Intensive behavioral therapy for primary enuresis

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ABSTRACT

Objective: To assess the effect of intensive behavioral therapy on Saudi children with primary enuresis.

Methods: Twenty-six children, aged 6-14-years, presented with complains of bed wetting during a 12-months period from January 2001 through to January 2002, ArAr Central Hospital, Kingdom of Saudi Arabia were studied in an interventional, non-randomized trial without control. After complete verbal autopsy, physical examination and laboratory investigation, they were offered intensive behavioral therapy. They were evaluated for response, regularity, esteem and recurrence of enuresis.

Results: Mean age of the study group was 9.6-years (SD = ± 2.6) and boys were affected almost twice of girls (P<0.05). Family history, social history and school performance did not show any significant (P>0.05) association with enuresis. Sixty point five percent were regular and out of those 27.9% never missed any visits. 91.7% were completely dry out of regular patients. There was 75% success rate in those, who visited 4-8 times while 25% in those, who visited 1-3 times. Ninety-six percent of the parents and 80.7% of the children were fully satisfied with this therapy. Socio-economic status seems to play a significant (P<0.05) role in regularity of follow up and response to behavioral therapy.

Conclusion: This result shows an excellent response to intensive behavioral therapy in primary enuresis if the follow up is regular.

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Childhood nocturnal enuresis has traditionally been regarded as a multifaceted problem. At present, there is no treatment modality that is exclusively successful in eliminating primary enuresis within a short time. Even though enuresis frequently resolves spontaneously with time, frequent bed wetting is often upsetting to both parents and children.[1] Physicians should realize that nocturnal enuresis could be an important problem not only for the child but also for entire family. Many mothers of enuretic children feel that doctors do not pay enough attention to this problem.[2]

Nocturnal urinary continence is dependent on 3 factors: 1. Nocturnal urine output, 2. Nocturnal bladder function and 3. Sleep and arousal mechanisms. Disturbance in nocturnal urine production, bladder functions and arousal mechanism have all been firmly implicated as pathogenetic factors in nocturnal enuresis.[3] Enuretic children are pathogenetically heterogeneous, and 2 main types can be discerned: 1. Diuresis-dependent enuresis; these children void as of excessive nocturnal urine production and impaired arousal mechanisms. 2. Detrusor-dependent enuresis; these

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children void as of nocturnal detrusor hyperactivity and impaired arousal mechanisms. The main clinical difference between the 2 groups is that desmopressin is usually effective in the former but not in the latter.[3] The prevalence of nocturnal enuresis is 7% in 5-year-olds, with a decrease of 1% per year and slight male predominance (1.4:1).[3] Urinary tract infection and constipation have an obvious association with enuresis, and they have to be ruled out before a diagnosis of functional enuresis is made, and therapy is started. Medication is usually used on an as-needed basis as most children relapse after cessation of treatment. Imipramine is well studied, commonly used, and cheap but potentially toxic and may be fatal in overdose.[4-9] Desamino-D-arginine vasopressin gives a response rate of up to 70% with few side effects but at the price of a high relapse rate, and high cost.[6,10] A review of the literature revealed 23 studies that have reported on the type or frequency of side effects with the use of desmopressin for the treatment of enuresis. Thirty-one side effects were reported in 717 patients. Seizure secondary to water intoxication is a potential serious complication of treatment with desmopressin and was reported in 6 patients.[7,11] In one study desmopressin showed an efficacy of 90.9% but relapse occurred in 60% of patients during the follow up period.[8,11,12] Anticholinergics should be reserved for those patients with significant diurnal symptoms or those who fail first-line pharmacotherapy. Overall patients and parents should be reassured by the high spontaneous cure rate.[5,9] Although moisture alarms have a good potential for a permanent cure, the child is mostly wet during treatment. Furthermore, it requires that the child make a remote association between the alarm event and a full bladder after the bladder has emptied, and alarm treatment suffers from poor compliance.[6,10] Active treatment should be tailored to the patient's age, motivation and parental wishes. Behavioral modification therapies yield the highest long term cure rate but require strong commitment and are more successful after the age of 7-years.[5,9] This is incorporated into motivational therapy, which consists of counseling, enhancement of self-responsibility and self efficacy with positive reinforcement for success. Many doctors approach to enuresis as a medical condition, relying exclusively on pharmacotherapy, despite all its consequences including a high rate of relapse. This approach perhaps ignores the fact that the most important aspect of treatment involves reassuring the family and child and helping the child to modify his behavior and take control.[10-15] However, it is not clear how well these approaches work for Saudi children and families. Therefore, we studied a series of children referred to a behavioral-developmental pediatric clinic with the complaints of bed-wetting for assessment and treatment. Since the literature shows that parents' education and other socio-demographic characteristics are associated with enuresis and treatment response, we wanted to assess the effect of these factors, in addition to the effect of compliance with our management.

