Original Article

Alarm Therapy and Desmopressin in the Treatment of Patients with Nocturnal Enuresis

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Abstract

Purpose: The purpose of this study was to compare the rates of success, relapse, and compliance to treatment in patients undergoing alarm therapy or receiving desmopressin for primary monosymptomatic nocturnal enuresis (PMNE). **Materials and Methods:** This retrospective study was performed by reviewing the medical files of patients undergoing alarm therapy (Group 1) or receiving desmopressin (Group 2) for PMNE, between January 2010 and July 2014. Patients undergoing treatment in the 3rd and 6th month as well as 1st year follow-up data were analyzed. Two groups were compared with regard to treatment success, relapse rate, and compliance to treatment. **Results:** Group 1 included 64 and Group 2 included 70 children. Relapse rates at the 3rd month, 6th month, and 1st year were 67.2%, 71.9%, and 17.0% for Group 1 and 74.3%, 80.0%, and 21.4% for Group 2, respectively. There was no statistically significant difference between relapse rates at any point of follow-up. **Conclusions:** Alarm therapy and desmopressin have the same success rate and relapse rates for PMNE. Compliance with alarm therapy is higher and we recommend it as the first-line treatment. On the other hand, desmopressin has low side effects and can also be used.

Keywords: Alarm therapy, children, desmopressin, enuresis

Introduction

Urinary incontinence is fairly frequent in children. It is defined as voluntary or involuntary wetting of clothing or bed for a period of at least 3 months, in children >5 years.[1] It is more frequently seen in boys. While its incidence is 15%–20% at 5 years of age, this decreases to 1%–2% at 17 years of age. The rate of spontaneous resolution is around 14%/year.[2]

Monosymptomatic nocturnal enuresis (MNE) is defined as nocturnal enuresis in children without any urinary tract pathology or day-wetting, and it constitutes more than 80% of enuresis.[3] Despite many reasons having been put forward regarding its etiology, it has not been clearly clarified. More than one factor being separately involved or multifactorial etiology is generally accepted for enuresis.[4] There are pharmacological and nonpharmacological treatments for enuresis. In addition to desmopressin and anticholinergics, antidepressants are also used as an alternative for pharmacological treatment. Nonpharmacological treatments include all methods of behavior modification and increased motivation.[5,6] This study has been carried out retrospectively for comparison of the efficacy of the two most widely used treatment methods in the treatment of nocturnal enuresis, desmopressin, and alarm therapy.

Materials and Methods

In this study, the medical data were retrospectively analyzed in 134 patients presenting between January 2010 and July 2014, with a complaint of nocturnal enuresis that were diagnosed as having primary MNE (PMNE). Patient data (history, physical examination, radiology results, and laboratory tests) were obtained from their medical files.

The 134 patients included in the study were divided into two groups, with 64 patients (Group 1) receiving alarm therapy and seventy patients (Group 2) receiving desmopressin therapy. The patients were called regularly for checkups and the efficacy

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of the treatment and drug-induced side effects were controlled. In the assessment, treatment response, compliance, and relapse rates were determined. A 90%–100% reduction in night wetting was considered as complete response, 50%–90% reduction in night wetting as moderate response, and a reduction of <50% was considered to be unresponsive.

Third and 6th month data were assessed to consider the impact of alarm therapy and desmopressin on enuresis, and response to treatment and relapses was analyzed.

The statistical analysis of data was carried out using SPSS 16.0 (Statistical Package for the Social Sciences, Chicago, IL, USA). In testing the significance of the percentage (%) success rate of the device and desmopressin and relapses, Chi-square analysis was used. In addition, whether there is a significant difference in the treatment period on success percentages in each group (device, Minirin) was analyzed in one group with Chi-square test.

Results

The average age of the 134 patients included in the study was 6–15 years. The mean age of the 91 male and 43 female patients in both groups was 10 years. The mean age of the 39 male and 25 female patients in Group 1 was 10.4 years. Full response was seen in 43 patients (67.2%) at the 3rd month control and in 46 patients (71.9%) at the 6th month control. However, in 21 patients (32.8%) treated with the same therapy, no response was observed at the 3rd month and in 18 patients (28.1%) at the 6th month. Reasons included familial reasons and noncompliance with alarm device. Relapse was observed in 11 (17.2%) of the cured patients.

