

# PEDIATRIC UROLOGY



**Original Article** 

# The effectiveness of biofeedback therapy in children with monosymptomatic enuresis resistant to desmopressin treatment

Desmopressin tedavisine dirençli monosemptomatik enurezis olan çocuklarda biyolojik geribildirim tedavisinin etkinliği

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#### **ABSTRACT**

**Objective:** To investigate the effect of biofeedback therapy on children with desmopressin- resistant primary monosymptomatic enuresis (MsE).

Material and methods: The study comprised both retrospective and prospective sections. A total of 262 medical files of patients who were diagnosed as enuresis between November 2012 and January 2015 were retrospectively screened. Patients with neuropathic bladder, daytime voiding problems, anatomical pathology and enuresis-related diseases were excluded from the study. The demographic data and family characteristics of 29 children with desmopressin- resistantprimary MsE were recorded. After biofeedback treatment patients whose frequency of enuretic episodes decrease by more than 50% were included in the successful biofeedback treatment group (SBTG), while other patients were categorized in the unsuccessful biofeedback treatment group (USGBT). The outcomes of uroflowmetry, voided volume, postvoiding residue (PVR) and total bladder volume/age-adjusted normal bladder capacity (TBV/NBC) were recorded before and at the sixth month of the treatment

Results: The mean age of 29 patients included in the study was 9.14±3.07 (6-15) years. Of patients, 16 were male (55.2%) and 13 were female (44.8%). Before biofeedback treatment the frequency of enuresis was 25.1±5.76 days/month, while after treatment this was calculated as 8.52±10.07 days/month. After treatment 8 patients (28.6%) achieved complete dryness. Twenty patients (69%), benefited from biofeedback (SBTG), while there were 9 patients (31%) in the USBTG group. There was no significant difference between the SBTG and USBTG groups in terms of age, body mass index and sex. The average bladder capacity of the patients increased from 215 mL to 257 mL after biofeedback treatment (p<0.001). The TBV/NBC value before treatment was 0.66, while after treatment it was 0.77 (p<0.001). There was a statistically significant difference between the SBTG and USBTG groups in terms of presence of MsE in mother, and both parents (p=0.001, p=0.016, respectively).

**Conclusion:** Biofeedback therapy is a safe, simple, and minimally invasive treatment modality in children with MsE resistant to desmopressin treatment. This treatment, which was found to increase total bladder capacity, may be recommended for children with MsE when conventional desmopressin treatment fails.

**Keywords:** Age adjusted normal bladder capacity; desmopressin resistant enuresis; EMG biofeedback; monosymptomatic enuresis; uroflowmetry.

#### ÖZ

Amaç: Desmopressine dirençli primer monosemptomatik enuresis'li (MsE) çocuklarda biofeedback tedavisinin etkinliğinin değerlendirilmesi amaçlanmıştır.

Gereç ve yöntemler: Bu çalışma retrospektif ve prospektif kısımlardan oluşmaktadır. Kasım 2012 ve Ocak 2015 tarihleri arasında enuresis tanısı alan 262 hastanın dosyası retrospektif olarak tarandı. Nöropatik mesane, gündüz işeme problemi, anatomik anomalisi ve enurezisle ilişkili hastalığı olanlar çalışma dışında tutuldu. Desmopressin dirençli primer MsE'li yirmi dokuz çocuğun demografik verileri ve ailesel özellikleri kaydedildi. Biofeedback tedavisi sonrasında enurezis sıklığı %50'den daha fazla düzelen hastalar başarılı biofeedback tedavisi grubu (BBTG); diğer hastalar başarılı olmayan biofeedback tedavisi grubu (BOBTG) olarak değerlendirildi. Üroflometri, işeme hacmi, rezidüel idrar ve total mesane hacmi / yaşla uyumlu normal mesane kapasitesi (TMH/NMK) sonuçları; tedavi öncesinde ve tedavinin 6. ayında kaydedildi.

