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## Therapeutic approaches to children with enuresis: A retrospective study

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### Abstract

Enuresis is a common pediatric condition and there are different treatment options. This study aimed to evaluate treatment options for enuresis in a sample of the child and adolescent psychiatry clinic. The data and treatment results of 98 patients (mean age: 10.38±2.15 years, range=6-16 years) diagnosed with enuresis between 1 May 2015 and 1 October 2020 were retrospectively reviewed. We found that 57 of the patients had previously applied to the hospital for enuresis, and 14 of them have applied to child and adolescent psychiatry, 10 of them to pediatric surgery, 20 of them to other branches of pediatrics, and 13 of them to the urology clinic. In previous hospital applications, behavioral treatment only had been applied to 40.4% of the patients, and pharmacotherapy had been applied in 59.6% of the patients. On the other hand, in the child and adolescent psychiatry clinic, 26.5% of the patients received behavioral treatment only, and 73.5% used drugs along with behavioral treatment, and the most frequently preferred drugs were imipramine (oftenest) and desmopressin. Also, the rates of psychiatric comorbidity in those who received medical treatment were significantly higher than those who treated behavioral treatment only. In conclusion, this study revealed that different clinical branches apply different treatment approaches to enuresis. In child and adolescent psychiatry, imipramine was the most commonly used agent in medical treatment, and this has been attributed to the high rate of psychiatric comorbidity

**Keywords:** Enuresis, child/adolescent, pharmacotherapy, behavioral therapy, treatment

### Introduction

Enuresis refers to repeated urinary incontinence into bed or clothes (whether involuntary or intentional) that is not consistent with one's development age (5 years or more) [1]. Enuresis is classified into two groups as primary or secondary depending on the type of onset and course. If it continues since infancy without any dry period, it is called primary enuresis. When it occurs at any age after at least 6 months of toilet training and the dry period, it is defined as secondary enuresis [1, 2]. In addition, enuresis is categorized into three groups according to the time of the day when the problem is seen: nocturnal only, diurnal only, and nocturnal and diurnal [1,2]. The prevalence of enuresis is highly variable, and its overall prevalence ranged from 2.3 to 25%, however, 10-15% of enuretic children show spontaneous recovery every year [3, 4].

Although enuresis tends to improve spontaneously with age, it usually leads to psychosocial and emotional negative effects on the life of both the child and his/her family and impairs the quality of life, as well as its deep impact on a child's self-esteem [5-8].

Therefore, the aim of the treatment is to solve the enuresis problem in the early period before the child's self-esteem decreases and serious unfavorable psychosocial effects occur.

It has been stressed that if enuresis has become an important problem for the child and family and the child is older than 6 years old, it should be treated [9].

There are many different treatment options for enuresis, but the treatment modality varies according to the type, frequency, and severity of enuresis, the age and emotional state of the child, and the motivation of the child and his/her family [9]. Behavioral treatments such as behavior modification, enuresis alarm, restricting fluid intake at night and pharmacotherapy including desmopressin, anticholinergic agents, and tricyclic antidepressants constitute two groups of treatment options [9-11]. The first and most important step in the treatment of enuresis is to motivate the child to the treatment. Thus, the recommended first line treatment is psychoeducation and behavioral treatments. When behavioral approaches are inadequate or unsuccessful, pharmacological agents are added to the treatment. The most preferred treatment is the combination of conditioning therapy by alarm and receiving desmopressin, in this context. However, a clinical evaluation showing the pharmacological agents preferred in clinical practice in the treatment of enuresis in our country is limited to a few studies and studies have been conducted in different clinical

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branches [11,12]. For this reason, in this study, the treatment options for children with enuresis were examined retrospectively and cross-sectionally, and it was aimed to obtain information about the treatment practices in children and adolescents treated with the diagnosis of enuresis.

