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Stepwise Approach for Treatment of Enuresis in Children

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Abstract

Introduction: Many parents believe that enuresis will be cured with age. Yet, left untreated, the problem may persist into adulthood. Enuresis can be subdivided into primary versus secondary, or monosymptomatic versus polysymptomatic.

Aim of the study: is to determine the efficacy of sequential therapy for treatment of enuresis

Subjects and Methods: This retrospective study was conducted between April 2014 and April 2020. It included 87 patients with enuresis. Patients were collected from two hospitals: Bugshan Hospital in Jeddah (53 patients) and Nasr City Insurance Hospital (34 patients). All patients were subjected to the following: through medical examination to know the type of enuresis, whether primary or secondary. Also, to know if enuresis was monosymptomatic or polysymptomatic. Renal function tests All patients received behavioral therapy for four months with follow-up on its results. Those who did not respond received sequential therapy (anticholinergics for 4 months). Then to follow up with those who did not respond to give Desmopressin.

Results: 60.9% of our patients responded to behavioral therapy, and 33.3% of our patients improved on behavioral and anticholinergic medications. Only 5.8% of our patients needed desmopressin. 10 patients (out of 87, or 11.5%) were discovered to have diabetes mellitus.

Conclusion: A stepwise approach for treatment of enuresis in children is effective. Secondary

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1. Introduction

Enuresis is a common problem in children worldwide. Many parents believe that enuresis will be cured with age and does not need any treatment. Yet, left untreated, the problem may persist into adulthood [1]. The International Children's Continence Society defined enuresis as intermittent incontinence that occurs exclusively during sleeping periods, while daytime incontinence and enuresis were defined as combined intermittent incontinence during "awake" periods and while sleeping [2]. Iscan and Ozkayn, 2020, added the condition that the age be at least 5 years to the previous definition [3].

The prevalence of enuresis in children is usually in the range of 10–30% at age 6, 5% at age 10, and 0.5–1% among teenagers and young adults [4]. The pathophysiology of primary nocturnal enuresis involves the inability to awaken from sleep in response to a full bladder, excessive nighttime urine production, and decreased functional capacity of the bladder [5].

Enuresis may be secondary to other medical conditions such as constipation, obstructive sleep apnea, diabetes mellitus, diabetes insipidus, chronic kidney disease, and psychiatric disorders [6]. Enuresis can be subdivided into primary and secondary, or monosymptomatic and polysymptomatic, types [4]. Primary enuresis refers to children who have never achieved six months of continuously dry nights. Secondary enuresis refers to children who previously attained at least six months of nighttime dryness but who have relapsed [7].

In monosymptomatic enuresis, the only symptom is nighttime bed-wetting. Polysymptomatic enuresis involves urgency, frequency, or dribbling [8]. Treatment of enuresis includes behavioral therapy in the form of limited oral intake before bedtime. also awaken the child to urinate after sleeping. These exercises may be more effective than alarm therapy [9]. Treatments also include medications in the form of anticholinergics that increase bladder capacity, and antidepressants may also be used as they increase bladder capacity. However, they have dangerous side effects known as cardiotoxicity. Hormonal therapy in the form of desmopressin binds to V2 receptors in the collecting duct, which increases the permeability of water, which in turn decreases urine output [10].

So, the current study aimed to determine the efficacy of sequential therapy (that included behavioral, anti-cholinergic, and hormonal therapy) for the treatment of enuresis.

2. Subjects and methods

2.1. Subjects

This prospective study was conducted between April 2014 and April 2020. It included 87 patients who were suffering from enuresis.

Patients were collected from two hospitals:

- Bugshan Hospital, Jeddah, Saudi Arabia (N = 53).
- Nasr City Insurance hospital, (N=34).

The total number of our patients was 87. Their ages ranged between 6 and 15 years.

Inclusion criteria

Child above 5 years of age, without any detected renal anomalies by ultrasound such as hydro-nephrosis or hydroureter, with normal renal functions (blood urea and serum creatinine), and commitment to regular follow-up for at least 18 months were included.

Exclusion criteria

Children who were less than 5 years of age, with detectable renal anomalies by ultrasound such as hydronephrosis or hydroureter, with abnormal renal functions (high blood urea or high serum creatinine or both), with irregular follow-up, or with parasitic infestations were excluded.

2.2. Methods

All patients were subjected to the following:

- Thorough medical history and thorough physical examination are necessary to detect family history and type of enuresis, whether primary or secondary. Also, to know if enuresis was monosymptomatic or polysymptomatic.
- Renal functions tests (blood urea, and serum creatinine)
- Urine analysis and specific gravity to exclude diabetes insipidus
- Pelvi-abdominal ultrasound to detect hydroureter or hydronephrosis
- HbA1c (Glycated hemoglobin) to detect diabetes mellitus that was repeated during follow up after 6 months
- Stool analysis to exclude parasitic infestations

All patients received behavioral therapy for four months with follow-up on its results. Those who did not respond received sequential therapy (anticholinergics for four months) in the form of oxybutynin chloride 0.4 mg/kg in two divided doses [4]. Then, to follow up with those who did not respond, give hormonal therapy in the form of Desmopressin at a starting dose of 0.2 mg, then gradual withdrawal over six months to avoid relapse. Improvement was considered significant if frequency of enuresis decreased by at least 50%

2.3. Statistical analysis

Recorded data were analyzed using the Statistical Package for Social Sciences (SPSS), version 20.0. The confidence internal was set to 95% and the margin of error accepted to 5% so the *P-value < 0.05* was considered significant

3. Results

The patients Socio-demographic characteristics were listed in Table 1. All our patients (n=87) were suffering from deep sleep with difficulty of arousal. HbA1c was high at 10 patients out of 87 (11.5%). Side effects of anticholinergics were limited. It occurred in the form of abdominal pain (9 patients out of 87-9.19%). This abdominal pain was mild and it did not need to stop the medicine. Headache occurred in (7 out of 87-8%). It was mild and it did not need to stop the medicine. There was no significant difference between the 2 groups in any of the parameters mentioned. HbA1c was high at 10 patients out of 87 (11.5%). Other results were listed in Tables 2 and 3.

