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URODYNAMIC EFFECTS OF PROPIVERINE HYDROCHLORIDE IN CHILDREN AND ADOLESCENTS WITH NEUROGENIC DETRUSOR OVERACTIVITY – RESULTS OF A PROSPECTIVE LONG-TERM STUDY

Hypothesis / aims of study

In the late 1970s, clean intermittent catheterization (CIC) in combination with anticholinergics was introduced as a treatment option for neurogenic detrusor overactivity (NDO), both in adults and children. The most commonly used drug is oxybutynin. However, there is increasing evidence of serious side-effects with oxybutynin. Anticholinergic effects, e.g. dry mouth, constipation and tachycardia, can occur, leading to discontinuation of the medication in 28% of cases when it is taken orally and in up to 65% when it is given intravesically. Serious adverse effects involving the CNS, e.g. hallucinations, drowsiness and cognitive impairment, can also occur in children treated with oral and intravesical oxybutynin. This is particularly important because the combined use of CIC with anticholinergics should be started in early childhood, preferably even in newborns. Thus, not only efficacy but also tolerability and the route of administration of the antimuscarinic drug are of interest, and influence patient compliance.

Propiverine hydrochloride (HCl) has a dual mode of action with both anticholinergic properties and Ca^{2+}-modulating effects. The efficacy of propiverine HCl for treating NDO was shown in spinal-cord injured adults and in children with NDO of different origin. It was as effective as oxybutynin, but its side-effects were less frequent and less severe. Particularly of note, oxybutynin is associated with a higher incidence of cognitive impairment than other anticholinergics like propiverine. After convincing short term results of a prospective study with propiverine HCl in children with NDO, our prospective study, initiated in 2003 and still ongoing, presents the first long-term data of propiverine HCl in children and adolescents suffering from neurogenic detrusor overactivity.

Study design, materials and methods

17 children and adolescents (10 female, 7 male) with an average age at last consultation of 13.0 years (range 6.0 - 19.1) suffering from NDO (in 14 cases due to myelomeningocele, twice due to perinatal hypoxia and once due to spinal cord injury) were enrolled. The patients were evaluated during long-term treatment with propiverine HCl, which was administered in body weight-adapted doses, aiming at 0.8 mg/kg body weight/day divided into 2 doses. Special attention was given to the urodynamic parameters during treatment because of their high prognostic value: maximum detrusor pressure, maximum cystometric capacity, and bladder compliance. Furthermore, the achievement of an age-related normal cystometric capacity according to the formula proposed by Palmer et al. was calculated. Attention was also paid to dilatation processes (no / slight / pronounced dilatation) of the upper urinary tract, continence (0 = completely continent, 1 = wet only once daily, mostly during night, 2 = incontinence episodes less frequent than 50% between catheterizations, 3 = incontinence episodes more frequent than 50% between catheterizations), and manifestation of urinary tract infections (UTI). The efficacy, tolerability, and safety of the medication was graded (1 = very good, 2 = good, 3 = sufficient, 4 = insufficient).

Results

Average follow-up of the patients was 3.6 (range 2.0 – 5.9) years. Maximum detrusor pressure was on average 33.0 $\pm$ 4.84 cm H_2O, bladder compliance 20.0 $\pm$ 5.39 ml / cm H_2O. Maximum cystometric capacity was within normal range according to the Palmer formula in 11 patients, in 6 patients it was reduced to an average of 61% of normal values. In 4 cases parameters deteriorated (2 cases due to low-compliance bladder, 2 cases due to a tethered cord syndrome), a co-medication with intravesical oxybutynin was necessitated in 6 patients. Continence situation was quite satisfying (1.2 $\pm$ 0.22 on average), recurrent UTI manifested in 2 patients only. Ultrasound examinations documented that upper urinary tract was not dilatated in 11, slightly dilatated in 3, a pronounced dilatation was documented in 3 patients. Propiverine HCl was very well tolerated (average scale 1.3 $\pm$ 0.19). The efficacy evaluation achieved good results (average scale 2.0 $\pm$ 0.28).

Interpretation of results

The present study reports the first prospective data on the long-term efficacy of propiverine HCl for NDO in children and adolescents. It showed clinically relevant improvements in all urodynamic outcomes, paralleled by clinically relevant improvements in incontinence scores.

Especially the key-parameter according to McGuire, maximum detrusor pressure, proved to be within safe ranges by documenting average values of 33.0 cmH_2O during treatment. Therefore, a deterioriation of the upper urinary tract can be ruled out. Moreover, all patients had either a normal (11) or an acceptable (6) maximum cystometric capacity, defined as values within two-thirds of normal bladder capacity. Crucial long-term parameters, e.g. dilatation of the upper urinary tract or recurrent UTI were well under control in 65% and 88% of cases, respectively.

Regarding the attrition rate, the patients` compliance for continuous intake of propiverine HCl was extremely high. However, in about one-third of the patients, which were very difficult to treat, an additional co-medication with intravesically applied oxybutynin was unavoidable.

Concluding message

In conclusion, in the present long-term study propiverine HCl was very effective, well tolerated, and safe for treating NDO in children and adolescents. Probably because of its dual mode of action, comprising anticholinergic and Ca^{2+}-modulating effects, propiverine HCl had pronounced effects on all urodynamic parameters and on the subjective benefit of the patients.

References

1. AVAILABLE ON REQUEST FROM CORRESPONDING AUTHOR

Specify source of funding or grant	**no**
Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require eithics committee approval because	**only usually clinical practice was documented**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**No**