## Materials and Methods

Between 1 May 2015 and 1 October 2020, 146 children between the ages of 6 and 16 who were diagnosed and treated with monosymptomatic enuresis at the child and adolescent psychiatry outpatient clinic were retrospectively evaluated. Only patients who were treated under the supervision of a child and adolescent psychiatry clinic were included in the study. 48 patients with incomplete data were excluded from the study, thus, a total of 98 patients who attended regular control visits were included in the study. Data on the patients' age, gender, type of enuresis and the kind of onset, family history, previous treatments and their results, comorbidity status, the treatment model and results preferred in our clinic were obtained from hospital files and computer records. Enuresis and comorbid psychiatric disorders were diagnosed with a regular psychiatric interview in line with the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA 2013) criteria [1]. The evaluation was performed by a child and adolescent psychiatrist in a psychiatric interview. If children with enuresis have the direct physiological effect of a substance (e.g. a diuretic, antipsychotic, or selective serotonin reuptake inhibitor (SSRI) antidepressant) or a general medical condition (e.g. diabetes, a urological problem including urological anomalies and/or bladder instability, urinary tract infection, spina bifida or seizure disorder), intellectual disability and autism spectrum disorder were excluded from the study. The response rates of the patients were evaluated, based on the preceding. Accordingly, a 90-100% reduction in the number of wetting was considered as a complete response, a 50-90% reduction as a moderate response, and a decrease below 50% as unresponsive [11,13]. The study was approved by the local Ethics Committee of the Medical Faculty of the Inonu University and performed in accordance with Good Clinical Practice procedures and the current revision of the Declaration of Helsinki (No:2020-1228).

## Statistical Analysis

Statistical data were analyzed using SPSS 23.0 (IBM SPSS, Version 23.0, IBM Corporation, Armonk, NY, USA). Normality was tested using the one-sample Kolmogorov-Smirnov test. The numerical and categorical data were presented as mean  $\pm$  standard deviation (SD), number (n), median (min-max), and percentage (%) whenever appropriate. During statistical analyses, statistical comparisons were performed with the chi-square test and Mann-Whitney-U-Test. The p-value of  $<0.05$  was accepted as an indication of statistical significance.

## Results

### Sociodemographic and clinical characteristics of participants

Our sample consisted of 98 children and adolescents diagnosed with enuresis according to DSM-5. The mean age of the participants was  $10.38 \pm 2.15$  years (minimum 6- maximum 16) and 61.2% (n=60) of them were male and 38.8% (n=38) were female. According to the starting type of enuresis, 63.3% (n=62) of the sample were primary and 36% (n=36) were secondary. According to the time of occurrence of enuresis, 70.4% (n=69) of

the patients were enuresis nocturna (night-time, only), 7.1% (n=7) enuresis diurna (daytime, only), and 22.4% (n=22) nocturnal and diurnal enuresis. In terms of the frequency of enuresis, 42 patients (42.9%) had enuresis problems every day, 18 patients (18.4%) a few days a week, and 38 patients (38.8%) once a week or less. Regarding the recurrence during the day, 77.6% (n=76) of the patients exhibit enuresis problem once a day, and 22.4% (n=22) more than once a day. Also, 63.3% (n=62) of the patients had a positive family history of enuresis. 58.2% (n=57) of all cases had at least one comorbid psychiatric disorder. The most common accompanying comorbid disorders were attention deficit hyperactivity disorder and conduct disorders (35.7%, n=35), depressive disorder (11.2% (n=11), anxiety disorders (8.2%, n = 8), and trauma and stressor-related disorders, respectively. Descriptive statistics of the participants' clinical characteristics and demographic variables are shown in Table 1.

