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LONG-TERM EFFICACY AND TOLERABILITY OF PROPIVERINE HYDROCHLORIDE IN CHILDREN AND ADOLESCENTS WITH NEUROGENIC DETRUSOR OVERACTIVITY

Hypothesis / aims of study

The established treatment of children with neurogenic detrusor overactivity consists of the use of anticholinergics and clean intermittent catheterization four or five times a day in order to keep intravesical bladder pressure low. However, side effects of the anticholinergics often restrict their use in a sufficient dosage. Less frequent and less severe adverse events compared to oxybutynin both in adults and in children, were reported for propiverine hydrochloride (abbreviated as propiverine), a drug encompassing a dual mode of action: anticholinergic properties and additional Ca^{++}-channel modulating effects. Results of short-term treatments have been presented for different anticholinergics. However, long-term efficacy of anticholinergics, despite its wide-spread use, is only scarcely assessed in adults and in children. The goal of this prospective post marketing drug surveillance was to determine the long-term efficacy and tolerability of propiverine in children / adolescents suffering from neurogenic detrusor overactivity.

Study design, materials and methods

At two study centers 54 children / adolescents (average age 7.3 years; range 4 months – 19.6 years) suffering from detrusor overactivity due to an upper motor neuron lesion were enrolled, but 6 of those failed regular followup. Most of the 24 boys and 24 girls (42/48) suffered from congenital causes (myelomeningocele), few (6/48) from acquired causes of neurogenic detrusor overactivity.
15 patients were followed up 24 months, 16 patients were followed up 12 months, the others less than 12 months.
Mean treatment duration was 13.8 months (median 12 months), cumulating to 663 patient months.
Urodynamic follow up was conducted at start of medication (V1), after 3 (V2), 6 (V3), 12 (V4), 18 (V5) and 24 (V6) months of propiverine treatment. At each visit maximum detrusor pressure, maximum cystometric capacity, reflex volume (defined as starting of first hyperreflexive detrusor contraction), and compliance were evaluated urodynamically. Due to the non-interceding character of post marketing surveillance and dependent on the medical judgment by the responsible physician some patients were not evaluated at every visit. In order to perform paired Wilcoxon tests in the evaluation of these primary endpoints the last value under observation was carried forward to the final visit (LOCF).

Results

All urodynamically assessed efficacy parameters improved significantly in regards to the comparisons of the first versus the last visit (mean ± standard deviation): maximum detrusor pressure decreased from 51.4 (± 27.0) to 35.3 (± 23.6) cmH_2O, maximum cystometric capacity increased from 143.2 (± 107.3) to 195.2 (± 118.0) mL, reflex volume increased from 93.5 (± 85.4) to 147.7 (± 97.2) mL. Compliance improved from 12.8 (± 14.4) to 17.3 (± 12.8) mL/ cmH_2O. Urodynamic results were reflected also in clinical parameters: incontinence episodes of more than 50% between catheterizations decreased from 72.9% at V1 to 41.7% at the last visit.
Concerning tolerability 17 adverse events were documented in 9 patients. Considering the time under observation this results in 2.6 adverse events per 100 patient months. 18 patients discontinued treatment due to various reasons: switch to other anticholinergics (especially intravesical applications; n=5) or to botulinum toxin injections (n=1), tethered cord operations (n=2), treatment at other hospitals (n=3), no / insufficient propiverine intake (n=4) and adverse events (n=1).
Propiverine was applied with average daily dosages of 0.7 mg/kg body weight, which is slightly below the recommended dosage of 0.8 mg/kg body weight.

Interpretation of results

Propiverine proved to be effective in long-term treatment (up to 24 months) of neurogenic detrusor overactivity in children. This was shown in the primary urodynamic as well as in clinical parameters.
Due to its dual mode of action it is well tolerated, even in most of those cases, which had to be exposed to higher dosages in order to achieve control of involuntary detrusor contractions. Propiverine was well tolerated and safe even under conditions of long-term exposure.

Concluding message

Propiverine hydrochloride is very effective in the treatment of children with neurogenic detrusor overactivity in long-term followup. Because of its dual mode of action, tolerability presents with a favourable tolerability profile even in children who need higher doses. Propiverine hydrochloride is a preferable alternative to oxybutynin, the anticholinergic most frequently used in children with NDO to date.

FUNDING: Apogepha Arzneimittel GmbH, Dresden, Germany

HUMAN SUBJECTS: **This study did not need ethical approval because According to the legal situation post marketing surveillance requires not a vote by an ethics committee. but followed the Declaration of Helsinki Informed consent was not obtained from the patients.**