (1.35) in the combination therapy group. Mean (SD) IPSS question 7 score was 3.37 (0.85) at baseline and 3.31 (1.09) respectively.

All parameters improved significantly from baseline ( $p < 0.001$ ) in both groups. At end of study, mean (SD) nocturia episodes changed by -1.5(1.2) in monotherapy and -2.0(1.9) in combination group ( $p = 0.057$ ). The IPSS nocturia question score changed by -1.51 (1.09) and -1.4 (1.03) respectively ( $p = 0.894$ ). The IPSS storage subscore improved more in Group II (-42.6% vs -53%,  $p = 0.023$ ).

The subgroup analysis among the various baseline subgroups showed that all subgroups improved from baseline without reaching statistical significance and without intergroup differences ( $p > 0.05$ ). There were no major adverse events related to pharmacotherapy.

### Interpretation of results

To our knowledge, this is the first analysis of a randomized population focusing on the efficacy of the combination of Solifenacin and Tamsulosin on nocturnal frequency in patients with BPE associated OAB who present with storage LUTS.

The improvement with combination therapy was greater as compared to monotherapy (adjusted mean change from baseline in nocturnal frequency: monotherapy, -1.5; combination, -2.0) with a trend for statistical significance ( $p = 0.057$ ). Similar were the observations in the 24h frequency (adjusted mean change from baseline: monotherapy, -3.5; combination, -4.4) ( $p = 0.073$ ). Interestingly, patients receiving Tamsulosin monotherapy reported similar improvement in their IPSS Question 7 score as compared to combination therapy (-1.51 vs. -1.4).

### Concluding message

Both monotherapy and combination treatment were effective in nocturia management in patients with BPE and OAB, with a trend for better improvement in the combination arm. The latter should be reserved for those with predominately storage LUTS.

### References

1. Irwin D, Milsom I, Hunskaar S, Reilly K, Kopp Z, Herschorn S, Coyne K, Kelleher C, Hampel C, Artibani W, Abrams P. population-based survey of urinary tract incontinence, overactive bladder and other lower urinary tract symptoms in five countries: Results of the EPIC study. *Eur Urol* 2006;50:1306-15.

Disclosures

**Funding:** None **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** This is a post hoc analysis of a previously registered study which was approved by the local ethics committee (Hippokrateion General hospital of THessaloniki and Aristotele University Bioethics committee). **Helsinki:** Yes **Informed Consent:** Yes