### Features of previous seeking treatment for enuresis

It was learned that 57 of the patients (58.2%) had previously applied to the hospital for enuresis, and 14 of them (24.6%) have applied to child and adolescent psychiatry, 10 (17.5%) of them to pediatric surgery, 20 (35.1 %) of them to other branches of pediatrics, and 13 (22.8%) of them to the urology clinic. Behavioral treatment only had been applied to 40.4% (n=23) of the patients who applied for treatment, and pharmacotherapy had been applied in 59.6% (n=34) of the patients. The agents preferred in pharmacological treatment were anticholinergics (n=28), desmopressin (n=4), and imipramine (n=2), respectively. In our sample, there was no patient using an enuresis alarm. While 52.6% (n=30) of the patients who received treatment showed a partial response to the treatment, 47.4% (n=27) did not respond. Data on features of previous treatment status for enuresis are presented in Table 2.

### The treatment preferences of the previously clinics applied

We found that 12 of the patients who received only behavioral treatment were treated in child and adolescent psychiatry, 2 in pediatric surgery, and 9 in other pediatrics branches. There were no patients who received only behavioral therapy in the urology clinic. Imipramine had been prescribed only in child and adolescent psychiatry, desmopressin had been prescribed in pediatric surgery and urology, and anticholinergics had been prescribed by all clinics except child and adolescent psychiatry. Table 3 shows the treatment preferences of the previously clinics applied.

### Treatment options in the child and adolescent psychiatry clinic, and treatment response

It was determined that 26.5% (n=26) of the patients who applied to child and adolescent psychiatry received behavioral treatment only, and 73.5% (n=72) used drugs along with behavioral treatment, and it was observed that psychoeducation was also applied to all patients who received pharmacotherapy. The most frequently used psychotropic drug in pharmacotherapy in child and adolescent psychiatry clinic was imipramine (52%, n=51), on the other hand, desmopressin was preferred for 21 patients (21.4%). Regarding treatment response, we determined that 44.9% (n=44) of the patients showed a complete response to the treatment, 40.8% (n=40) showed a partial response to the treatment, and 14 patients (14.3%) did not respond to the treatment. Treatment options in the child and adolescent psychiatry clinic,

and treatment response are summarized in Table 4.

### Clinical variables affecting drug use in the treatment of enuresis

Regarding the clinical variables predicting drug use in the treatment of enuresis, it was found that age, gender, types, frequency, and severity of enuresis and response to previous treatment did not affect the medical treatment decision, while the presence of psychiatric comorbidity and previous seeking treatment for enuresis and previous treatment modality played a significant role in the decision to initiate medication. Accordingly, we determined that the rates of psychiatric comorbidity (68.1% vs. 30.8%, respectively,  $p=0.001$ ) and previous treatment admissions for enuresis (66.7% vs. 34.6%, respectively,  $p=0.005$ ) in those who received medical treatment were significantly higher than those who treated behavioral treatment only. In addition, the rate of previously receiving combined treatment was significantly higher in the group receiving medical treatment than those who received behavioral treatment only (66.7% vs. 22.2%, respectively,  $p=0.023$ ). Data on clinical variables affecting drug use in the treatment of enuresis are presented in Table 5.

**Table 1.** Sociodemographic and clinical characteristics of participants

	Number (%) or mean±SD
<b>Age (mean-years±SD)</b>	10.38±2.15
<b>Gender (n,%)</b>	
Male	60 (61.2)
Female	38 (38.8)
<b>Starting type of the enuresis (n,%)</b>	
Primary	62 (63.3)
Secondary	36 (36.7)
<b>Occurrence type of the enuresis (n,%)</b>	
Enuresis nocturna (night-time, only)	69 (70.4)
Enuresis diurna (daytime, only)	7 (7.1)
Nocturnal and diurnal	22 (22.4)
<b>Frequency of enuresis (n,%)</b>	
Everyday	42 (42.9)
A few days a week	18 (18.4)
Once a week or less	38 (38.8)
<b>Recurrence during the day (n,%)</b>	
Once a day	76 (77.6)
More than once a day	22 (22.4)
<b>Family history of enuresis (n,%)</b>	
Yes	57 (58.2)
No	41 (41.8)
<b>Psychiatric comorbidity (n, %)</b>	
Yes	57 (58.2)
No	41 (41.8)
<b>Types of psychiatric comorbidity (n,%)</b>	
Attention deficit hyperactivity disorder and conduct disorders	35 (35.7)
Depressive disorder	11 (11.2)
Anxiety disorders	8 (8.2)
Trauma and stressor-related disorders	3 (3.1)

