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Madersbacher H[1], Hessdoerfer E[2], Martan A[3], Nurkjewicz W[4], Bruenjes R[5], Shah J[6]
1. Neurourology Unit, University Hospital of Innsbruck, Austria, 2. Consultant, Urology, Berlin, Germany, 3. Dept. Gynecol., University Prague, Czech Republic, 4. Dept. Urology, Warsaw, Poland, 5. Apogepha Arzneimittel GmbH, Dresden, Germany, 6. Urology and Nephrology, UCLH, London, UK

SAFETY, TOLERABILITY AND EFFICACY OF PROPIVERINE LONG-TERM TREATMENT

Aims of study

To gain data of propiverine hydrochloride (propiverine) long-term administration regarding safety, tolerability and efficacy.

Study design, materials and methods

In this open-label, prospective, multicenter, multinational study 464 patients (safety population) suffering from symptoms of overactive bladder (frequency, urgency, urge incontinence; 92.9%) or neurogenic detrusor overactivity (7.1%) were included.
15 mg of propiverine b.i.d. (group A) or t.i.d. (group B) were administered orally for up to 6 months (464 patients) or up to 12 months (330/464 patients). The mean treatment duration in the ITT population (454 patients, age 57.7 ± 14.3 years, 374 (82.4 %) women) was therefore 266 days.
After the initial visit (pre-treatment visit) there were examination visits (V2, 3 and 4 after 3, 6 and 9 months, respectively). The final visit was V3 or V5 after 6 months or after 12 months, respectively.
Evaluation
Safety: adverse events (body system and frequency; at V2, V3, V4, V5), vital parameters (blood pressure, pulse rate; at V1, V2, V3, V4, V5), ECG (at V1, V3, V5), lab parameters (blood analysis, urinalysis; at V1, V2, V3, V4, V5).
Tolerability: at V2, V3, V4, V5.
Efficacy: micturition frequency and incontinence episodes (bladder diary after V1, V2, V3 and V4), King‘ s Health Questionnaire (V1, V3 and V5), evaluation of efficacy (V3 and V5).
The safety population consisted of 464 patients (378 in group A, 87.3% did not change dose during study; 86 in group B, 58.1% did not change dose).
The PP population consisted of 421 patients.

Results

Safety: no relevant changes in haematology, clinical chemistry, urinalysis, vital signs, and ECG were observed.
Adverse events (AE’s) were experienced by 314 patients (67.7%), 69.0% in group A, 61.6% in group B; premature withdrawals due to adverse events: 15.6% in group A and 13.5% in group B. 40.3% of the patients reported gastrointestinal disorders,13.1% eye disorders (blurred vision 6.7%) and 20.7% various types of infections - UTI 8.6%; influenza 3.9%.
30 serious adverse events in 26 patients (group A: 25 in 22 patients; group B: 5 in 4 patients) were reported. Within the first 182 days of treatment 48.3% of the patients experienced at least one related AE. During the second half year this decreased to 35.5%; e.g. the rate of dry mouth (the most frequent AE) decreased from 27.8% in the first half to 20.9% in the second half of the study.
Tolerability was judged to be good or very good by more than 90% of the patients at V3 and V4.
Efficacy: the *micturition frequency* / 24 h in group A decreased from 11.7 ± 5.5 by 2.0 ± 4.8 (V2), 2.6 ± 5.9 (V3), and 2.8 ± 6.2 (V4) (all changes $p<0.0001$ compared to baseline). In group B (baseline 11.9 ± 4.9) the decreases were 1.6 ± 2.9 (V2), 1.7 ± 3.2 (V3), and 1.7 ± 3.8 (V4) (all changes $p<0.005$).
The *number of incontinence episodes* / 24 h in group A decreased from 2.1 ± 3.1 by 0.9 ± 2.2 (V2), 1.3 ± 2.9 (V3), and 1.5 ± 3.2 (V4) (all changes $p<0.0001$). In group B (baseline 1.7 ± 2.5) the decreases were 0.5 ± 1.5 (V2), 0.5 ± 1.7 (V3), and 0.7 ± 1.4 (V4) (all changes $p<0.05$).
In both groups the efficacy was judged to be good or very good by about 70% of the patients and investigators.

The sum score for *quality of life* in group A improved (baseline 39.7) by 14.2 (first half of study) and by 24.6 (second half). In group B (baseline 47.1) the improvements were 14.2 (first half) and 20.2 (second half; p<000.1 in all cases).

Interpretation of results

The number of withdrawals due to AE´s was 15.6% (group A) and 13.5% (group B) for propiverine and are thus comparable with the results of other anticholinergic drugs (1). With propiverine AE´s decreased during treatment with propiverine, e.g. dry mouth from 28 to 21%; for tolterodine 28% of dry mouth were reported, however there is no information about a variation in time.

Concluding message

The treatment with propiverine, a drug with a dual mode of action, was safe (no noteworthy QT prolongations and no ECGs worsening). The incidence of AE´s decreased during the study course and the global assessment of tolerability was excellent. The efficacy and the quality of life improved during the study period.

Reference:

1. Tolterodine long-term treatment results in 1669 patients. Eur Urol 2000; 37 (suppl 2): 1-175

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