Methods. We report a prospective case series with an interventional, non-randomized trial, based on before and after comparison without control. We included 26 children aged 6-14-years, referred from primary health care centers to the hospital, during a period of 12-months between January 2001 and January 2002, with the complaint of bed wetting during the night. These children did not receive any remarkable medical care before referral to our clinic. Most of the children were recruited with in the first 6 months of study, but a few were recruited until the 9th month. Their follow up ranges from a minimum of 3-months to maximum of 1-year. Included are those children who wet only at night and during sleep, and who never experienced a sustained period of dryness. All organic causes of enuresis, on the basis of the medical history, physical examination findings, fasting blood sugar and urine test results were excluded. The cases which were difficult to follow due to nomadic life style and lack of home telephone were also excluded from the study. All parents or legal guardians gave their written informed consent before the children were enrolled in the study. Permission was also taken from hospital authority, and the "Research Ethics Committee" approved the study. The study was conducted in ArAr Central Hospital, a centrally located 350-bed hospital serving a low socio-economic community in Northern Saudi Arabia. The northern part of the country is sparsely populated, and there are high rates of poverty and joblessness and low rates of literacy. After completion of history, physical examination and laboratory investigation, the children were offered "Intensive Behavioral Therapy," which was a multi-component strategy that included meetings of focus groups, explanation of physiology of urination, plan for pre-sleep routine, and restriction of fluid intake before bed time, positive reinforcement by star chart and simple incentives and bladder training. The charts and files of enrolled children were reviewed at the end of each month. Every child was assessed on the basis of enuresis free nights per month, parental response to the enuresis treatment, the child's subjective response to the treatment, recurrence of the bed-wetting, and the child's regularity of follow up. This last factor was considered in 2 categories: number of visits attended and whether or not the child ever missed an appointment. We planned to conduct minimum 2 sessions per month for the first month and one session per month thereafter. We

Table 1 - Characteristics of subject children.

Characteristics	Frequency	(%)
Age groups (n=26)		
6-9 years	18	(69.2)
10-14 years	8	(30.8)
Sex (n=26)		
Male	17	(65.4)
Female	9	(34.6)
Time for enuresis (n=26)		
Day and Night	1	(3.8)
Only night	25	(96.1)
Family History (n=26)		
Siblings with enuresis	1	(3.8)
Enuretic parents	4	(15.4)
No family history	21	(80.8)
Development (n=26)		
Normal	25	(96.1)
Delayed	1	(3.8)
Socio-economic status		
Higher	6	(23.1)
Lower	14	(53.8)
Middle	6	(23.1)

expected most of the children to respond within the period of 3 months (4-6 visits), but also anticipated that the number of sessions needed for complete dryness would depend upon the personality, attitude and socioeconomic status of the children and their parents which were assessed by interview. The success of each child was assessed using the enuresis chart on which parents marked enuresis free nights with a star. The percentage of dry nights per month was calculated, using 30-days to represent 100%. The subjects were then divided into 5 categories, on the basis of their percentage of dry nights at the conclusion of treatment 1. Zero percent no response, 2. 25% 7-8 nights free of enuresis/month, 3. 50% 14-16 dry nights/month, 4. 75% 21-24 dry nights/month, and 5. 100% all nights dry/month. Almost all of the children wet virtually every night prior to initiation of treatment, the number of dry nights listed under "response" below indicates both the number of additional dry nights, as well as the total number of dry nights per month: Patients were also contacted through telephone after the completion of therapy and assessments, at which time data were collected on recurrence or relapse.

