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PROPIVERINE HYDROCHLORIDE IMMEDIATE (IR) AND EXTENDED RELEASE (ER): COMPARISON OF EFFICACY AND TOLERABILITY IN PATIENTS WITH OVERACTIVE BLADDER

Aims of study

The primary objective was to evaluate the efficacy of propiverine hydrochloride immediate release (IR) and propiverine hydrochloride extended release (ER) in comparison with placebo in patients with overactive bladder in terms of incontinence episodes/24 hours.
Secondary objectives were number of micturitions/24 hours, urge episodes/24 hours, volume of micturition, efficacy evaluation by patient and investigator, quality of life (King's Health Questionnaire), adverse events (AEs), blood pressure/pulse rate, ECG, haematology, clinical chemistry and urinalysis, evaluation of tolerability by patient and investigator.

Materials and methods

This clinical study was designed as a double-blind, double-dummy, randomised, placebo-controlled study with 3 parallel groups comparing IR 15 mg twice daily, ER 30 mg once daily and placebo at a ratio of 2:2:1.
After a run-in period of 7 days, the patients were treated for 32 days with regular assessments of efficacy and tolerability using pre-post comparisons.
The safety population consisted of 988 patients (89.5% females and 10.5% males). Its mean age was 56.1 years and its mean BMI was 26.6 kg/m^2 in the males and 27.0 kg/m^2 in the females (comparable between the groups). The ITT population consisted of 786, and the pp population of 735 patients. A total of 973 (98.5%) patients experienced their incontinence with urge.

Results

Efficacy:In the ITT population the baseline values for the incontinence episodes within 24 hours were comparable (3.29 in the IR group, 3.38 in the ER group, 3.50 in the placebo group). The number of incontinence episodes decreased by 2.26 in the IR group, by 2.46 in the ER group, and by 1.75 in the placebo group.
Changes were statistically significantly different for both treatments versus placebo ($p<0.0001$).
The number of micturitions within 24 hours was statistically significantly ($p<0.001$) more reduced in both propiverine groups than in the placebo group.
The number of urge episodes within 24 hours was statistically significantly ($p<0.05$) more reduced in both propiverine groups than in the placebo group.
The treatment groups did not differ regarding the increase in volume of micturitions within 24 hours.
The mean volume of the single micturitions increased statistically significantly more in both propiverine groups than in the placebo group, although the liquid intake was comparable between groups.
The efficacy assessed by the investigators and patients was statistically significantly better in both propiverine groups than in the placebo groups.
The improvement in QoL was less consistent, although the propiverine groups were slightly better than the placebo group.

Safety;38.5% of the patients experienced AEs in the IR group, 34.3% of the patients in the ER group, and 20.3% of the patients in the placebo group.
26 (2.6%) patients dropped out prematurely due to a AE: 14 (3.5%) in the IR group, 11 (2.8%) in the ER group, and 1 (0.5%) in the placebo group. Gastrointestinal disorders and nervous system disorders were the most frequent AEs leading to withdrawal from the study.
The difference in incidence of AEs between propiverine and placebo was mainly caused by propiverine's anticholinergic effects.

The most frequent adverse event was dry mouth with 22.8 % of the patients of the IR group, 21.7 % of the patients of the ER group and 6.4 % of the placebo group.
“Eye disorders” were experienced by 6.6% of the patients of the IR group, 7.2% of the ER group and 2.5% of the placebo group. All other system organ classes accounted for less than 5% of the patients each.
Other safety parameters (blood pressure/pulse rate, ECG, laboratory, urinalysis) did not show any results of concern. The overall tolerability was rated very good or good by 85% of the investigators and patients.

Concluding message

Propiverine IR 15 mg b.i.d. and propiverine ER 30 mg s.i.d. reduce effectively the number of incontinence episodes per 24 hours within a treatment period of 32 days.
Both formulations also decrease the number of urge episodes per 24 hours.They decrease the number of micturitions within 24 hours resulting in an increase of the volume of single micturitions without increase of the total 24 h urine output and despite unchanged liquid intake.
Both formulations are safe.

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