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INFLUENCE OF PROPIVERINE ER 30 MG ONCE DAILY ON COGNITIVE FUNCTION IN ELDERLY FEMALE AND MALE PATIENTS WITH OVERACTIVE BLADDER: A NON-INTERVENTIONAL STUDY TO ASSESS REAL LIFE DATA

Hypothesis / aims of study
The overactive bladder (OAB) affects women and men with almost identical prevalence and increases in both genders with aging; in the EPIC trial, 11.8% of the total adult population was affected. Due to the increasing life expectancy, the number of elderly people with OAB and urinary incontinence is growing. Likewise, the prevalence of cognitive impairment and dementia increases with aging. Anticholinergic agents are first-line drug treatment of OAB or urgency incontinence but they have the potential to further decrease cognitive function due to muscarinic receptor inhibition in the central nervous system. Oxybutynin is well known to significantly reduce cognitive function and should therefore not be prescribed in elderly patients. Propiverine is an anticholinergic agent with calcium channel blocking properties licensed for the treatment of OAB in adults; however, data on cognitive function during treatment with propiverine is sparse. Therefore, the aim of this study was to evaluate the influence of propiverine ER 30 mg once daily on cognitive function in elderly patients with OAB under real-life conditions.

Study design, materials and methods
In this non-interventional study, female and male patients with OAB were prospectively enrolled between August 2011 and March 2012 if they fulfilled the following inclusion criteria: age 70 years or older, symptoms of OAB, no treatment of OAB with anticholinergics within the last 4 weeks prior to study inclusion, and no contraindication for anticholinergic treatment as indicated in the patient information leaflet. Folstein's Mini Mental State Examination (MMSE) test was used to assess cognitive function and the Patient Perception of Bladder Condition (PPBC) questionnaire was used to assess drug efficacy. MMSE is a screening test which consists of 5 domains with 11 questions resulting in a score between 0 and 30 (30-27 = normal cognitive function; 26-20 = mild; 19-10 = moderate; 9-0 = severe cognitive dysfunction). PPBC is a 6-item questionnaire evaluating the subjective bladder condition resulting in a score from 1 to 6; a higher score indicates more severe bladder problems. MMSE and PPBC were completed at baseline and after 12 weeks of treatment with propiverine ER 30 mg once daily. Post-void residual urine (PVR) and number of pads/24 h were recorded before and after 4 and 12 weeks of treatment with propiverine ER 30 mg. PVR and patient-reported adverse drug reactions (ADR) were monitored as safety parameters.

Results
Of 225 enrolled patients (safety population), 201 patients (124 women, 74 men, 3 not reported; mean age: 75.8 years, range: 70-93 years) fulfilled the inclusion criteria and were included in the analysis; of those, 136 patients (68%, 100 woman, 34 men, 2 not reported) experienced urgency incontinence episodes. The mean MMSE at baseline showed a score in the lower normal range (mean: 27.0); after 12 weeks of treatment with propiverine ER 30 mg once daily, no significant change of the MMSE score (mean 27.1) was observed (figure 1a). At study begin, 66 patients (33%; 32 women and 34 men) had mild to moderate cognitive impairment (mean MMSE score 23.7); these patients also showed no significant changes of the mean MMSE score after 12 weeks (mean MMSE score 24.1; figure 1b). The mean PPBC score improved significantly from 4.4 at baseline to 2.9 at week 12 ($p<0.001$). Patients experiencing incontinence episodes exhibited a higher burden as documented by a higher PPBC score before treatment (4.5 vs. 4.2); however, no differences were found between patients with or without incontinence after 12 weeks of treatment (2.9 vs. 2.8). At baseline, incontinent patients used a mean number of 2.7 pads per 24 h; at study end, the number of pads was significantly reduced by 52%. After 12 weeks, 66 (31.3%) and 66 patients (31.3%) used 0 or only 1 pad/24 h, respectively. Average PVR did not change significantly during the 12 weeks of treatment (20.7 ml at baseline vs. 21.7 ml at week 12). Treatment with propiverine ER 30 mg was well tolerated; ADRs appeared in only 38 patients (17%); dry mouth was the most frequently mentioned ADR (9.8%).