Bulgular: Çalışmaya alınan 29 hastanın yaş ortalaması 9,14±3,07 (6-15) yıl idi. Hastaların 16'sı (%55,2) erkek, 13'ü (%44,8) kızdı. Biofeedback tedavisi öncesinde enurezis sıklığı 25,1±5,76 (gün/ay) iken tedavi sonrasında 8,52±10,07 (gün/ay) olarak hesaplandı. Tedavi sonrasında hastaların 8'inde (%28,6) tam kuruluk olduğu görüldü. Biofeedback tedavisinden fayda gören (BBTG) hasta sayısı 20 (%69) iken, 9 (%31) hasta BOBTG grubunda değerledirildi. BBTG ve BOBTG grupları arasında yaş, vücut kitle indeksi ve cinsiyet açısından anlamlı fark saptanmadı. Biofeedback tedavisi sonrasında hastaların ortalama mesane kapasitesinin 215 mL'den 257 mL'ye yükseldiği bulundu (p<0,001). TBV/NBC değeri tedavi öncesinde 0,66 iken, tedavi sonrasında 0,77 oldu (p<0,001). BBTG ve BOBTG grupları arasında; annede MsE varlığı ve hem annede hem babada MsE varlığı açısından, istatistiksel olarak anlamlı fark olduğu saptandı (sırasıyla; p=0,001, p=0,016).

**Sonuç:** Biofeedback tedavisi, desmopressin tedavisine dirençli MsE'li çocuklarda, güvenli, kolay ve minimal invaziv tedavi yöntemidir. Total mesane kapasitesini artırdığı saptanan bu tedavi; klasik desmopressin tedavisinden fayda görmeyen MsE'li çocuklar için önerilebilir.

**Anahtar Kelimeler:** Yaşla uyumlu normal mesane kapasitesi; desmopressine dirençli enurezis; EMG biofeedback; monosemptomatik enurezis; üroflometri.

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### Introduction

Enuresis or intermittent nocturnal incontinence is a frequent and important symptom in the childhood period. [1,2] According to the definition of the International Children's Continence Society (ICCS), all urine leakage during sleep in children above the age of 5 without lower urinary tract symptoms (frequent urination, urgency, etc.) is called monosymptomatic enuresis (MsE). [3] While the prevalence of MsE in 7- year- old children is between 5-10%, it spontaneously resolves with time and the prevalence in adults is between 1-2%. [4,5] As it can cause loss of confidence and intense psychological stress in children, it is recommended that MsE be treated at the ages of 6-7. Alarm treatment and desmopressin are recommended as the first choice in evidence-based treatment. [1] While desmopressin treatment is effective in 70% of the patients, 30% of the patients are resistant to treatment.

Electromyographic (EMG) biofeedback is a muscle-training method which transforms myoelectric signals in the muscles into visual and audible signals. EMG ensures perception of varying signals of skeletomuscular activity and transmits the interpreted data to the user as visual or audible stimuli. Using surface electrodes to identify changes in skeletomuscular activity, the user is visually or audibly warned. Biofeedback may be used both to strengthen weak muscles and reduce the tonus of spastic muscles. <sup>[6]</sup> A variety of publications have shown biofeedback treatment is effective in the treatment of chronic dysfunctional voiding and non-monosymptomatic enuresis (NMsE). <sup>[7,8]</sup> It is reported that in patients with NMsE, the enuresis component is resolved at a rate of 64% with EMG biofeedback treatment. <sup>[7]</sup> Additionally bladder capacity increases with biofeedback treatment.

Many studies have revealed a worse response to desmopressin treatment in children with primary MsE associated with a small bladder capacity compared with those with a normal capacity. <sup>[4,10]</sup> However, there is no information available on the bladder capacity increasing effect of biofeedback treatment, for this special patient group. In our study we planned to search the efficacy of biofeedback treatment in children with primary MsE resistant to desmopressin treatment.

#### Material and methods

#### Design of the study

In this prospectively designed study, each participant signed an informed consent form in accordance with the Declaration of Helsinki involving Human Subjects, and this study was approved by the Research and Ethical Review Board of Çanakkale Onsekiz Mart University.