**Table 2.** Features of previous seeking treatment for enuresis

	Number (%)
<b>Previous seeking treatment for enuresis (n,%)</b>	
Yes	57 (58.2)
No	41 (41.8)
<b>Previous clinic visited for treatment (n, %)*</b>	
Child and adolescent psychiatry	14 (24.6)
Pediatric surgery	10 (17.5)
Other branches of pediatrics	20 (35.1)
Urology	13 (22.8)
<b>Previous enuresis treatment (n, %)**</b>	
Behavioral therapy only	23 (40.4)
Behavioral therapy + pharmacotherapy	34 (59.6)
<b>Previous pharmacotherapy (n, %)**</b>	
Imipramine	2 (5.9)
Desmopressin	4 (11.8)
Anticholinergics	28 (82.4)
<b>Response to previous treatment (n, %)*</b>	
Partial response	30 (52.6)
No response	27 (47.4)

\*After patients who do not apply for treatment were excluded.  
\*\*After patients receiving behavioral therapy only were excluded

**Table 3.** The treatment preferences of the previously clinics applied

	Behavioral therapy	Imipramine	Desmopressin	Anticholinergics
<b>Child and adolescent psychiatry (n, %)</b>	12 (85.7)	2 (14.3)	0 (0)	0 (0)
<b>Pediatric surgery (n, %)</b>	2 (20)	0 (0)	2 (20)	6 (60)
<b>Other branches of pediatrics (n, %)</b>	9 (45)	0 (0)	0 (0)	11 (55)
<b>Urology (n, %)</b>	0 (0)	0 (0)	2 (15.4)	11 (84.6)

**Table 4.** Treatment options in the child and adolescent psychiatry clinic, and treatment response

	Number (%)
<b>Treatment options (n,%)</b>	
Behavioral therapy only	26 (26.5)
Behavioral therapy + pharmacotherapy	72 (73.5)
<b>Pharmacotherapeutic drug preferences (n,%)</b>	
Imipramine	51 (52)
Desmopressin	21 (21.4)
<b>Response to previous treatment (n,%)</b>	
Complete response	44 (44.9)
Partial response	40 (40.8)
No response	14 (14.3)

**Table 5.** Clinical variables affecting drug use in the treatment of enuresis

	Pharmacotherapy		p-value*
	Yes (n=72)	No (n=26)	
<b>Gender (n,%)</b>			
Male	47 (65.3)	13 (50)	0.171
Female	25 (34.7)	13 (50)	
<b>Age (mean-years±SD)</b>	10.57±2.23	9.85±1.87	0.097
<b>Starting type of the enuresis (n,%)</b>			
Primary	45 (62.5)	17 (65.4)	0.794
Secondary	27 (37.5)	9 (34.6)	
<b>Occurrence type of the enuresis (n,%)</b>			
Enuresis nocturna (night-time, only)	52 (72.2)	17 (65.4)	0.796
Enuresis diurna (daytime, only)	5 (6.9)	2 (7.7)	
Nocturnal and diurnal	15 (20.8)	7 (26.9)	
<b>Frequency of enuresis (n,%)</b>			
Everyday	32 (44.4)	10 (38.5)	0.745
A few days a week	12 (16.7)	6 (23.1)	
Once a week or less	28 (38.9)	10 (38.5)	
<b>Recurrence during the day (n,%)</b>			
Once a day	59 (81.9)	17 (65.4)	0.083
More than once a day	13 (18.1)	9 (34.6)	
<b>Family history of enuresis (n,%)</b>			
Yes	25 (34.7)	11 (42.3)	0.492
No	47 (65.3)	15 (57.7)	
<b>Psychiatric comorbidity (n, %)</b>			
Yes	49 (68.1)	8 (30.8)	0.001
No	23 (31.9)	18 (69.2)	
<b>Previous seeking treatment for enuresis (n,%)</b>			
Yes	48 (66.7)	9 (34.6)	0.005
No	24 (33.3)	17 (65.4)	
<b>Previous enuresis treatment (n,%)</b>			
Behavioral therapy only	16 (33.3)	7 (77.8)	0.023**
Behavioral therapy + pharmacotherapy	32 (66.7)	2 (22.2)	
<b>Response to previous treatment (n,%)</b>			
Partial response	16 (33.3)	7 (77.8)	0.476**
No response	32 (66.7)	2 (22.2)	

