

FACTORS INFLUENCING DESMOPRESSIN TREATMENT OUTCOMES IN CHILDREN WITH MONOSYMPTOMATIC ENURESIS NOCTURNA

Monosemptomatik Enürezis Nokturnası Olan Çocuklarda Desmopressin Tedavi Sonuçlarını Etkileyen Faktörler

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ABSTRACT

Objective: Desmopressin has been used in the treatment of monosymptomatic enuresis nocturna. However, data on the factors affecting desmopressin treatment success remain insufficient. This study aimed to evaluate the factors that influence desmopressin treatment outcomes in children with monosymptomatic enuresis nocturna.

Material and Methods: A total of 115 children aged over five years with primary monosymptomatic enuresis nocturna were included in this study. All patients were treated with 120 mg desmopressin daily. After three months of treatment, the patients were divided into two groups: group 1 (successful) included children who achieved dryness, while group 2 (unsuccessful) included those who continued bedwetting despite treatment. The factors influencing the success of desmopressin treatment were evaluated.

Results: The mean maternal age was significantly higher in group 1 compared to group 2 (34.8 vs. 32.4 years, $p = 0.044$). The number of enuretic nights per week and enuresis episodes per night were significantly greater in Group 2 (6.8 vs. 6 nights, $p = 0.030$; 1.7 vs. 1.4 episodes, $p = 0.040$). Multivariate analysis revealed that children with mothers aged over 33 years were 3.5 times more likely to respond to desmopressin treatment (odds ratio: 3.5 [1.2-10.5], $p = 0.023$).

Conclusion: Factors influencing desmopressin treatment success included maternal age, frequency of enuretic nights per week, and the number of enuresis episodes per night. Among these, maternal age was identified as the only independent predictor of treatment outcomes. This association may be attributed to the increased maternal experience and enhanced adherence to treatment protocols.

Keywords: Deamino Arginine Vasopressin; Desmopressin; Enuresis; Monosymptomatic Enuresis Nocturna; Nocturnal Enuresis

ÖZET

Amaç: Desmopressin monosemptomatik enürezis nokturna tedavisinde kullanılır. Ancak, desmopressin tedavisinin başarısını etkileyen faktörlere ilişkin veriler yetersizdir. Bu çalışma, monosemptomatik enürezis nokturnası olan çocuklarda desmopressin tedavisinin sonuçlarını etkileyen faktörleri değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu çalışmaya, primer monosemptomatik enürezis nokturnası olan beş yaş üstü toplam 115 çocuk dahil edildi. Tüm hastalara günlük 120 mg desmopressin tedavisi uygulandı. Üç aylık tedaviden sonra hastalar iki gruba ayrıldı: 1. grup (başarılı) kuruluğa ulaşan çocukları içerirken, 2. grup (başarısız) tedaviye rağmen yatak ıslatmaya devam edenleri içeriyordu. Desmopressin tedavisinin başarısını etkileyen faktörler değerlendirildi.

Bulgular: Ortalama anne yaşı, grup 1'de grup 2'ye kıyasla önemli ölçüde daha yüksekti (34,8'e karşı 32,4 yıl, $p = 0,044$). Haftada enüretik gece sayısı ve gece başına enürezis atakları Grup 2'de önemli ölçüde daha fazlaydı (6,8'e karşı 6 gece, $p = 0,030$; 1,7'ye karşı 1,4 atak, $p = 0,040$). Çok değişkenli analiz, 33 yaş üstü ananelere sahip çocukların desmopressin tedavisine yanıt verme olasılığının 3,5 kat daha fazla olduğunu ortaya koydu (olasılık oranı: 3,5 [1,2-10,5], $p = 0,023$).

Sonuç: Desmopressin tedavisinin başarısını etkileyen faktörler; anne yaşı, haftada enüretik gece sayısı ve gece başına enürezis sayısı olarak bulundu. Bunlar arasında, anne yaşı tedavi sonuçlarının tek bağımsız öngörücüsü olarak bulundu. Bu ilişki, artan anne deneyimi ve tedavi protokollerine artan uyumla ilişkili olabilir.

