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Alloussi S[1], Mürtz G [2], Braun R[3], Gerhard U[2], Heinrich M[4], Hellmis E[5], Marschall-Kehrel A[6], Niklas K[7], Rössler T[8], Seibt B[9], Wiedeking B[10], Hanisch J[11]
1. Department of Urology and Paediatric Urology, Neunkirchen, Germany, 2. Dresden, 3. Leipzig, 4. München, 5. Duisburg, 6. Oberursel, 7. Saarlouis, 8. Rottweil, 9. Zwickau, 10. Essen, 11. Basel

# EFFICACY, TOLERABILITY AND SAFETY OF PROPIVERINE HYDROCHLORIDE IN COMPARISON TO OXYBUTYNIN IN CHILDREN WITH IDIOPATHIC DETRUSOR OVERACTIVITY – A MULTICENTER OBSERVATIONAL COHORT STUDY

Hypothesis / aims of study

Antimuscarinics are the mainstay for the treatment of children suffering from idiopathic detrusor overactivity. Oxybutynin still presents the most widely used antimuscarinic drug, despite its limited tolerability. A more favourable tolerability and safety profile has been reported for propiverine (1), a compound comprising a dual mode of action with antimuscarinic and calcium-channel-modulating effects (2). Therefore, this study aims at a comparative assessment of efficacy, tolerability and safety of propiverine (Mictonetten®) and oxybutynin in children with urinary incontinence due to idiopathic detrusor overactivity.

Study design, materials and methods

Our pharmacoepidemiological study presents the results of 621 children suffering from urinary incontinence due to idiopathic detrusor overactivity, which had been treated in 16 study centers. According to the individual symptomatology idiopathic detrusor overactivity was assumed, so urodynamic verification of the diagnosis was not necessarily performed. This diagnostic procedure is in accordance with the algorithm of the ICI (3). Children suffering from daytime- and nighttime symptoms were included, children with nighttime symptoms only were not eligible. 437 children were treated with propiverine, 184 with oxybutynin. The age range of the cohort varied from 4 – 14 years, antimuscarinic treatment was started on average at 7.5 (propiverine) and at 9.2 (oxybutynin) years of age.

Results

The primary efficacy outcome, the achievement of continence, demonstrated statistically equivalent efficacy of propiverine and oxybutynin. According to the multivariate adjusted comparison, conducted additionally, a trend for superior efficacy of propiverine compared to oxybutynin resulted. The subjective assessment of the investigators corresponded to the clinical outcomes (table 1).

Tab. 1: Efficacy and dosages

| | Propiverine | | Oxybutynin | |
|---|---|---|---|---|
| | Pre treatment | Post treatment | Pre treatment | Post treatment |
| Continence (%) | 0 | 61.6 | 0 | 58.7 |
| Incontinence episodes/week | 6.2 | 1.8 | 6.4 | 1.3 |
| Micturition Frequency/day | 9.2 | 6.6 | 9.1 | 6.5 |
| Dosage/day (mg) | 15.1 | 15.5 | 9.8 | 9.6 |
| Dosage (mg/kg body weight/day) | 0.54 | - | 0.31 | - |
| Final assessment of investigators (continent + improved) (%) | - | 82.6 | - | 85.9 |

In higher dosage groups of propiverine a trend towards superior efficacy compared to oxybutynin was demonstrated. Furthermore, in the propiverine-treated children an increment of dosages corresponded to improved efficacy. In the oxybutynin-treated children higher dosages did not correspond to improved efficacy: in the highest dosage group efficacy rates even deteriorated compared to lower dosages. This corresponds to the finding, that 57.6% of our children in the oxybutynin-group were exposed to 10 – 15 mg/day, dosages being recommended for adults, whereas in the propiverine group only in 34 out of 437 children (7.8 %) 30 mg, eqivalent to dosages applicable in adults, were administered.

Treatment periods comprised on average 208 days in the propiverine-group, and 303 days in the oxybutynin-group. Continence was documented after 186 days of propiverine, and after 259 days of oxybutynin treatment on average. Another analysis, contrasting applied treatment periods and the achieved continence rates, revealed a positive correlation between continence rates and treatment periods.

In the propiverine-treated patients adverse events manifested in 3.9%, in those treated with oxybutynin the incidence rate of adverse events was more than 4-fold higher (16.3%). No serious adverse events occurred. Adverse events manifested earlier in the propiverine- compared to the oxybutynin-group, discontinuation rates were 1.6% and 4.4%, respectively.

Interpretation of results

The study confirms the equieffectiveness of propiverine and oxybutynin in children suffering from urinary incontinence due to idiopathic detrusor overactivity. In the multivariate adjusted analysis a trend of superior efficacy for propiverine compared to oxybutynin was demonstrated. Our data also elucidated that treatment modalities can be further optimized: Propiverine dosages (0.54 mg/kg body weight/day on average) could possibly be increased, thus further improving continence rates, whereas the administered oxybutynin dosages (0.31 mg/kg body weight/day on average) documented at least in the highest dosage group declining continence rates. Furthermore, the topic of minimum treatment periods, a prerequisite for a successful outcome, must be addressed, because treatment failures are not only attributable to inappropriate diagnoses and insufficient dosages but also to inadequately short treatment periods.

Advantages of propiverine in regards to tolerability and safety were confirmed. Therefore, propiverine should be preferred to oxybutynin in the paediatric population, especially in cases requiring acceptable tolerability and safety.

Concluding message

Both propiverine and oxybutynin are effective in the treatment of urinary incontinence due to idiopathic detrusor overactivity in children. The trend of an even superior efficacy of propiverine, documented for the higher dosage groups, must be emphasized. Adequate diagnosis, bodyweight adapted dosages, dose titration and treatment periods of preferrably at least 4 months or longer are the determining factors for treatment success.

References

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