The medical files of 262 patients applying to Çanakkale Onsekiz Mart Urology and Children's Health and Diseases Department

from November 2012 to January 2015 with the diagnosis of enuresis were retrospectively screened. Patients with the diagnosis of enuresis above the age of 5, with dry periods no longer than 6 months, and complaints not resolving in spite of desmopressin treatment were identified. Urination habits and defecation history, detailed physical investigation including neurological examination, complete urinalysis, fasting blood sugar, uroflowmetry and urinary system ultrasonography were retrieved from patient files. Patients with neuropathic bladder, daytime voiding problems, anatomical pathology and enuresis-related diseases (such as adenoid hyperplasia and obstructive sleep apnea- hypopnea syndrome) were excluded from this study. Thirty-two patients with primary MsE, resistant to desmopressin treatment were reached by telephone contact and called to the urology clinic.

The families of 29 patients gave permission for biofeedback treatment. Information about MsE history in the family, family education level and income level were requested from these patients. Uroflowmetric measurements, upper urinary system evaluation with ultrasound and residual urine postvoiding residue (PVR) tests were performed. Before uroflowmetry, children typically were waited until they felt the urge to urinate. Voided volume and total PVR were evaluated together as total bladder volume (TBV). Age-adjusted normal bladder capacity (NBC) was calculated using the Koff formula [(age+2) x 30]. As TBV was affected by the patient's age, TBV/NBC values were also calculated.

For EMG biofeedback treatment children were laid in supine position. Two superficial EMG electrodes were placed just in front of the anus at 3 and 9 o'clock positions, and one electrode was placed on the leg. Initially rest activity was measured. Then using pelvic floor exercises taught by the urotherapist, the pelvic floor muscles were contracted and muscle activity was measured, then biofeedback therapy was initiated. The children were shown a caterpillar, a fish or a plane on the screen and told them to imagine that they were these creatures, and objects and to try to avoid any obstacles that appeared. At each session, the pelvic floor muscle activity was measured and patients were advised to practice the exercises at home for half an hour each day. At the end of 6 weeks of biofeedback treatment, they were advised to continue with the instructed exercises as before. Data obtained before treatment and at 6 months after treatment were assessed and compared. The patients with frequency of enuresis decreasing by more than 50% were assessed as the Successful Biofeedback Treatment Group (SBTG), while patients with 50% or less improvement were included in Unsuccessful Biofeedback Treatment Group (USBTG).[4]

#### Statistical analysis

Statistical analysis was performed with Statistical Package for the Social Sciences 20.0 statistical software package (IBM Corp., Armonk, NY, USA). For descriptive statistics mean ± standard deviation, numbers and percentages were used. The normal distribution of the sample data was checked with the Shapiro-Wilk test. The baseline characteristics of the groups with SBTG and N-SBTG were compared using a T-test or Mann-Whitney U test for continuous variables and a chi-square test or Fisher's exact test for categorical variables. The Mann-Whitney U test was also performed to test the significance of pairwise differences using the Bonferroni correction to adjust for multiple comparisons. Similar assessments were completed for results before and after biofeedback treatment. All statistical tests were two-tailed, and statistical significance was defined as p<0.05.

#### **Results**

The mean age of the 29 patients included in the study was 9.14±3.07 (6-15) years. Of patients 16 were boys (55.2%) and 13 were girls (44.8%). Before biofeedback treatment the frequency of enuresis was 25.1±5.76 days/month, while after treatment this was calculated as 8.52±10.07 days/month. Eight patients (28.6%) were observed to be fully dry. Twenty (69%) patients in the successful biofeedback group experienced 50% or more drop in the frequency of enuretic episodes with biofeedback treatment, while there were 9 patients who had 50% or less benefit from biofeedback treatment (31%) (Figure 1). There was no difference between the SBTG and USBTG in terms of age, body mass index and sex. The average bladder capacity of patients after biofeedback treatment rose from 215 mL to 257 mL (p<0.001). The TBV/NBC value was 0.66 before treatment and rose to 0.77 after treatment (p<0.001). The basic characteristic values in the SBTG and USBTG groups before and after biofeedback treatment are summarized in Table 1.