Table 1: Socio-demographic characteristics of the study group.

Variables		Values
Age (years)		9.3±2.4 (6-15)
Gender	Female	37 (42.5%)
	Male	50 (57.5%)
Symptom	Mono-symptom	50 (57.5%)
	Poly-symptom	37 (42.5%)
Type	Primary	58 (66.7%)
	Secondary	29 (33.3%)
Family History	No	50 (57.5%)
	Yes	37 (42.5%)
HbA1c	Normal	77 (88.5%)
	High	10 (11.5%)

Table 2: Sequential therapy of the studied patients.

Variables	Values
Patients who received Behavioral therapy	87 (100%)
Patients who Improved on behavioral therapy	53 (60.9%)
Patients who received Anti-Cholinergic	34 (39.1%)
Patients who improved on behavioral therapy plus Anti-Cholinergic	29 (33.3%)
Patients who needed hormonal therapy	5 (5.8%)

Table 3: Comparison between patients who needed medical therapy and those who improved on behavioral therapy alone.

Variables		Sequential Therapy		*P-value*
		Behavioral therapy only	Behavioral and medical Therapies	
Age (years)		9.2±2.4	9.5±2.5	0.604
Gender	Male	29 (54.7%)	21 (61.8%)	0.516
	Female	24 (45.3%)	13 (38.2%)	
Symptom	Mono-symptom	32 (60.4%)	18 (52.9%)	0.494
	Poly-symptom	21 (39.6%)	16 (47.1%)	
Type	Primary	38 (71.7%)	20 (58.8%)	0.214
	Secondary	15 (28.3%)	14 (41.2%)	
Family History	No	32 (60.4%)	18 (52.9%)	0.494
	Yes	21 (39.6%)	16 (47.1%)	

HbA1c	Normal	45 (84.9%)	32 (94.1%)	0.189
	High	8 (15.1%)	2 (5.9%)	

4. Discussion

Our study included 50 males (57.5%) and 37 females (42.5%). This was in accordance with the results of Nevéus *et al.*, 2000, who stated that boys are affected more frequently than girls [11]. A family history of enuresis was positive in 37 patients out of 87. This was in contrast to Rees et al. 2012, who found positive family histories in most of their studied children [12]. This difference may be related to the denial of many parents that they were wet during their childhood. HbA1c was normal in 77 patients out of 87 (88.51%). While it was high, only 10 patients out of 87 (11.5%) had a P value greater than 0.05, which is considered not significant. This showed the importance of excluding secondary causes of enuresis, such as diabetes mellitus, before starting our protocol of therapy. even to be repeated after six months to exclude the presence of diabetes in those patients with partial improvement of their symptoms.

Our results showed non-significant improvement in either monosymptomatic or polysymptomatic cases with the sequential desmopressin protocol. These results are similar to those of Butler, 2001, who showed that combinations of therapy are effective as they were done in this study [13].

Also, that sequential therapy was effective in improving enuresis, whether primary or secondary. This showed the efficacy of sequential therapy in improving even secondary causes of enuresis, such as diabetes mellitus.

Sequential therapy decreased enuresis, whether there was a positive family history or not. These results were in concordance with Neveus *et al.*, 2010, who stated that combination therapy will improve the prognosis of the disease and the outcome of treatment. As it is documented, a positive family history makes patients more resistant to treatment [15]. The combination of desmopressin and anticholinergics decreased the relapse rate after stopping desmopressin. Relapse of enuresis usually occurs after stoppage of desmopressin [16].

The side effects of desmopressin and anticholinergics were limited and occurred in the form of abdominal pain and headache [17]. The number of affected children with these side effects was 10 out of 87 patients (11.5%). These side effects occurred with anticholinergics only, with no recorded side effects for minirin. In this study, the use of antidepressants was avoided because of their serious side effects, such as fatal arrhythmias. HbA1c was high in 10 patients out of 87 (11.5%). Enuresis improved with blood sugar control combined with the sequential therapy. This showed the importance of the stepwise approach for managing enuresis by excluding secondary causes before the start of treatment.

Conclusion

A stepwise approach (first behavioral, then medical therapy) for the treatment of enuresis in children is effective. Secondary causes of enuresis should be excluded first before applying the approach. The exclusion of diabetes mellitus should be

done after starting treatment if the enuresis is partially improving.

Ethical considerations: This study was approved by the Research Ethics Committee, Western Region, Ministry of Health, Saudi Arabia. Also approved by the Ethics Committee of Health Insurance Institutes in Egypt.

Patient consent: Approval and consent to participate: In-formed written consent from patients who were invited to participate in the research was obtained.

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