

## SLEEPING THROUGH THE NIGHT AND SOLIFENACIN: CAN ANTIMUSCARINICS REDUCE NOCTURIA IN OAB PATIENTS?

### Hypothesis / aims of study

Nocturia is a symptom with numerous etiologies which can be challenging for clinicians to diagnose and treat. A common initial approach to nocturia is to consider treatment based on three broad etiologic categories: nocturnal polyuria, bladder storage dysfunction, or inappropriate emptying. If bladder storage dysfunction (secondary to overactive bladder [OAB]/detrusor overactivity) contributes to nocturia in a subset of patients, might these patients see improvements in their nocturia symptoms with antimuscarinic drug treatment? We evaluated reductions in episodes of nocturia using data from a large, pooled population of patients with OAB treated with the newly approved antimuscarinic agent, solifenacin succinate (VESIcare<sup>®</sup>). A responder analysis was performed to determine whether the proportion of participants whose nocturia 'responded' to treatment differed when treatment with solifenacin was compared with placebo. Solifenacin treatment has demonstrated statistically significant reductions in incontinence, urgency, and frequency in multiple placebo-controlled clinical trials of OAB, and thus seemed appropriate to evaluate the impact of an antimuscarinic agent on nocturia.

### Study design, materials and methods

Data from 3-day voiding diaries completed by patients with symptoms of overactive bladder (voiding  $\geq$  8 daily voids and one episode of incontinence or one episode of urgency per 24 hrs) was collected from four trials; similarities in trial designs and baseline demographics allowed appropriate pooling. Ad hoc analyses were performed on data from the four placebo-controlled studies evaluating 12 weeks of solifenacin treatment at the 5 mg and 10 mg once-daily dosing strengths (5 mg was evaluated in two studies; data from a single within-study tolterodine 2 mg BID active control arm was not included in the pooled analysis). Changes from baseline to endpoint in episodes of nocturia were analyzed. Nocturia was defined as a night-time void that caused an interruption of sleep. Responders were defined as patients reporting a mean of  $> 1$  nocturia episode/24 hrs at baseline and  $\leq 1$  nocturia episode/24 hrs at endpoint; this responder endpoint is consistent with a definition of nocturia as two or more episodes per night [1].

### Results

In the responder analysis as defined above, a statistically and clinically significantly greater percentage of patients reported  $\leq 1$  episode of nocturia following solifenacin treatment when compared with placebo. Forty-five percent (159/355) and 44% (298/679) of patients treated with solifenacin 5 mg and 10 mg, respectively, reported  $\leq 1$  episode of nocturia at study endpoint versus 35% (228/647) of patients in the placebo group ( $P = 0.004$  for solifenacin 5mg;  $P = 0.001$  for solifenacin 10mg). Among all patients in the subgroup reporting nocturia at baseline, solifenacin treatment provided a 50% or greater reduction in nocturia in a significant percentage (43% [214/494] for 5mg and 44% [452/1036] for 10mg versus 36% [364/1005] for placebo;  $P < 0.01$  for 5mg and  $P < 0.001$  for 10mg). Finally, as shown in the table below, statistically significant reductions in the number of nocturia episodes/24 hrs were demonstrated for patients treated with solifenacin when compared with placebo.

Parameter	Placebo	Solifenacin 5 mg	Solifenacin 10 mg
NOCTURIA	N = 1005	N = 494	N = 1035
Mean baseline	1.8	2.0	1.8
Mean actual change [P]	-0.4	-0.6 [p = 0.025]	-0.6 [p < 0.001]
Median % change [P]	-25.0%	-35.5% [p = 0.021]	-36.4% [p < 0.001]

#### Interpretation of results

In a clinically significant group of patients, solifenacin improved nocturia associated with overactive bladder. In fact, the results reported here may underestimate clinical efficacy because patients with nocturia due to other causes (such as nocturnal polyuria) were included in this pooled population. Despite this, solifenacin was the first antimuscarinic medication associated with significant reductions in nocturia in an OAB population.

#### Concluding message

With improved clinical triage of nocturia patients, solifenacin may play an important therapeutic role in the treatment of nocturia in patients with OAB.

#### References

1. Management of overactive bladder. N Engl J Med 2004; 350(8): 786-99.

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