Table 2 - Response in different age and sex groups (n=26).

Age* (Years) Sex**	Response				
	No response	**25% reduction**	**75% reduction**	**Complete dryness**	**Total**
6-9	0	8	1	9	**18**
Row %	0	44.4	5.6	50	**100**
Col %	0	80	33.3	75	**69.2**
10-14	1	2	2	3	**8**
Row %	12.5	25	25	37.5	**100**
Col %	100	20	66.7	25	**30.8**
Total	**1**	**10**	**3**	**12**	**26**
Row %	**3.8**	**38.5**	**11.5**	**46.2**	**100**
Col %	**100**	**100**	**100**	**100**	**100**
Male	1	8	0	8	**17**
Row %	5.9	47.1	0	47.1	**100**
Col %	100	80	0	66.7	**65.4**
Female	0	2	3	4	**9**
Row %	0	22.2	33.3	44.4	**100**
Col %	0	20	100	33.3	**34.6**
Total	**1**	**10**	**3**	**12**	**26**
Row %	**3.8**	**38.5**	**11.5**	**46.2**	**100**
Col %	**100**	**100**	**100**	**100**	**100**

* significance of response to different age group *P*=0.18 and ** male and female *P*=0.06

Statistical analysis. Data are reported as means ± SD, percentages, rates, and proportions. Chi-square tests were mainly used for comparison among different categorical predictor and outcome variables. A *P* value of less than 0.05 was considered to indicate statistical significance. The success rate was calculated in percentages (total numbers of dry nights divided by total number of wet nights, multiplied by 100.) A database was constructed in Microsoft Excel to record all relevant information while the analyses were carried out using Epi-Info 2000.

Results. The demographic and socio-economic characteristics of the patients are reported in **Table 1**. The mean age was 9.6 years (SD =± 2.6) while modal age groups were 8 and 11-years and boys were referred almost twice (1.9:1) as often as girls ($P<0.05$) **(Table 1)**. However, child's age or sex was not significantly associated with either visit attendance or treatment response **(Table 2)**. At the completion of intervention, 91.7% of the children who attended all visits reported complete dryness, compared to 53.8% of those who did not attend all visits (1-8 visits only) ($p<0.05$). Among those who visited 1-3 times the success rate was 25% and those who visited 4-8 times 75% with success defined as complete dryness at the end of therapy. **(Tables 3 & 4)**. Family history, social history and school performance were all largely negative. Five of the children had a positive family history of enuresis. The children's performance in school as reported by parents was good and parents did not report any significant social problems **(Table 1)**. Parents responded well and 96% were fully satisfied with this therapy. Similarly, 80.7% of the children were also happy as reported by their parents as well as themselves. **(Table 3)** Education and income seem to play a significant role ($P<0.05$) in regularity and response **(Tables 5 & 6)**.

Discussion. The treatment approach for enuresis is controversial due to the lack of consensus as to the exact causes of nocturnal enuresis. Despite the high relapse rate, side effects, and availability of other treatment modalities, drug therapy with imipramine or desmopressin still appears to be the most common choice. In addition, one can find reports of novel treatment approaches such as acupuncture, anticholinergic calcium antagonist, oral synthetic androgen mesterolone, diclofenac sodium suppository, bell and pad, and hypnosis.[12-20] Despite the popularity of pharmacotherapy, there is support in the literature that it should not be the first intervention attempted. Rather, non-punitive behavioral techniques should be the first approach considered, with pharmacotherapy reserved for those who do not

Table 3 - Regularity and other outcome variables.

