

Effectiveness of Tolterodine in Non-Neurogenic Voiding Dysfunction

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*The efficacy of tolterodine was analysed in children with non-neurogenic voiding dysfunction, using dysfunctional voiding symptom score (DVSS). Of 44 patients (mean age 9.3 yrs; M:F = 25:19), 36 received long acting tolterodine tartrate at a dose of 2mg OD and 8 at a dose of 4mg OD. The mean (SD) DVSS before and after the treatment was 17.1 (2.8) and 12.0 (2.4). There was a significant improvement in the mean DVSS score at the end of the treatment (Student's *t* test $P < 0.01$). The dysfunctional symptoms were cured in 28(63.6%), improved in 14(31.8%) and failed to show improvement in 2 (4.6%). Over all 95% were compliant with the single daily medication. Our results demonstrate that long acting tolterodine is effective in children with voiding dysfunction. The single daily dose has good compliance and minimal side effect profile.*

Key words: *Bladder instability, Dysfunctional voiding, Overactive bladder.*

VOIDING dysfunction is characterized by a variety of symptoms including urgency, frequency, urge incontinence, often associated with day time or night time wetting, constipation, leg crossing and crouching (Vincent's curtsey). While behavioural modification, bladder training and biofeed back remain the mainstay of treatment, anticholinergic medications are necessary to control the overactive bladder. These medications often have side effects like dry mouth, flushing and constipation.

Tolterodine, a potent high-affinity competitive muscarinic receptor antagonist, has been used successfully in adults with voiding dysfunction. Fewer side effects have been reported compared to oxybutynin as tolterodine is a bladder selective anticholinergic agent(1). The aims of the present study were to assess the efficacy and tolerability of single daily dose, long acting

tolterodine in children with non-neurogenic voiding dysfunction.

Subjects and Methods

Children with symptoms of voiding dysfunction seen in the outpatients between November 2003 and October 2005 were evaluated by history and clinical examination including examination of spine and anal tone. An X-ray of the spine was performed to exclude spinal dysraphism or sacral agenesis. In addition uroflowmetry and renal ultrasonogram (with post void residual volume) were performed. Children with evidence of obstructive uropathy or neurological abnormality were excluded. Dysfunctional voiding was defined as urgency, frequency, wetting and various holding manoeuvres in the absence of neurological abnormality or obstructive uropathy. Urodynamic evaluation or MRI scan was not routinely performed.

Patients who had never been treated earlier with medications for dysfunctional voiding were included. Long acting tolterodine tartrate was used at the dose of 2 mg once daily in children less than 10 years, and 4 mg once daily in older children, for a duration of 3 months. Patients with constipation also received oral lactulose to prevent worsening of constipation. Dysfunctional voiding symptoms score (DVSS) described earlier^(2,3) was completed by the parents/ children at the beginning and the end of the treatment. In addition, a subjective evaluation of efficacy was assessed using a standardized questionnaire. Complete cure was defined as >90% reduction in wetting episodes, improvement as reduction of at least half and failure as a reduction of less than half. The severity of side effects were defined as follows: mild: does not interfere with patient's usual function; moderate: interferes to some extent with the patient's usual function; and severe: interferes significantly with patient's usual function. The compliance was defined as good: child always taking the medication; fair: child taking the medications most of the time and poor: child not taking the medication consistently. Written consent of the child and the parent to participate in the study was obtained in all cases.

Results

Of 51 patients with symptoms of bladder dysfunction, 7 were excluded due to

underlying problems (3 occult spinal dysraphism, 2 meatal stenosis; 2 posterior urethral valve). Of 44 patients (mean age 9.3 yrs; M:F = 25:19), 36 received long acting tolterodine tartrate at a dose of 2 mg OD (mean age 8.2 years) and 8 at a dose of 4 mg OD (mean age 14.3 years).