\*The chi-square test and Fisher's exact test (as appropriate) were used to test group differences. Bold font indicates statistical significance: p < 0.05.

\*\*After patients who do not apply for treatment were excluded.

## Discussion

In this study, we specifically investigated the treatment preferences among children with enuresis in a clinical sample. Enuresis is a disorder that can pose long-term psychosocial risks and problems in the lives of children and adolescents and their families, negatively affects self-esteem, and may require treatment [5-8,14]. There are a variety of treatment alternatives for enuresis including behavioral and motivational therapy, enuretic alarm device, and pharmacotherapy. However, the consensus in the treatment of enuresis is the application of a stepwise treatment model [14,15]. Treatment should be started with psychoeducation (providing education and information to children and their families about the condition) first. Simple behavioral treatments such as fluid restriction, waking the child to urinate, daily motivation, exercises to increase bladder capacity are first-line treatment approaches [14-16]. Complex behavioral treatment methods such as enuretic alarm and dry bed training are recommended for patients over 7 years of age, but it has been reported in current studies that enuretic alarm therapy can also be applied to children aged 5 years [9-11,16]. Pharmacologic treatment is proposed when nonpharmacologic treatment interventions fail and social problems occur in the life of the child and family, and should be initiated in children seven years or above. However, the most commonly used therapeutic approach in enuresis is combined treatment strategies, and in this context, the most preferred treatment is the combination of conditioning therapy by alarm and receiving desmopressin. Treatment is accepted as successful when the patient reaches continence for 14 consecutive nights for 16 weeks. Nonresponse to treatment is described as a decrease below 50% in frequency and severity enuresis, partial response is defined as a 50-90% decrease [13].

Desmopressin, anticholinergic agents, and imipramine constitute medical treatment alternatives. However, none of these drugs are curative, and these drug options are used to temporarily reduce the frequency and severity of enuresis. It has been produced evidence of the superiority of desmopressin in previous studies [17-20]. A prior study has demonstrated that those taking desmopressin were 4.6 times more likely to stay dry for 14 consecutive nights than placebo [17]. However, it has been documented to be more effective in those with normal bladder capacity and those with nocturnal polyuria [18,19]. In addition, high recurrence rates have been reported following discontinuation of the drug [11]. Anticholinergics (e.g., oxybutynin, and hyoscyamine) reduce detrusor muscle tone and increase bladder capacity, and should be preferred only when the first-line treatment approaches (alarm or desmopressin) are unsuccessful in the treatment of enuresis [18,21,22]. A positive effect can be expected from anticholinergics in patients who do not describe lower urinary tract symptoms during the day but whose bladder capacity is restricted due to nocturnal detrusor overactivity. However, it has been emphasized that monotherapy with anticholinergics does not have a major effect on the treatment of enuresis [18]. Tricyclic antidepressants (e.g., imipramine and desipramine), another important treatment option, are thought to act by suppressing detrusor overactivity and increasing bladder capacity through their anticholinergic and myorelaxant effects. Also, it has been suggested that they suppress rapid eye movement (REM) sleep and facilitates awakening via central noradrenergic stimulation. Another possible mechanism of action is that they decrease nocturnal urine production by increasing vasopressin release [23,24]. In general, it has been shown to provide a positive effect in 50% of the patients, but it is common for symptoms to recur after the treatment is discontinued. Studies have revealed their efficacy, especially in

cases when standard treatment approaches (alarm, desmopressin, anticholinergics) have failed. However, due to their negative side effect profile and concerns about potential toxicity, TCAs are currently recommended to be used only in tertiary treatment and reference centers [9,14,23,24].