Anahtar Kelimeler: Deamino Arjinin Vazopressin; Desmopressin; Enürezis; Monosemptomatik Gece İdrar Kaçırma; Nokturnal Enürezis

INTRODUCTION

According to the International Children's Continence Society's standardization of terminology, enuresis is both a symptom and a condition characterized by intermittent incontinence during sleep. Enuresis without other lower urinary tract (LUT) symptoms and without bladder dysfunction was defined as monosymptomatic enuresis nocturna (MEN) (1). According to the International Classification of Diseases-10 (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) criteria, children older than five years who have at least two enuresis episodes per week for three consecutive weeks require treatment (2,3).

Seven of the 100 boys who went to bed at the age of seven are still enuretic into adulthood⁴. MEN significantly affects children, both emotionally and socially. Thus, treatment is recommended after the age of five, considering mental status, family expectations, social challenges, and cultural factors (4). First-line treatment involves urotherapy, including regular eating and drinking habits, normal daytime fluid intake, reduced fluid intake before sleep, and waking of the child at night to urinate (5). An arginine vasopressin analog, desmopressin, is a second-line treatment option with a success rate of more than 70% in MEN treatment (6). However, data on the factors affecting desmopressin treatment success remain insufficient. This study aimed to evaluate the factors influencing desmopressin treatment outcomes in children with MEN.

MATERIALS AND METHODS

The medical records of children with enuresis were retrospectively evaluated, and data were recorded prospectively. Verbal informed consent was obtained from the parents of all the participating children. The study was conducted according to the principles of the World Medical Association Declaration of Helsinki and Ethical Principles for Medical Research Involving Human Subjects⁷. Ethics committee approval was obtained from the Local Ethics Committee (Approval number: 2023.09.421).

Children older than five years with primary MEN were included in this study. All patients underwent a detailed history-taking process, including daytime

symptoms and defecation patterns, bladder diary, and physical examination. Urinalysis was performed to exclude urinary tract infections. Patients with non-monosymptomatic enuresis nocturna, secondary enuresis, or bladder-bowel dysfunction were excluded. Demographic and familial data, such as gender, age, body mass index (BMI), parents' ages, birth details, nutritional history, and neurological development, were recorded. Initially, general lifestyle modification was recommended. Subsequently, a sublingual tablet of 120 µg/day (Minirin®, Ferring International Center, Saint-Prex, Switzerland) was prescribed. The frequency of enuresis was tracked using a calendar, and treatment success was evaluated after three months. The patients were divided into two groups: Group 1 (successful treatment) and Group 2 (unsuccessful treatment). The groups were compared based on the recorded data. The Statistical Package for the Social Sciences version 24 (SPSS IBM Corp.; Armonk, NY, USA) was used for data analysis (7). Independent t-tests were used to compare independent groups, whereas the chi-square and Fisher's exact tests were used to analyze categorical data. Multivariate analysis was performed using logistic regression for parameters that were significant in univariate analysis. Data were analyzed at a 95% confidence level and considered significant when the p-value was < 0.05.

RESULTS

The study included 115 patients (35 female and 80 male) with a mean age of 9.7 years (range: 5-16 years). The demographic, familial, and pretreatment characteristics of the patients are shown in Table 1. The mean number of enuretic nights per week was 6.2, while the mean number of episodes of enuresis per night was 1.4. Of these, 91 (79.1%) responded to desmopressin treatment (Table 1).

When stratified by treatment response, no significant differences were observed between the groups in terms of gender, age, BMI, paternal age, family history, gestational duration, birth weight, mode of delivery, breastfeeding duration, age at walking and speaking, or sleep duration ($p \geq 0.05$). However, the mean maternal age was significantly higher in Group 1 (34.8 vs. 32.4; $p=0.044$). Additionally, Group 2 exhibited significantly higher enuretic nights per week (6.8 vs. 6; $p=0.030$)

and enuresis episodes per night (1.7 vs. 1.4; $p=0.040$) (Table 2).

Multivariate regression analysis identified maternal age as an independent predictor of desmopressin treatment outcome ($p=0.023$). Children whose mothers were older than 33 years had a 3.5 times greater likelihood of responding to desmopressin treatment (odds ratio: 3.5 [1.2-10.5]) (Table 3).

