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PROPIVERINE ER AND EFFECTS OF FLEXIBLE DOSING IN 1335 PATIENTS WITH OAB: RESULTS OF A NON-INTERVENTIONAL STUDY

Hypothesis/ aims of study
Patients with overactive bladder (OAB) show a wide range of individual symptom severity. Therefore, flexible dosing of antimuscarinics is an established and useful option in clinical practice to achieve the best balance between maximum therapeutic effect and tolerability. For most OAB drugs given once daily, two different dosages are available, recommending the lower one as starting dose. In contrast, therapy with propiverine ER can be initiated with either 30 mg or the higher dose of 45 mg once daily. The aim of this study was to assess for the first time the effectiveness and tolerability/safety of propiverine ER 30 mg or 45 mg in patients with OAB under real life conditions, to evaluate the number of patients who opted for dose-adjustment, and to determine treatment differences between patients who remained on the starting dose and those who changed dosage.
Study design, materials and methods
This was a non-interventional study of female and male OAB patients carried out between May 2012 and January 2013. During the observational period of 12 weeks, patients were treated with either propiverine ER 30 mg or propiverine ER 45 mg once daily. Micturition- frequency/24h, urgency episodes/24 h, incontinence episodes/24 h, mean voided volume, the number of pads/24 h, and the Patient Perception of Bladder Condition (PPBC) score were recorded at baseline (Visit 1), after 4 weeks (Visit 2) and 12 weeks (Visit 3). Patients could opt for dose adjustment of propiverine after 4 weeks (i.e. from 30 to 45 mg or 45 to 30 mg once daily, depending on the starting dose). Post-void residual urine (PVR) and adverse drug reactions (ADR) were monitored as safety parameters.
Results
Data from 1335 patients (857 female, 437 male, 41 not reported; mean age: 65.7 years, range 18 - 93 years) were collected and all patients were included into the study. 1069 patients (80.1%) started therapy with propiverine ER 30 mg. 791 (59%) patients were treated with propiverine ER 30 mg and 182 (14%) patients with propiverine ER 45 mg throughout the study. At week 4, dosage was increased from 30 to 45 mg in 161 and decreased from 45 to 30 mg in 28 participants.
Patients who started with propiverine ER 30 mg and changed to propiverine ER 45 mg (dose-escalators) and those who received propiverine ER 45 mg throughout the study had higher baseline values than patients treated with propiverine ER 30 mg throughout the observational period (Table 1).
Table 1: Baseline value (mean ± standard deviation)

Parameter	Dosage throughout the study		p-value*	Dose-escalators (30 mg → 45 mg)	p-value#
	30 mg	45 mg			
Micturition-frequency/24 h [n]	13.3 ± 4.3	14.4 ± 4.3	0.0002	14.6 ± 4.8	0.0003
Urgency episodes/24 h [n]	9.9 ± 6.3	11.3 ± 5.9	0.0014	11.8 ± 6.8	0.0005
Incontinence episodes/24 h [n]	3.1 ± 3.6	4.8 ± 4.6	<0.0001	4.4 ± 4.8	0.0023
Mean voided volume [ml]	172 ± 80	154 ± 77	0.0007	164 ± 67	0.52
Number of pads/24 h [n]	2.4 ± 2.3	3.5 ± 2.5	<0.0001	3.2 ± 3.2	0.0012
PPBC score	4.6 ± 0.8	4.8 ± 0.8	<0.0001	4.8 ± 0.8	0.0051

In the overall population, all effectiveness parameters showed significant improvement from baseline to week 12 regardless of dose regimens.
Patients treated with propiverine ER 45 mg throughout the study showed significantly greater improvement in all parameters compared with patients treated with propiverine ER 30 mg
throughout the study (Table 2).

