

Efficacy of Trazodone in the Treatment of Nocturnal Enuresis in School Age Children

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Abstract

Background: This study aimed to evaluate the efficacy of trazodone in the treatment of nocturnal enuresis in school age children. **Methods:** Nine patients (7 male and 2 female) with nocturnal enuresis, resistant to regular treatments, received trazodone (25 mg/day, for the first week and 50 mg/day for the second week). **Results:** Marked improvement was observed in one case, while partial improvement was observed in more than 50% of the cases. **Conclusion:** Trazodone seems to be a promising new approach for the treatment of children with primary nocturnal enuresis (German J Psychiatry 2008; 11: 7-9).

Keywords: trazodone, nocturnal enuresis, treatment

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Introduction

Enuresis, defined as the involuntary discharge of urine, is one of the most common disorders in school age children, when they are expected to have achieved full bladder control at night (Mark and Frank, 1995; Alexopoulos et al., 2006). Social problems, emotional distress such as feeling of shame, isolation, feeling of embarrassment and fear are the consequences of nocturnal enuresis in those children (Spee-van der Wekke et al., 1998). Several therapeutic approaches have been used for treatment of nocturnal enuresis, including behavioural therapy methods such as improving awareness of urgency, ability to initiate urination, ability to inhibit urination while awake, ability to inhibit urination during sleep, alarm systems (Pennesi et al., 2004; Butler and Robinson, 2002) and pharmacological treatments such as tricyclic antidepressants (TCAs), desmopressin, indomethacin, or diclofenac (Tullus et al., 1999; Cendron and Klauber, 1998; Sener et al., 1998). None of these approaches have been completely successful, but phar-

motherapeutic approaches may be more accepted by both physicians and children. However, none of these drugs does lead to complete dryness and most children return to their previous wetting frequency after discontinuation of the medication (Moffatt et al., 1993). Moreover, several side effects are associated with TCA, and high relapse rates with desmopressin bring to attention that efforts should be made to evaluate the efficacy of drugs with less side effects for the treatment of nocturnal enuresis. Trazodone is an antidepressant acting as a serotonin reuptake inhibitor, a partial agonist of serotonin 5-HT_{1A} and an antagonist of 5-HT₂ receptors. Trazodone is well absorbed after oral administration, with mean peak plasma levels obtained within 0.5 to 2 hours after ingestion. Common adverse reactions encountered with trazodone are drowsiness, nausea/vomiting, headache and dry mouth (Odagaki et al., 2005; Balsara et al., 2005). This study was conducted to assess the efficacy of trazodone in the treatment of nocturnal enuresis in school age children.

Table 1: Response to trazodone treatment in children with primary nocturnal enuresis

Gender	Improvement			Total
	Complete	Partial	None	
Female	0	1	1	2
Male	1	4	2	7
Total	1	5	3	9

Patients and Methods

Subjects of this study were 9 school children with the diagnosis of primary nocturnal enuresis (PNE) in the Paediatric Department of Yasuj University of Medical Sciences. Patients were referred to the Pediatric Department for treatment. The patients received trazodone monotherapy, starting with 25 mg/day. Dose was increased to 50 mg/day after one week of initial treatment. Enuresis was considered to be present when children wet their bed at least two times for 3 or 4 weeks.

The study was performed in accordance with the Declaration of Helsinki and subsequent revision and was approved by local ethics committee of our institute. Informed consent was obtained from each parent before entering of their child into the study. A self-administered questionnaire was used, consisting of two parts, the first was used to record the demographic features of the subjects and the second part contained questions regarding the frequency of bed wetting before and after treatment with trazodone, drugs used before or after the trial and possible side effects of trazodone.

Results

Patients recruited for the study were 7 boys and 2 girls, aged 6–15 years. Dramatic improvement with complete elimination of enuresis two weeks after the initiation of treatment was achieved in one child. A significant decrease in frequency of nocturnal enuresis was observed in five other children (Table 1). The rate of decrease was ranging from 33% to 67% in these patients. No marked improvement was observed in the rest of 3 cases. The most common noticed side effect of the drug was sedation, but tolerance developed to the sedative effects of the drug after one week. Another side effect observed in the study was dizziness. Table 2 summarised the side effects of trazodone.

Discussion

A variety of approaches, including pharmacotherapeutical treatment, have been used for treatment of primary nocturnal enuresis but most of them have not achieved a satisfactory result. The relapse of enuresis after withdrawal of the

Table 2: Side effects of trazodone in studied subjects

Gender	Female	Male	Total
No side effect	2	4	6
Sedation	0	2	2
Dry mouth	0	0	0
Orthostatic hypotension	0	0	0
Dizziness	0	1	1

treatment is another dilemma in managing of PNE. It is currently argued that a potentially dangerous drug such as imipramine with hazardous side effects should not be recommended in treatment of nocturnal enuresis, as a benign disorder. Therefore, efforts should be made to assess other drugs with less side effects. The current study was designed to determine the efficacy of trazodone in the treatment of nocturnal enuresis. Results showed a significant and rapid improvement of nocturnal enuresis in some study patients. Regarding the beneficial effects of imipramine, peripheral antimuscarinic effects seem not to be important in PNE (Korczyński et al., 1997). Therefore imipramine may exert its effects through serotonergic mechanisms.

Considering the fact that the patients in this study had been resistant to standard treatment, trazodone might be a suitable alternative for management of children with PNE. According to our best knowledge, this is the first experience with trazodone in the treatment of enuresis. Limitations of this study include the small number of cases, lack of serum drug level controls and the open label design.

In conclusion, our findings demonstrated that trazodone appears to be a promising new approach for the treatment of children with PNE. Randomised placebo controlled study are needed to confirm these findings.

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