DISCUSSION

The treatment of nocturnal enuresis can be divided into two categories: nonpharmacological and pharmacological. Nonpharmacological treatment mainly involves motivation treatment and alarm treatment. Pharmacological treatments include

desmopressin, anticholinergics, imipramine, sertraline, and combination therapy. Desmopressin (1-deamino-8-D-arginine vasopressin) is a synthetic analog of arginine vasopressin and has achieved dryness rates of 60-80% in large-scale studies (8-10). Our findings align with these, reporting a response rate of 79.1%.

The prevalence of enuresis decreases with age. The incidence of enuresis is approximately 10% at the age of seven and 5% at 10 years of age. The spontaneous recovery rate was 15% per year (11). The Desmopressin Response in Primary nocturnal enuresis (DRIP) study is the largest prospective international multicenter study performed with desmopressin in patients with primary enuresis (12). This study demonstrated that age is a significant demographic predictor (increased efficacy

Table 1. Demografic, Familial and Pretreatment Characteristics of The Patients

Gender (male / female)	80/35
Age (years) *	9.7±2.9
Body mass index (kg/m ²) *	18.9±4.7
Family history	72 (%62.6)
Maternal age (years)*	34.2±4.8
Paternal age (years)*	38.4±4.9
Number of children in the family *	2.8±1.4
Gestational duration (weeks) *	38.9±1.8
Gestational duration (preterm / term)	10/105
Birth weight (gram) *	3262.7±580.7
Birth weight (low / normal / high)	9/96/10
Mode of delivery (vaginal / caesarean)	84/31
Duration of breastfeeding (months) *	5.6±3.2
Duration of breastfeeding (≤6month, >6month)	87/28
Duration of breastfeeding with formula (months) *	12.2±10.6
Duration of breastfeeding with formula (≤24month,>24month)	104/11
Walking start age (years)*	11.1±4.3
Speaking start age (years)*	13.5±6.4
Number of enuretic nights per week *	6.2±1.5
Number of enuresis per week ≤5	31 (27.0%)
Number of enuresis per week >5	84 (73.0%)
Number of enuresis per night *	1.4±0.6
Number of enuresis per night <2	75 (65.2%)
Number of enuresis per night ≥2	40 (34.8%)
Duration of sleep (hours) *	9.1±1.5
Response to desmopressin therapy	91 (%79.1)

*: mean ± standard deviation, kg/m²: kilogram square meter

Table 2. Comparison of Parameters Between Groups

	Groups		p
	Group 1	Group 2	
Number of patient	91	24	
Gender (male / female)	28/63	7/17	0.881
Age (years) *	9.6±3.0	10.0±2.5	0.549
Body mass index (kg/m ²) *	18.9±5.0	18.8±3.5	0.573
Family history	58 (%63.7)	15 (%62.5)	0.941
Maternal age (years)*	34.8±4.9	32.4±4.0	0.044
Paternal age (years)*	38.5±5.1	37.8±4.5	0.617
Number of children in the family *	2.7±1.5	2.8±1.3	0.703
Gestational duration (weeks) *	38.9±2.0	39.3±0.8	0.603
Gestational duration (preterm / term)	9/82	1/23	0.185
Birth weight (gram) *	3284±602	3193±512	0.335
Birth weight (low / normal / high)	8/74/9	1/22/1	0.362
Mode of delivery (vaginal / caesarean)	67/24	17/7	0.648
Duration of breastfeeding (months) *	5.6±3.3	5.6±2.9	0.588
Duration of breastfeeding (≤6month, >6month)	71/20	16/8	0.262
Duration of breastfeeding with formula (months) *	11.7±10.7	13.9±10.2	0.958
Duration of breastfeeding with formula (≤24month, >24month)	84/7	20/4	0.147
Walking start age (years)*	12.3±4.8	12.9±3.0	0.950
Speaking start age (years)*	15.3±11.0	16.0±3.7	0.210
Number of enuretic nights per week *	6.0±1.6	6.8±0.9	0.030
Number of enuresis per week ≤5	29 (31.9%)	2 (8.3%)	0.021
Number of enuresis per week >5	62 (68.2%)	22 (91.7%)	
Number of enuresis per night *	1.4±0.6	1.7±0.7	0.040
Number of enuresis per night <2	64 (70.3%)	11 (45.8%)	0.025
Number of enuresis per night ≥2	27 (29.7%)	13 (54.2%)	
Duration of sleep (hours) *	9.1±1.5	9.1±1.6	0.990