The present study revealed that more than half of the patients applied to a number of clinics including child and adolescent psychiatry for enuresis treatment before applying to our clinic. Urology, pediatric surgery, child and adolescent psychiatry, and other branches of pediatrics were the most frequently applied clinics, and behavioral therapy had been applied to 40% of the patients, and pharmacotherapy had been applied to 60%. There was no patient using an alarm. The reason why pharmacological treatment is preferred rather than behavioral treatment may be the desire of both physicians and family to respond to the treatment as soon as possible. Before applying to our clinic, the agents preferred in pharmacological treatment were anticholinergics, desmopressin, and imipramine, respectively. The most preferred drug group was anticholinergics. These results differ from those recommended in treatment guidelines. Because enuresis alarms and desmopressin are emphasized in the initial active therapies in the treatment guidelines [14]. Our conflicting results may have resulted from patients' admission to different clinics and different treatment modalities at each clinic. For example, while behavioral therapy and imipramin were not used in the urology clinic, the most used methods in the child psychiatry clinic were behavioral therapy and imipramin. Again, desmopressin was preferred only by pediatric surgery and urology. Also, we detected that almost half of the patients did not respond to the treatment, and the remaining half showed a partial response, before applying to our clinic. This result may be due to the less preference of behavioral and motivational therapy. Because although behavioral and motivational therapy requires longer treatment than pharmacological treatment, it is known that relapse rates are lower and more successful [11].

Regarding the treatment options in our clinic, it was found that 26.5% of the patients received behavioral therapy only, and 73.5% of the patients received combined therapy. The most preferred agent in pharmacotherapy was imipramine, and it has been prescribed for more than half of the patients. The other preferred pharmacological agent was desmopressin and was prescribed for one-fifth of patients, but anticholinergics were not prescribed for any patients. The pharmacotherapy profiles of children with enuresis in our study contradict the data reported in the literature. Although there are various treatment alternatives in the treatment of enuresis, it is reported that desmopressin treatment is the most preferred treatment method in daily practice [11,14]. The reason why imipramine is preferred over desmopressin in our clinic may be the high rate of psychiatric comorbidity in patients, with a frequency of 58%. In our population, the most common comorbid psychiatric disorders were attention deficit hyperactivity disorder and conduct disorders, and depressive disorder. On the other hand, imipramine is not only a treatment option for enuresis, but also for treatment-resistant enuresis in children with ADHD [25,26]. Our results suggest that the presence and type of comorbid psychiatric comorbidity play an effective role in the treatment of choice for enuresis.

Several limitations of the present study should be addressed. These were that our sample size was relatively small, the sample lacked a control group, and the study was in retrospective design, which prevents us from generalizing our results. Therefore, future prospectively planned multicenter studies with larger samples

to evaluate treatment options in enuresis will be substantially valuable. Despite its limitations, our study presents considerable important data on child and adolescent psychiatry practices in the treatment of enuresis in our country. As a result, this study extends the outcomes of the previous studies in children with enuresis.

## Conclusion

In conclusion, this study revealed that different clinical branches apply different treatment approaches to enuresis. In child and adolescent psychiatry, behavioral therapy only was performed on a quarter of the patients, and behavioral therapy and pharmacotherapy were applied together to the rest of the patients. Imipramine was the most commonly used agent in medical treatment, and this was attributed to the high rate of psychiatric comorbidity.

## Conflict of interests

*The authors declare that they have no competing interests.*

## Financial Disclosure

*All authors declare no financial support.*

## Ethical approval

*Local Ethics Committee of Inonu University approved the study (protocol no: 2020-1228)*

**Data Accessibility:** *The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.*

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