The mean (S.D) DVSS before starting and after completing the treatment was 17.1 (2.8) and 12.0 (2.4). There was a significant improvement in the mean DVSS score at the end of the treatment (Student's t test $P < 0.01$). Subjective evaluation from questionnaire revealed cure of dysfunctional symptoms in 28 (63.6%), improvement in 14 (31.8%) and no improvement in 2 (4.6%). Only two patients reported mild side effects in the form of dry mouth and hyperpyrexia. The compliance was good in 39 patients (88.6%), fair in 3 (6.8%) and poor in 2 (4.6%). *Table I* summarizes the compliance versus cure rate. No patient discontinued the medication during the period of study due to side effects.

Discussion

Dysfunctional voiding is a common problem encountered in children with wetting and recurrent urinary infection. Overactive detrusor and poorly coordinating sphincter play an essential role in the pathology of dysfunctional voiding. Anticholinergic medications are widely used as a first line

TABLE I—Treatment outcome and compliance in patients (n=44) with voiding dysfunction, receiving single daily dose tolterodine

Compliance	Cured	Improved	Failed	Total
Good	28	11	0	39
Fair	0	3	0	3
Poor	0	0	2	2
Total (%)	28 (63.6%)	14 (31.8%)	2 (4.6%)	44

Key Message

- Single daily dose, long-acting tolterodine has a good efficacy in controlling dysfunctional voiding symptoms with minimal side effects.

therapy in the management of children with dysfunctional voiding. However non-selective anticholinergic agents like oxybutynin have significant muscarinic side effects and are not well tolerated by children. Although selective anticholinergics like tolterodine have been used successfully in adults there are limited reports of its use in children(1).

Goessl(4) and Munding(5) reported the first successful and safe use of tolterodine in children with dysfunctional voiding. Others have demonstrated that tolterodine is superior to oxybutynin, with respect to adverse events, allowing more compliance and more effective treatment in children(6,7). Ayan(8) combined behavioural modification along with tolterodine successfully in children with dysfunctional voiding. Conventional tolterodine has to be taken twice daily and sometimes this makes the children non-compliant(9). However, long acting tolterodine has to be taken only once daily and improves compliance(10). The dose recommended is 2 mg and 4 mg once daily for children weighing <35 and >35 kg respectively(11).

Our results demonstrate that tolterodine is effective in controlling dysfunctional symptoms in most patients with minimal side effects. The present study also shows that the long-acting formulation has a good patient compliance due to single daily dosing. Larger studies are warranted to further strengthen or negate this evidence.

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Evaluation of Immunogenicity and Tolerability of a Live Attenuated Hepatitis A Vaccine in Indian Children

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An open non comparative study of a live attenuated H2 strain Hepatitis A vaccine of Chinese origin was carried out in 143 healthy Indian children aged 1 to 12 years (mean age 4.87 + 2.76 years; 88 boys, 55 girls). At baseline, all were negative for IgG HAV antibodies and had normal hematological and biochemical indices. Two months after a single dose of the vaccine (given subcutaneously), 137 children (i.e. 95.8%) developed protective antibodies of IgG >20 mIU/mL. The hematological and biochemical parameters remained within normal limits. There were no adverse events in any except mild fever in one child. In conclusion, live attenuated H2 strain Hepatitis A vaccine in a single dose was found to be immunogenic and safe in Indian children.

Key words: *Immunogenicity, Live attenuated hepatitis A vaccine, Tolerability.*

HEPATITIS A Virus (HAV) has a worldwide distribution, and accounts for more than 1.4 million cases of viral hepatitis annually(1). In recent years, India and other transitional economies are showing a significant epidemiological shift of HAV infections from high endemicity to intermediate endemicity(2,3). Increasing numbers of older children and adults,

especially in urban 'developed' areas, are now susceptible to HAV with considerable increase in morbidity, costs and mortality related to the disease. Further, such areas (of transitional endemicity) are prone to recurrent and explosive epidemics of the disease as seen in Shanghai (China) and Kerala (India)(4,5). As such, WHO has now recommended hepatitis A vaccination programs in areas of intermediate