*: mean ± standard deviation, kg/m²: kilogram square meter

Table 3. Multivariate Analysis

	Odds Ratio*	p
Maternal age **	3.5 (1.2-10.5)	0.023
Number of enuretic nights per week ***	0.4 (0.1-1.9)	0.236
Number of enuresis per night ****	0.4 (0.2-1.2)	0.105

*: 95% confidence interval, **: Mother age ≤33 and > 33 compared, ***: Number of Enuresis per Week ≤5 and >5 compared, ****: Number of Enuresis per Night ≤1 and >1 compared

with increased age). According to a study by Montaldo et al., the mean age of children who responded to desmopressin treatment was 10 years (13). The number of patients who did not respond to the treatment was 8 years. However, in our study, there was no significant difference in age between the groups. Therefore,

patient age did not affect desmopressin treatment outcomes.

Although enuresis is more common in males, the effect of gender on the response to desmopressin treatment has not been demonstrated (12-14). In this study, we found that gender did not affect the treatment

success. According to Yanaral et al., BMI was higher in enuretic children than in the control group (15). However, there is insufficient data on the relationship between enuresis and BMI. In the present study, BMI had no effect on treatment success.

The relationship between family history and enuresis nocturna has been demonstrated in many studies. The frequency of enuresis in children with a history of enuresis in parents is 44-77% (16). However, no relationship has been found between family history and desmopressin response (14). In our study, there was no correlation between the response to desmopressin therapy and family history of enuresis. However, informing parents has been shown to play a role in the treatment of enuresis nocturna. There is insufficient evidence to demonstrate a relationship between the age of the parent and desmopressin treatment outcomes (8). In our study, maternal age was higher in patients who responded to desmopressin treatment. Maternal age was the only significant predictive factor in the multivariate analysis. Children with mothers older than 33 years of age were more likely to respond to treatment. This may reflect greater maternal experience and compliance with treatment protocols.

Parental involvement plays a critical role in the management of nocturnal enuresis in children, particularly in enhancing treatment adherence. Studies have shown that when parents are actively engaged in the treatment process by supporting behavioral interventions, maintaining treatment schedules, and providing emotional encouragement, children demonstrate significantly higher compliance rates (17). Furthermore, parental understanding of the condition reduces punitive responses and fosters a supportive environment, both of which are essential for a child's psychological well-being and long-term treatment success (18). Evidence also suggests that structured parental guidance and education can improve outcomes (19). Thus, involving parents not only improves adherence, but also strengthens the therapeutic alliance between the clinician, child, and family, ultimately enhancing the overall effectiveness of treatment.

Many studies have reported a relationship between the severity of enuresis and response to treatment.

The DRIP study demonstrated that the number of wet nights per week (increased efficacy with fewer wet nights) and nocturnal diuresis were significant predictive clinical variables (12). Onol et al. reported that the most important factor that determines the response to enuresis treatment is the number of enuresis per week (20). An enuresis of more than five per week makes the response to treatment difficult. According to Kruse et al., children with more than one enuresis at night do not respond to treatment (14). In our study, both the number of enuretic nights per week and the number of enuresis per night affected the response to treatment.

Breastfeeding provides cognitive and neurological developmental advantages in children compared with infant formulas. Although enuresis was higher in infants fed formula than in infants fed breastfed, there are insufficient data concerning the relationship between treatment response and breastfeeding (21). In our study, no relationship was found between breastfeeding and the response to desmopressin treatment.

The retrospective nature and relatively small number of patients in this study highlights its limitations. However, the prospective data collection illustrated the strengths of the present study.

CONCLUSION

Our study identified maternal age, frequency of enuretic nights per week, and number of enuresis episodes per night as the primary factors influencing the success of desmopressin treatment. The multivariate analysis revealed that maternal age was the only independent predictor. This association may be attributed to the increased maternal experience and enhanced adherence to treatment protocols. Therefore, the influence of parental involvement on treatment adherence should also be considered. The relationship between maternal age and treatment response warrants further investigation using larger prospective studies.

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