Variables	Frequency	(%)
Regularity (n=26)		
1-8 visits	14	(53.8)
Never missed an appointment	12	(46.2)
Response date (n=26)		
No response	1	(3.8)
25% reduction	10	(38.5)
75% reduction	3	(11.5)
Complete dryness	12	(46.2)
Enuresis chart filling (n=26)		
Not filled	4	(15.3)
Incomplete	5	(19.2)
Complete	17	(65.3)
Parent response (n=26)		
Not satisfied	1	(3.8)
Satisfied	25	(96.1)
Child response (n=26)		
No satisfied	5	(19.3)
Satisfied	21	(80.7)

Table 4 - Comparison between regularity and response of subject children (n=26).

	Response				
Regularity	**No response**	**25% reduction**	**75% reduction**	**Complete dryness**	**Total**
1-8 visits	1	9	3	1	**14**
Row %	7.1	64.3	21.4	7.1	**100**
Col %	100	90	100	8.3	**53.8**
Never missed a visit	0	1	0	11	**12**
Row %	0	8.3	0	91.7	**100**
Col %	0	10	0	91.7	**46.2**
Total	**1**	**10**	**3**	**12**	**26**
Row %	**3.8**	**38.5**	**11.5**	**46.2**	**100**
Col %	**100**	**100**	**100**	**100**	**100**

* significance of response with regularity in follow up $P=0.0003$

Table 5 - Asociation of soco-economic status, education and family income with regularity of subject children (n=26).

Socioeconomic status	**Regularity**		
	1-8 visits	**Never missed a visit**	**Total**
High	0	6	**6**
Row %	0	100	**100**
Col %	0	50	**23.1**
Middle	6	0	**6**
Row %	100	0	**100**
Col %	42.9	0	**23.1**
Low	8	6	**14**
Row %	57.1	42.9	**100**
Col %	57.1	50	**53.8**
Total	**14**	**12**	**26**
Row %	**53.8**	**46.2**	**100**
Col %	**100**	**100**	**100**

**p*=0.0022

Table 6 - Association of socio-economic status (education and family income) with response of therapy (n=26).

Age* (Years) Sex**	Response				
	No response	**25% reduction**	**75% reduction**	**Complete dryness**	**Total**
High	6	0	0	0	**6**
Row %	100	0	0	0	**100**
Col %	50	0	0	0	**23.1**
Middle	1	4	1	0	**6**
Row %	16.7	66.7	16.7	0	**100**
Col %	8.3	40	33.3	0	**23.1**
Low	5	6	2	1	**14**
Row %	35.7	42.9	14.3	7.1	**100**
Col %	41.7	60	66.7	100	**53.8**
Total	**12**	**10**	**3**	**1**	**26**
Row %	**46.2**	**38.5**	**11.5**	**3.8**	**100**
Col %	**100**	**100**	**100**	**100**	**100**
P=0.01					

