Treatment of Nocturnal Enuresis in Children With Attention Deficit Hyperactivity Disorder

Boris Chertin,* Dmitry Koulikov, Wael Abu-Arafeh, Yoram Mor, Ofer Z. Shenfeld and Amicur Farkas

From the Departments of Urology, Shaare Zedek Medical Center, Jerusalem, Faculty for the Health Science, Ben-Gurion University of the Negev, Be'er Sheva and Chaim Sheba Medical Center, Faculty of Medicine, Sackler School of Medicine, Tel Aviv University (YM), Tel Aviv, Israel

Purpose: Children with attention deficit hyperactivity disorder disproportionately experience voiding dysfunction and persistent nocturnal enuresis due to a combination of sphincter and detrusor overactivity and nocturnal polyuria. The different treatment approaches to nocturnal enuresis often fail in these patients. Therefore, we performed a prospective study to compare the efficacy of combination therapy with desmopressin and oxybutynin vs the tricyclic antidepressant imipramine in patients with attention deficit hyperactivity disorder who have nocturnal enuresis.

Materials and Methods: A total of 54 patients with attention deficit hyperactivity disorder and nocturnal enuresis were randomly stratified into 2 groups. Demographic data on patient age and gender were identical in the 2 groups. Functional bladder symptoms were judged using the dysfunctional voiding symptoms survey. The initial dysfunctional voiding symptoms survey score was similar in the 2 groups. The total survey score was compared between the 2 groups in aggregate as well as specifically regarding the incidence of nocturnal enuresis following treatment.

Results: The first group consisted of 27 patients who received desmopressin and oxybutynin, and the second group of 27 was treated with imipramine. Of the 27 children in each group 23 (85%) received methylphenidate for attention deficit hyperactivity disorder. The mean ± SD initial dysfunctional voiding symptoms survey score in groups 1 and 2 was 20.5 ± 3.3 and 20.9 ± 4.1, respectively. Following treatment the mean survey score decreased significantly in groups 1 and 2 (6.5 ± 2.5 and 9.4 ± 2.1, respectively, $p < 0.001$). However, between groups analysis showed that the dysfunctional voiding symptoms survey score was significantly lower in group 1 than in group 2 (mean 6.5 ± 0.5 vs 9.6 ± 0.4, $p < 0.001$). There was also a statistically significant decrease in the incidence of nocturnal enuresis in group 1 (survey question 2 score 0.9 ± 0.2 vs 2.9 ± 0.2).

Conclusions: Our data show that there is a high incidence of voiding dysfunction in children with attention deficit hyperactivity disorder. Combination therapy with desmopressin and oxybutynin is a feasible, safe and effective treatment for nocturnal enuresis in these children.

Key Words: bladder, oxybutynin, nocturnal enuresis, attention deficit disorder with hyperactivity, deamino arginine vasopressin

Attention deficit hyperactivity disorder is relatively common, affecting approximately 3% to 5% of children in the Western world. ADHD manifests as impulsive, hyperactive, inattentive behavior.[1,2] Symptoms present before age 6 years and they are noted in 2 distinct settings (home and school).

Bedwetting or NE is a common clinical disorder in Western countries.[3–5] It is well known that NE may have a profound psychological and social impact on the affected child. Furthermore, almost all studies of the comorbidity between primary NE and psychopathology in children suggest an increased prevalence of behavioral disorders in general and of ADHD in particular.[6–9] Some investigators pointed out that the combination of nocturnal polyuria with bladder and sphincter overactivity may be responsible for almost 25% of NE episodes in children with ADHD.[7] Different treatment modalities have been suggested for NE in children with ADHD, including urotherapy, DDAVP and the tricyclic antidepressant imipramine. However, none of these therapies have shown significant effectiveness for ADHD with voiding dysfunction.[7,8] Therefore, we performed a prospective study to compare the effectiveness of combined treatment with DDAVP and oxybutynin vs the tricyclic antidepressant imipramine.