Interpretation of results
This is the first non-interventional study evaluating the influence of propiverine on cognitive function and subjective perception of bladder condition in patients aged 70 years or older. The study confirmed the clinical observation that propiverine 30 mg once daily does not influence cognitive function in elderly patients. Even patients with mild cognitive impairment did not show a deterioration of cognitive function during anticholinergic treatment with propiverine. Real-life data is sparse, especially in the elderly population. The results of this study are in line with those of an earlier preliminary report showing that propiverine does not influence the MMSE score in female and male patients with moderate cognitive dysfunction (dementia) when co-administered with donepezil, a cholinesterase inhibitor. Efficacy of propiverine treatment was confirmed by the improvement of the subjective perception of bladder condition scale (PPBC-questionnaire) and decrease of the number of pads/24 h. Treatment with propiverine ER 30 mg once-daily was well tolerated and the adverse event profile is similar to that was reported previously. Propiverine ER 30 mg once-daily did not alter PVR volume in this cohort of elderly patients.

Concluding message
Propiverine ER 30 mg once-daily does not cause cognitive dysfunction under real-life conditions in females and males aged 70 years and or older even if they had mild cognitive impairment at baseline. Furthermore, elderly patients reported significant improvements of the subjective perception of their bladder condition and number of pads/24 h. PVR remained unchanged during treatment with propiverine.

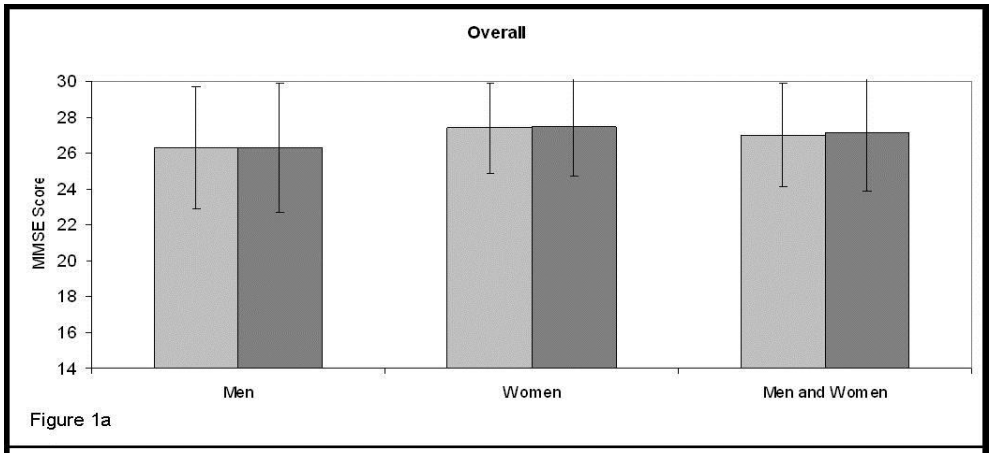

Figure 1a

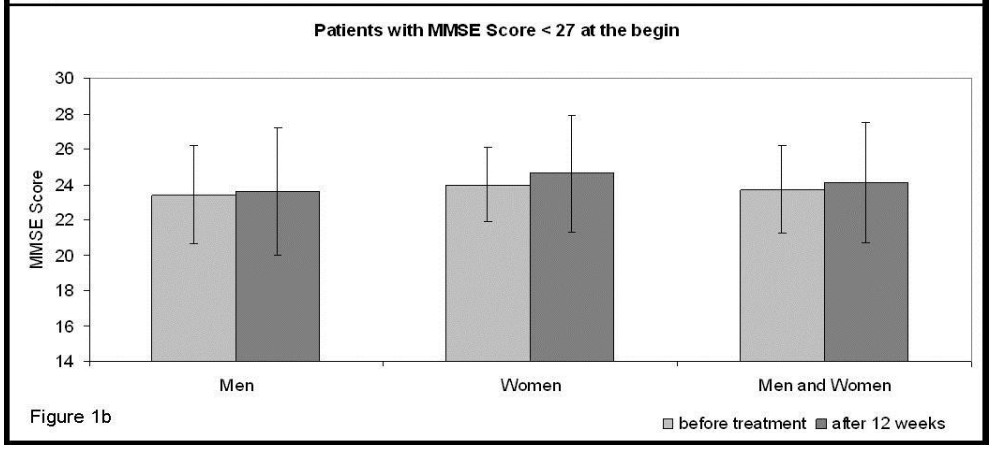

Figure 1b

Disclosures
Funding: Apogepha Arzneimittel GmbH, Dresden, Germany **Clinical Trial:** Yes **Registration Number:** EK-BR-37/11-1 **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Ethics committee of the Sächsische Landesärztekammer EK-BR-37/11-1 **Helsinki:** Yes **Informed Consent:** Yes