The mean age of the 52 male and 25 female patients, in Group 2, was 9.7 years. Of the seventy patients receiving desmopressin therapy, full response was seen in 52 patients (74.3%) at the 3rd month control and in 56 patients (80.0%) at the 6th month control. However, in 18 patients (25.7%), no response was observed at the 3rd month and in 14 patients (20.0%) in the 6th month. No side effects causing the discontinuation of desmopressin treatment were observed in this group. Relapse was observed in 15 (21.4%) of the cured patients [Table 1].

No statistical difference was found between the two groups for success rates or relapse rates at the 3rd or 6th month follow-up.

Discussion

The pathophysiology of nocturnal enuresis includes mechanisms such as high nocturnal urine output, decreased nocturnal bladder capacity, or decreased detrusor activity and impaired sleep arousal.

Despite there being many methods (behavioral and pharmacological) for treatment, none have provided complete cure, mainly due to the pathophysiology not being fully understood.[7] Most children with enuresis do not show obvious mental and urological pathology and do not have urinary tract infections. Their functional day-and-night bladder capacity is generally normal; however, the increased urine produced overnight exceeds functional bladder capacity and involuntary urination occurs.[8] Under normal conditions, nocturnal vasopressin secretion is higher during the nights. This condition leads to 50% less urine output at night.[4] Sufficient antidiuretic hormone is not secreted in these children and this leads to increased urine production. This situation is thought to be the case in 2/3rd of enuretic children to varying degrees.[9]

Desmopressin has been available in intranasal and tablet forms for the treatment of primary nocturnal enuresis; however the easiest method of sublingual melt is the most recently developed form.[10] Desmopressin sublingual melt form was used in all our patients; there were no complaints from parents regarding usage.

In general, desmopressin is a safe medication that has been used for many years,[11] with its most dangerous known side effect being water intoxication that can rarely be accompanied by convulsions and this is seen most commonly with its nasal form.[12]

No side effects causing the discontinuation of desmopressin treatment were observed in our study. We believe that the limitation of drinks particularly in the evenings (such as water, milk, and soft drinks) in all patients was the reason why water intoxication was not reported in any of the patients.

Studies have shown the importance of the balance between the bladder capacity of children with MNE and nocturnal urine. Nocturnal urine output seen during dry nights under desmopressin therapy has been determined to be significantly lower than wet nights, with desmopressin showing an antidiuretic effect.[13]

Table 1: Data values of enuresis nocturnal groups

	Male/ female	Age (years)	Response to treatment		Relapse (%)	*P*
			3 months later (%)	6 months later (%)		
Nocturnal enuresis alarm device group (*n*=64)	39/25	10.4±2.2 Minimum-maximum (6-15)	43 (67.2)	46 (71.9)	11 (17.2)	0.779
Nocturnal enuresis medication group (*n*=70)	52/18	9.7±2.6 Minimum-maximum (6-16)	52 (74.3)	56 (80.0)	15 (21.4)	0.421
P			0.366	0.612	0.535	

Chi-square tests: Significance *P*<0.05

In 41 systematic reviews of 2760 patients published by Glazener and Evans,[14] all forms of desmopressin were shown to reduce wetting at least 1 day/week in comparison with placebo. In addition, findings show that the number of wet nights per week is rapidly decreased with desmopressin therapy; however, relapse is commonly seen after treatment is discontinued. Desmopressin treatment is generally discontinued in the 3rd and 6th months, thus relapse rates are high. We believe that treatment should continue for at least 1 year to reduce relapse rates. In our study, we observed a significant difference in relapses of patients given a break after 6 months and those treated for a year. We did not encounter any serious problems in terms of adverse drug reactions in long-term use.

In another recent study, Lottmann *et al*.[15] published an article describing the long-term efficacy and safety of desmopressin therapy. The study following 744 patients with a mean age of 8.7 ± 2.5 years, with male patients constituting 71%, reported an average of 6 wet days a week. When all patients were evaluated following 3 and 6 months of desmopressin treatment, the percentage of patients with over 50% dryness achieved per week was reported as 40.5% (301/744), with those with <50% dryness achieved reported as 3% (23/744). In addition, when the patients leaving the study were considered, it has been determined that 16% of patients left the study due to finding the treatment ineffective, 8% of their own choice, and 11% for unknown reasons.

