563

Veenboer P W[1], Huisman J[2], Chrzan R J[3], Kuijper C F[3], Dik P[2], de Kort L[1], de Jong T[2]
1. *University Medical Center Utrecht,* ***2.*** *Wilhelmina Children's Hospital Utrecht,* ***3.*** *Emma Children's Hospital Amsterdam*

BEHAVIORAL EFFECTS OF LONG TERM ANTIMUSCARINIC USE IN SPINAL DYSRAPHISM: A CASE CONTROL STUDY

Hypothesis / aims of study
Antimuscarinic drugs are frequently prescribed to children with neurogenic lower urinary tract dysfunction in spinal dysraphism (SD). These drugs are known to pass the blood-brain barrier and may cause central nervous system (CNS)-side effects, like cognitive problems and hallucinations. The effects of long-term use of these drugs on cerebral functioning have not been studied yet. The aim of this study was to explore the possible association between long-term antimuscarinic use and behavioral problems in children with spinal dysraphism and neurogenic bladder dysfunction.

Study design, materials and methods
After obtaining EBR approval, children with SD (both open and closed) aged 6-18 years were recruited from two centers. At center A, antimuscarinics were prescribed in selected patients only when detrusor overactivity was diagnosed. At center U, antimuscarinic agents were basically prescribed from birth onwards in all patients. Patients from center A not using antimuscarinics were matched to patients from center U who had been using antimuscarinics lifelong, Parents of the participants were asked to fill-out a Child Behavior's Check List (CBCL), a 120-question questionnaire, which is a validated and broadly used screening tool for behavioral problems. Outcomes were clustered into various subdomains: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior and aggressive behavior. The broader subcategories internalizing, externalizing and total problems were also scored.
Demographics, data on level of the lesion, type of lesion and hydrocephalus/drain (and if applicable, number of revisions) were retrieved for each patient. Cases and controls were matched for these characteristics. Data were compared between groups. For statistical analysis, SPSS 20.0® was used, with $p < 0.05$ regarded statistically significant. The difference between users of oral and intravesical oxybutynin was assessed separately.

Results
These are also shown in **Table 1** (continuous scores) and **Table 2** (categorized). After a 6-month data-collection period, data of 32 children (16 in each group) were analyzed. Median age in the case-group was 10.6 years and 10.5 in the control-group (p = 0.877); both groups consisted of 8 boys and 8 girls. In each group, 9/16 had hydrocephalus with a drain. No significant difference in CBCL-score Total Problems could be found between the case-group and the control-group (medians 52.0 vs. 59.5, respectively; p = 0.39). When looking at categorized data, 2/16 (12.5%) children in the control-group and 4/16 (25.0%) children in the case group had problems in the clinical range (p = 0.172). Categorized scores are also visible in **Table 1.** On none of the subdomains of the CBCL, differences could be found between the two groups. Patients using intravesical oxybutynin (n = 4) had the same amount of clinical behavioral problems in total than those using oral drugs (1/4 vs. 1/12; p = 0.607); this was also the case for internalizing and externalizing clinical problems (1/4 vs. 1/12; p = 0.245 and 0/4 vs. 1/12; p = 0.450, respectively). Median scores of CBCL were also the same for oral and intravesical users (median 51.0 vs. 54.5; p = 0.361).

Table 2. CBCL-outcomes, continuous scores (non-categorical). A T-score of 50 is completely normal for a child of that particular age and sex. IQR = interquartile range (25th percentile – 75th percentile). [a] p-value of difference between the groups as found using the Wilcoxon matched-pair signed-rank test.

Type of problems	Median T-Score Cases (IQR) (n = 16)	Median T-Score Controls (IQR) (n = 16)	p-value[a]
Total (IQR)	**52.0 (45.5 – 55.8)**	**59.5 (45.8 – 64.5)**	**0.393**
Internalizing problems (IQR)	53.5 (45.0 – 60.5)	60.5 (46.3 – 66.0)	0.485
Externalizing problems (IQR)	47.5 (40.0 – 52.5)	51.0 (44.5 – 61.0)	0.170

Table 1. Categorized T-scores. Given are the fractions and percentages of subclinical, borderline and clinical problems in each group. [a] p-value of cases compared to controls using the McNemar-Bowker-test

Type of problems	Cases (n = 16)	Controls (n = 16)	p-value[a]
Total			
• **T-scores in subclinical range**	**13/16 (81.3%)**	**8/16 (50.0%)**	**0.172**
• **T-scores in borderline range**	**1/16 (6.3%)**	**4/16 (25.0%)**	
• **T-scores in clinical range**	**2/16 (12.5%)**	**4/16 (25.0%)**	

Internalizing problems			
• T-scores in subclinical range	12/16 (75.0%)	8/16 (50.0%)	0.241
• T-scores in borderline range	2/16 (12.5%)	4/16 (25.0%)	
• T-scores in clinical range	2/16 (12.5%)	4/16 (25.0%)	
Externalizing problems			
• T-scores in subclinical range	14/16 (87.5%)	12/16 (75.0%)	0.392
• T-scores in borderline range	1/16 (6.3%)	1/16 (6.3%)	
• T-scores in clinical range	1/16 (6.3%)	3/16 (18.8%)	

Interpretation of results

Although possibly impaired by small numbers, this case-control study shows no difference in behavioural problems in those who had used antimuscarinics for a long period of time versus those who had not. The lack of long-term behavioural problems suggests in our point of view that antimuscarinics do not cause any structural damage to children's brains. This argument could be used to explain parents that long-term use of antimuscarinics is safe with respect to behavioural problems. Although this was a small study, it was the largest study to be achieved in our country. The number of children born with SD is diminishing due to ultrasonography and folic acid prophylaxis, and most children have antimuscarinics from birth on. A larger control group will therefore be very hard to compose. The strength of this study is that the children in our cohort were well-matched and that we used a validated questionnaire.

Concluding message

In a group of children with spinal dysraphism, no significant differences in behavior could be identified between children who chronically used antimuscarinics and those who did not.

Disclosures

Funding: None. **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** University Medical Center Utrecht Ethical Committee (METC UMC Utrecht) **Helsinki:** Yes **Informed Consent:** Yes