MATERIALS AND METHODS

A total of 54 patients with ADHD who were referred for NE were randomly stratified into 2 groups. Group 1 of 27 patients was treated with DDAVP and oxybutynin, while 27 in group 2 received imipramine. We excluded children with mental retardation, anatomical abnormalities of the urinary system on imaging and psychosis. The table shows clinical and demographic data on the 2 groups.

Functional bladder symptoms were judged using DVSS. A DVSS was designed at Hospital for Sick Children in Toronto for quantification voiding symptoms in children.[10] We used an established, modified form of that DVSS, consisting

* Correspondence: Department of Urology, Shaare Zedek Medical Center, Jerusalem, 91031, P. O. 3235, Israel (telephone: +972-2-6555560; FAX: +972-2-6555062; e-mail: bchertin@yahoo.com).

DOI:10.1016/j.juro.2007.03.171

Demographic and clinical data on 54 studied children

	Group 1	Group 2
No. boys	17	17
No. girls	10	10
Mean ± SD age (yrs)	8.07 ± 2.13	8.22 ± 2.19
Mean ± SD symptom duration	2.2 ± 0.87	2.2 ± 0.98
Mean ± SD initial DVSS score	20.9 ± 4.2	20.5 ± 3.3

of 10 questions, omitting the question on stressful events in the life of the child, as previously suggested (see Appendix).[6] Each question in the questionnaire was scored on a 0 to 3 scale, including 0—never, 1—less than half of the time, 2—about half of the time and 3—almost always.

The initial DVSS score was similar in groups 1 and 2 (mean ± SD 20.8 ± 4.18 and 20.5 ± 3.31, respectively, $p > 0.05$). The total DVSS score was compared between the 2 groups in aggregate as well as specifically regarding the incidence of NE following treatment (DVSS question 2). The child and parents were asked to complete the questionnaire together.

A bladder training program designed to decrease bladder overactivity and engage the child in the treatment process commenced at the beginning of the treatment protocol. It included an increase in daytime fluid intake, the need to respond to any sense of urgency in urination, timed voiding every 2 to 3 hours or during school breaks to establish cognitive control over voiding and treatment of encopresis, if it existed. During the bladder training program child compliance was evaluated and DVSS was reevaluated. Only children with compliance participated in the study. Since none of the children demonstrated significant improvement on DVSS, we proceeded with medical therapy.

Group 1 patients received DDAVP at an initial dose of 0.2 mg with an increase to 0.4 mg if the episodes of nighttime wetting did not decrease at least 50%. Also, oxybutynin was given at 0.2 mg/kg 3 times during the day. In group 2 imipramine was given at a dose of 25 mg. Patients were followed at least 1 year. Success was defined as symptom resolution for 6 months. We attempted to wean the children from the medications 1 year after treatment began, while continuing timed voiding, constipation treatment when indicated and dietary suggestions. GraphPad® Prism®, version 4.0 for Windows® was used for statistical evaluation with the paired and unpaired t test, and $p < 0.05$ considered significant.