respond to behavioral interventions.[18,19,21-24] Behavioral approaches assume that learning takes place to produce the cessation of wetting. Therefore, these approaches should theoretically be self-encouraging, health promoting interventions that are safe and effective if applied intensively and properly. However, it is not yet assessed whether these approaches work for Saudi Children and families, thus, the success rate in our study exceeded the improvements observe in other cited studies. It seems that the success rate of all methods were even not reached up to more than 50% in general, if do so, it might be a combination of treatments or the recurrence rate that is very high with a lots of side effects at high cost. Our findings show that at the completion of intervention, 91.7% of the children who attended all visit reported complete dryness, nevertheless, one can argue that it may largely be accounted for, by spontaneous remission but the results describe that the response appeared very promptly within 2-3-months. Some children who were recruited at the latter part of our study could not attend enough number of sessions even being regular. If they could have been recruited early, the success of the therapy would be higher. Also, this study describes that the mean age was 9.6-years (SD = ± 2.6) and majority were affected of 8-years and 11-years of age group, which is not consistent with previously published data.[3] Boys were affected almost twice as often (1.9:1) as girls ($P<0.05$), which supports an established difference between 2 sexes. However, child age and sex were not significantly associated with either visit attendance or treatment response.[1] Although there is a high rate of spontaneous remission added by, it seems that it can be fasten with behavioral therapy. Also the social, psychological, and emotional costs of drug therapy to children and families can be great. Yet, drug is still widely used, a study highlighted that a long term treatment with imipramine is not an option for all children and it can still be used for brief periods, such as camp, as the initial response recaptured after a medication-free period of time. Whereas a study investigating the differential response of children with enuresis to DDAVP and the bell and pad method of conditioning found that 70% improved with the DDAVP but at high cost with high rate of relapse and 86% improved with the alarm method, yielding non-significant differences, but a small trial showed that alarm treatment was better than drugs.[6,10,21,22,25-29] Another study showed a simila results and found that children with small pretreatment maximal functional bladder capacities did better with the bell and pad method in conjunction with retention–control training, while the children with larger bladder capacities responded to the bell and pad method alone. However, it should be noted that this was a qualitative difference in response, as 92.5% of the 40 children who completed the study met the outcome criteria of 14 consecutive dry nights, regardless of which group they were in.[23,30] A similar experiment that compared the therapeutic benefits of desmopressin in combination with the bell and to placebo found that the combination of desmopressin, and the alarm resulted in significantly drier nights.[24,31] On the contrary; we have used behavioral therapy alone and the success rate exceeded that of the combination therapy above.

Hogg and Husmann[32] particularly looked at the efficacy of DDAVP for children who had been refractory to conditioning treatment and imipramine, using a randomized double-blind placebo controlled crossover study, but in comparison of our study the results depicted that of the 52 children studied, 53% had a complete cessation of wetting, 19% were partial responders, and 28% had no or minimal response.[25] The locality covered in the study was predominantly inhabited by low socio-economic status and results showed a significant ($P<0.05$) role of economic status and educational level in response, follow up and regularity, this confirms the fact that enuresis is related to parents'education.[26,33] It was also found previously that enuresis in greater frequency in children who were undergoing psychosocial stress and in those living in socially disadvantaged circumstances.[27,34] Surprisingly, family history, social history and school performance did not show any significant ($P>0.05$) relation to enuresis in our study. Previously, it has been identified that nearly 75% of patients have a positive family history.[25-30] The reason of non-consistent with other studies is a small and referred sample size, which might be not representing the whole population. As the child's parents have the major responsibility for promoting growth and development, they must provide support and nurturance to the child to establish that growth and development with good emotional bond. If parents appreciate and recognize the child's abilities and competencies, the child can learn self-esteem. Therefore, in this type of therapies, the patients'self–esteem and their parents'satisfaction can play a pivotal role so as shown in our study that the parents responded well and 96% reported being fully satisfied, and 80.7% children were also happy. As previously showed in a study that physical and psychiatric symptoms in the child, poor academic achievement and lax parental attitudes to toilet training have association with enuresis.[27,34] In this study the results seem to have no association between any other behavioral problem and school performance, although behavioral problems were not academically studded using Child Behavior Checklist or other scales. Sibling relationships within the family allow each child to learn and experience competition and cooperation among peer, learn specific abilities have a definite effect on other children. Interestingly, this study showed that only one child's siblings were facing the same problem (**Table 1**). Thus, this case series demonstrates an excellent response to intensive behavioral therapy, which bolsters the rationale for the use of behavioral therapy; furthermore, the consequences are very few if measure in terms of relapse and no side effects as compared to drug therapies, but for the evaluation of long term effects desires further studies. Though this case-series depicted excellent results but cannot be generalized due to certain limitations such as uncontrolled study design, can not speak to the relative efficacy of drugs versus behavioral; it may be expensive/time consuming for the doctor; it may be hard for some parents (who have come to lots of appointments), and it may take long time to control. It also emphasizes the importance of good compliance and patients follow up. Finally, we recommend further scrutiny for such treatment modalities, as well as good training to pediatricians to deal with it.

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