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VILOXAZINE VERSUS IMIPRAMINE IN THE TREATMENT OF ENURESIS*

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Imipramine has often been prescribed in the treatment of eneuritic children. While the beneficial effect of imipramine in reducing the frequency of this disorder has been well established in many controlled trials, efficacy is less than 100 percent[1-3]. But it has been reported that tricyclic antidepressants, including imipramine, have some mild side effects due to their anticholinergic, antiseratoninergic and antihistaminic properties such as postural hypotension, dry mouth, constipation, tachycardia, perspiration, nausea, lethargy and insomnia. It should be noted that these particular drugs may cause severe hypotension, cardiac arrest, apnea, acute renal failure, convulsions and icterus, especially with their cardiotoxic and hepatotoxic effects when taken in higher doses in accidental fatal poisoning which is not uncommon in some countries[4,5].

Viloxazide, a non-tricyclic antidepressant that appears to possess minimal side effects in normal doses is not cardiotoxic nor hepatotoxic in excessive doses. This drug has also been used in the treatment of some psychiatric disorders in children[6]. A report from Scotland on its successful use in the treatment of enuresis with good tolerance encouraged us to evaluate its effectiveness in the treatment of this disorder as compared to imipramine[7].

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Material and Methods

The subjects for study were selected from among six-year-olds or over, presenting with nocturnal enuresis in the Department of Pediatrics of the Ulus Social Security Hospital who were considered suitable for drug therapy. The children's age, sex, weight, social economic level and history of bed-wetting were recorded. A physical examination was carried out and bacterial cultures were also taken. The children with an abnormality in the urine and those who did not come for control were excluded from the study.

Thirty-seven children were included in the study. There were 25 boys (68%) and 12 girls (32%). Their ages ranged from 6-17 years, the mean being 10. The children were grouped at random but they were well-matched according to age and socioeconomic level. Prior to the study most of the children had received simple preliminary methods of treatment including wakening the child to go to the toilet at night and fluid restriction.

Thirty-one children (84%) had primary and six (16%) secondary enuresis. In many there was a family tendency to enuresis; 14 children (38%) had enuretic brothers or sisters, 11 had a mother or father who had been enuretic as a child (30%), and eight (22%) an aunt or uncle.

The children were randomly assigned treatment with imipramine or viloxazine for a six-week period. Twenty-one were put on viloxazine and 16 on imipramine. The daily dose of the active drug taken half-an-hour before bedtime was 25 mg imipramine (Tofranil^{R}, 25 mg) or 50 mg viloxazine (Viloksan^{R}, 50 mg) for the six to ten year-olds, and the amount was doubled for those aged 11 years and over.

A check-list was given to the parents for them to mark off any symptoms that might later be recorded as side effects of the treatment. The children were re-assessed after six weeks of treatment. At this visit each child was examined and the number of wet nights during the six-week period was recorded together with a note on any side effects. The therapeutic index score was then made, the response to therapy being graded as follows: O-no improvement, 1-partial improvement and 2-complete cure.

The Kruskal-Wallis analysis was used to compare the two treatments.

Results

The response to therapy with imipramine or viloxazine is illustrated in Table I. At the end of the sixth week, no significant differences were recorded between the imipramine and viloxazine groups. In addition no significant side effects were observed in any of the groups during the therapy.

TABLE I: Some Clinical Features and the Effects of Drugs Used in the Treatment of Enuretic Children.

Group	Drug	Number of patients	Age (yrs)	Sex M:F	Type Primary: Secondary	Therapeutic index score
1	Imipramine	16	11.3 (7–15)	11:5	13:3	1.55
2	Viloxazine	21	10.1 (6–17)	14:7	18:3	1.29
	Total	37	10.0	25:12	31.6	

Discussion

The use of imipramine, which is practically a classical drug of choice in the treatment of enuresis[1-3], has also been supported by a previous study carried out at the same center[8]. Although we did not observe any side effects from imipramine in our study, its minor side effects are reported frequently. The main reason for this being that parents do not pay any attention to the mild side effects such as constipation or tachycardia. However it has been reported that viloxazine has a lower incidence of unwanted side effects particularly without its anticholinergic effects[6,7].

The present study demonstrates that viloxazine is as effective as imipramine in the treatment of enuresis. Thus, viloxazine may be chosen as an alternative drug or a preferable drug with its reported minimal and potentially no fatal side effects. In addition, it may be used primarily in the treatment of enuresis by parents who mostly use imipramine without consulting a physician. However, to draw any conclusions on its effectiveness, additional studies are needed.

Summary

The effectiveness of imipramine and viloxazine was evaluated in 37 children with enuresis. It was shown that both imipramine and viloxazine produced an improvement in the same degree in these subjects. No side effects were reported in the use of both these drugs in the study. It is therefore proposed that viloxazine may be used as an alternative drug instead of imipramine with advantages of potentially no fatal side effects.

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