Parameter	Dosage throughout the study		p-value
	30 mg	45 mg	
Micturition-frequency/24 h [n]	-5.6 ± 3.8	-6.4 ± 3.9	0.0023
Urgency episodes/24 h [n]	-6.8 ± 5.3	-7.9 ± 5.7	0.0033
Incontinence episodes/24 h [n]	-2.4 ± 3.1	-3.6 ± 3.9	<0.0001
Mean voided volume [ml]	+58 ± 61	+78 ± 63	<0.0001
Number of pads/24 h [n]	-1.4 ± 1.7	-2.3 ± 2.1	<0.0001
PPBC score	-2.1 ± 1.1	-2.3 ± 1.3	0.0097

Table 2: Change from baseline to visit 3
Figure 1 shows the changes of bladder diary variables in patients with propiverine ER 30 mg throughout the study and dose-escalators. After 4 weeks, dose-escalators showed less improvement for the most parameters compared with patients treated with propiverine ER 30 mg throughout the study. Therefore, dosage was increased at visit 2 in patients who were not satisfied with treatment effectiveness at that point. At visit 3 dose-escalators showed similar overall therapeutic improvements compared to baseline (Figure 1). Similar effects were observed between these two groups for the number of pads/24 h and the PPBC score (data not shown).

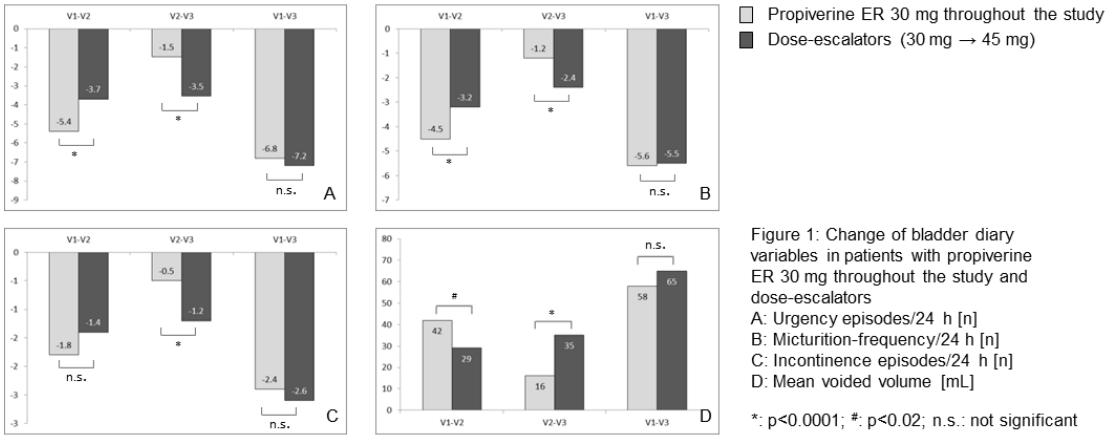

Figure 1: Change of bladder diary variables in patients with propiverine ER 30 mg throughout the study and dose-escalators
A: Urgency episodes/24 h [n]
B: Micturition-frequency/24 h [n]
C: Incontinence episodes/24 h [n]
D: Mean voided volume [mL]

*: $p<0.0001$; #: $p<0.02$; n.s.: not significant

In the overall population, patients reported a decrease of -1.1 pads/24 h after 4 and -1.6 after 12 weeks; 713 patients used fewer pads and 193 patients did not require pads anymore after 12 weeks. The PPBC score improved significantly from average 4.7 at baseline to 2.6 after 12 weeks (mean change: -2.1 ± 1.1).
Of 325 patients (24.3%) reporting ADRs, dry mouth (19.6%) was the most frequently reported, followed by constipation (6.0%) and dizziness (1.3%). The incidence of ADRs was independent of the dose regimen. Average PVR changed slightly regardless of dosage (19 ± 26 ml baseline, 18 ± 23 ml week 12) and no cases of acute urinary retention were reported.

Interpretation of results

These data show the benefit of flexible dosing of propiverine ER 30 mg and 45 mg for OAB patients. Propiverine ER 45 mg is significantly more effective than propiverine ER 30 mg. The decision of the physicians for prescribing the higher dose was based on the severity of symptoms. In addition, patients who were dissatisfied with the treatment effect can expect increased effectiveness from dose escalation. With dose adjustment after 4 weeks, most patients will be satisfied with propiverine ER after 12 weeks.

Concluding message

This study confirmed that propiverine ER with its two daily dosages of 30 mg and 45 mg can be considered as an effective and well tolerated treatment for patients with OAB under real life conditions. While propiverine ER 30 mg seems to be the ideal starting dose for the majority of patients, men and women with more severe symptoms can profit from propiverine ER 45 already at treatment begin or, if not satisfied with 30 mg, from dose escalation to 45 mg.

Disclosures

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