In our study familial MsE history was scrutinized. Maternal MsE negatively affected treatment success in children (p=0.001), while presence of paternal MsE or MsE in other family members did not affect treatment success. Again, there was a significant difference between SBTG and USBTG groups in terms of presence of both maternal and paternal MsE (p=0.016). Any significant difference was not observed between the groups who improved with treatment and those who did not in terms of mother's working status, and educational level, father's educational level, family income levels and presence of deep sleep in childhood. The evaluation of familial and clinical parameters in terms of results of biofeedback treatment is summarized in Table 2.

## Discussion

This is the first study to investigate the effects of biofeedback therapy on children with desmopressin resistant primary MsE. Enuresis is an important and frequently seen health problem dur-

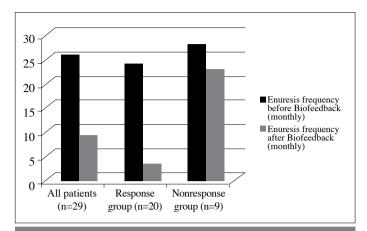


Figure 1. Monthly enuresis incidence in the groups of those who benefited from biofeedback treatment and those who did not

ing the childhood all over the world and it is predicted that there are over 50 million children with enuresis.<sup>[2]</sup> In accordance with the definition of the ICCS, MsE is defined as incontinence during sleep in a child who is older than 5 years old and who does not have any low urinary tract (LUT) symptoms.<sup>[3]</sup> The pathologic mechanisms of MsE are believed to include three factors: high night-time urine output, night-time low bladder capacity and increased detrusor activity and arousal disorder.<sup>[1]</sup>

Supportive treatment modalities (regulating the eating and drinking habits, reducing fluid intake in the hours before sleep etc.) are more successful than doing nothing, although the cure rate is not significantly high. So this treatment modalities should be used in conjunction with other treatment modalities. Alarm therapy and desmopressin are recommended in evidence-based first-line treatments.<sup>[1]</sup> Alarm therapy is helpful with a 60% complete response rate. However, this therapy has a high cessation rate because it interrupts the sleep of children and parents, and at least 5-12 weeks are required for the achievement of success. In addition, a low functional bladder capacity is an important predictor of failure of alarm therapy.<sup>[7,13]</sup>

Approximately two-thirds of MsE are related to the high night-time urine output mechanism and desmopressin treatment may resolve this problem with success rates around 70%. [1,7] Several studies have shown that patients with desmopressin resistant MsE had a significantly smaller age-adjusted functional bladder capacity (FBC). [4,10] Additionally, some reports have revealed the important role of reduced FBC in children with MsE refractory to desmopressin, anticholinergics, and alarm treatment. [9,14] Pelvic floor muscle training through biofeedback is a non-invasive, interactive urotherapy modality that teaches children how to control their lower urinary tract correctly with the goal of sustaining pelvic floor relaxation during voiding. [11] In biofeedback therapy, surface EMG electrodes are used to detect a change in skeletal muscle activity, which is then fed back to the user with