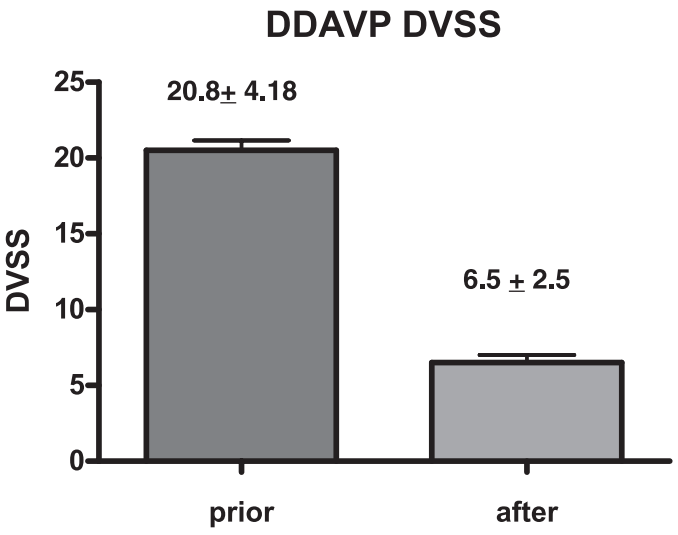

FIG. 1. DVSS before and after DDAVP and oxybutynin treatment

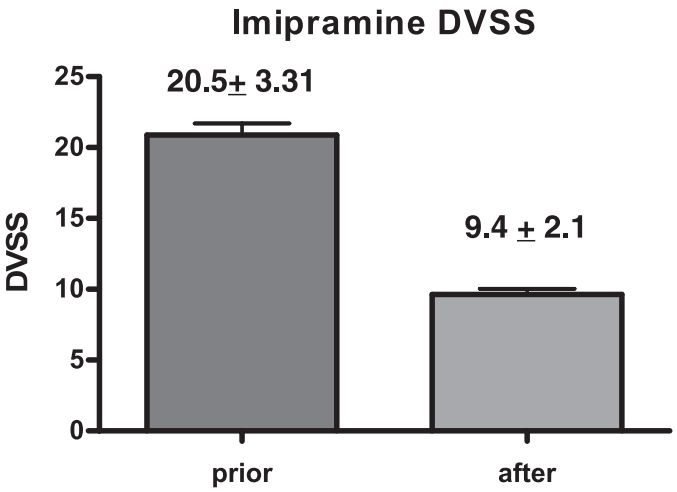

FIG. 2. DVSS before and after imipramine treatment

RESULTS

Demographic data on patient age and gender were identical in groups 1 and 2. There were 17 boys and 10 girls in each group. Mean age in groups 1 and 2 was 8.1 ± 2.1 and 8.2 ± 2.2 years, respectively. Of the 27 children in each group 23 (85%) received methylphenidate for ADHD. Of the 54 children in the 2 groups 39 (72%) had inattentive ADHD. Following treatment the DVSS score decreased significantly in group 1 from 20.8 ± 4.18 to 6.5 ± 2.5 and in group 2 from 20.5 ± 3.31 to 9.4 ± 2.1 (figs. 1 and 2, $p < 0.001$). However, between groups analysis showed that the posttreatment DVSS score was significantly lower in group 1 than in group 2 (mean 6.5 ± 0.5 vs 9.6 ± 0.4, $p < 0.001$, fig. 3). There was also a statistically significant decrease in the incidence of NE in group 1 vs group 2 (DVSS question 2 score 0.9 ± 0.2 vs 2.9 ± 0.2, $p < 0.0001$, fig. 4). None of the children in group 2 were completely dry during the study period.

DISCUSSION

NE can be a distressing, humiliating and perplexing experience for children and young people.[3–5] It may lead to

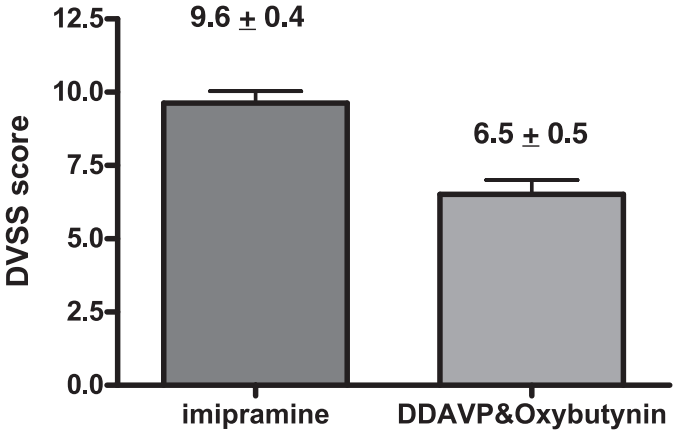

FIG. 3. DVSS in patients in 2 groups