Enuresis alarm within the nonpharmacological treatments is undoubtedly the most effective method for the treatment of MNE in children with difficulty waking up and has the lowest relapse rate.[16]

Enuresis alarm is a treatment method based on conditioning. It is based on the principle of learning to wake up when the bladder is full prior to bed wetting.[17] In addition to its mechanism of action, there are publications showing that functional bladder capacity is also increased.[18,19] The average cure rate after at least 12 weeks of treatment has been reported to be 70%.[20]

The most important known disadvantage of this treatment option is the late onset of effect, which disrupts the motivation of the family and child.[21] According to some previous systematic reviews and controlled studies, it has been shown to be the treatment option offering the highest dry rate for the child, with a cure rate of 60%–80% and a risk of relapse between 20% and 30%. It is recommended that treatment is not immediately discontinued following 14 continuous dry nights, and for alarm therapy to continue for 4 weeks of dryness.[22,23] The efficacy of alarm device and desmopressin used in the treatment of primary NE has been assessed and compared in many studies.

In one study, the efficacy and relapse rates after 3rd, 6th, 9th, and 12th months following 6-month treatment were compared. Almost 68% of 88 patients receiving desmopressin achieved full continence in the 6th month; however, only 10% continued with continence at the control 6 months following discontinuation of treatment (12th month). Nearly 63% of the 79 patients receiving alarm therapy achieved full response in the 6th month, and full continence continued in 56% of the patients at 6 months following discontinuation of treatment (12th month).[24]

In a randomized study carried out by Önol *et al*.[25] of 142 patients with PMNE with 12-month treatment and follow-up, evaluating the 6-month efficacy, 76.8% of 73 patients receiving desmopressin and 61.8% of 45 patients receiving alarm therapy were shown to respond to the treatment. At the 6th month control, 20 (30.7%) patients receiving alarm therapy (for reasons such as device incompatibility, distrust of device, and reluctance) and 4 (5.2%) patients given desmopressin were reported to have left the study. In the 12-month follow-up of 32 patients receiving alarm therapy and 54 patients receiving desmopressin remaining in the study, the treatment efficacy rates were reported as 75% and 77.8%, respectively. As in our study, no statistically significant difference was shown between the efficacy at the 6th and 12th months.

In a multicentric study published recently by Evans *et al*.[26] when the groups receiving desmopressin and alarm therapies were compared, over 50% reduction in bed wetting (days/week) was determined to be 37.5% and 32.2%, respectively, and no significant difference was reported in dryness rates in their long-term (1 year) follow-ups.

In a randomized prospective study of treatment efficacies in PMNE by Kwak *et al*.,[27] the treatment response and effects of 51 patients receiving desmopressin as first-line treatment for 12 months and 46 patients receiving alarm therapy were compared. Two patients in the group receiving desmopressin therapy and three patients from the group receiving alarm therapy left the study prior to completion of the treatment period, and one patient from each group left the study due to side effects (stomach pain, difficulty urinating) and low compliance. The efficacy following 3-month treatment was determined as 77.8% for desmopressin therapy and 82% for alarm therapy, while no supremacy could be determined between them; however in later follow-ups, the rate of relapse was reported to be 50% in patients receiving desmopressin and 12% in patients receiving alarm therapy in patients with full response.

Our study is consistent with previously published articles; in terms of both treatment options showing similar successful results in terms of safety and efficacy and desmopressin showing faster results. However, when relapse rates are compared in our study, while generally the relapse rate following desmopressin treatment is reported to be higher, no statistically significant difference was found. This difference in our study is thought to be related to continuity of treatment along with close follow-up, the education level of the families, as well as the confidence and reassurances given.

Conclusions

Alarm therapy and desmopressin have the same success rate and relapse rates for PMNE. Compliance with alarm therapy is higher and we recommend it as first-line treatment. On the other hand, desmopressin has low side effects and can also be used.

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Confiicts of interest

There are no conflicts of interest.

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