Table 1. Evaluation of biofeedb	oack treatment resul	ts in terms of basic demogra	phic and clinical paramet	ers
	All patients (n=29)	Successful Biofeedback Treatment Group (n=20)	Failed Biofeedback Treatment Group (n=9)	<b>p</b> *
Gender				
Boy	16 (55.2%)	11 (55%)	5 (55.6%)	0.647
Girl	13 (44.8%)	9 (45%)	4 (44.4%)	
Age (yrs)				
Mean	9.14	9.65	8.00	0.185
Standard deviation	3.07	3.24	2.39	
Body mass index (kg/m²)				
Underweight (<5 percentile)	0	0	0	
Normal (5-84 percentile)	19 (65.5%)	14 (70%)	5 (55.6%)	0.368
Overweight (85-95 percentile)	6 (20.7%)	4 (20%)	2 (22.2%)	
Obese (>95 percentile)	4 (13.8%)	2 (10%)	2 (22.2%)	
Enuresis frequency (monthly) Before biofeedback				
Mean	25.1	23.30	27.33	0.064
Standard deviation	5.76	6.03	2.23	
Range	12-30	12-30	25-30	
After biofeedback				
Mean	8.52	2.30	22.00	
Standard deviation	10.07	2.97	3.84	< 0.001
Range	0-30	0-10	15-30	
p**	<0.001	<0.001	0.011	
Voided urine volume (mL) Before biofeedback				
Mean	215.97	244.40	152.78	0.004
Standard deviation	83.00	80.00	48.99	
After biofeedback				
Mean	257.14	299.00	164.11	0.003
Standard deviation	120.17	116.96	62.71	0.003
p**	<0.001	<0.001	0.158	
Qa (mL/sn) Before biofeedback				
Mean	9.79	10.90	7.33	0.032
Standard deviation	0.78	4.61	1.22	

Mean         10.21         11.40         7.56         0.47           Standard deviation         0.90         5.40         1.50           Ostroiding residue (mL) before biofeedback         0.260         0.330         0.559           Mean         7.24         7.00         7.78         0.813           Standard deviation         7.97         8.64         6.66         6.66           Mean         6.90         6.50         7.78         0.83           Standard deviation         7.60         8.17         6.66         0.683           Standard deviation         2.0326         0.330         1         0.04           Standard deviation         84.13         81.34         48.11         0.04           Standard deviation         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         0.04           Mean         263.17         304.00         172.44         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.00         0.00         0.00         0.00         0.00         0.00         0.0	Table 1. Evaluation of biofeedback treatment results in terms of basic demographic and clinical parameters (Continued)						
Mean         10.21         11.40         7.56         0.47           Standard deviation         0.90         5.40         1.50           Ostroiding residue (mL) before biofeedback         0.260         0.330         0.559           Mean         7.24         7.00         7.78         0.813           Standard deviation         7.97         8.64         6.66         6.66           Mean         6.90         6.50         7.78         0.83           Standard deviation         7.60         8.17         6.66         0.683           Standard deviation         2.0326         0.330         1         0.04           Standard deviation         84.13         81.34         48.11         0.04           Standard deviation         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         0.04           Mean         263.17         304.00         172.44         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.05         0.00         0.00         0.00         0.00         0.00         0.00         0.0			Treatment Group	Treatment Group	<b>p</b> *		
Standard deviation         0.90         5.40         1.50         0.47           tw*         0.260         0.330         0.559         0.559           Description seldue (mL).           Standard deviation         7.24         7.00         7.78         0.813           Standard deviation         7.97         8.64         6.66         0.66           Standard deviation         7.60         8.17         6.66         0.83         0.83           Standard deviation         7.60         8.17         6.66         0.683         0.68	After biofeedback						
Standard deviation   0.90   0.30   0.559   0	Mean	10.21	11.40	7.56	0.047		
Service infeedback           Mean         7.24         7.00         7.78         0.813           Standard deviation         7.97         8.64         6.66           When         6.90         6.50         7.78         0.683           Standard deviation         7.60         8.17         6.66         6.04         6.04         6.04         6.04         7.24         8.11         6.04         6.04         8.13         8.13         8.13         8.13         8.13         8.13         8.13         8.12         8.12         8.12         8.12 <td>Standard deviation</td> <td>0.90</td> <td>5.40</td> <td>1.50</td> <td>0.047</td>	Standard deviation	0.90	5.40	1.50	0.047		
Refore biofeedback           Mean         7.24         7.00         7.78         0.813           Standard deviation         7.97         8.64         6.66         6.66           Refere biofeedback           Mean         6.90         6.50         7.78         0.683           Standard deviation         7.60         8.17         6.66         0.683           Refere biofeedback           Mean         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         0.05           After biofeedback         8.12         159.44         0.04           Mean         263.17         304.00         172.44         0.05           Standard deviation         121.92         120.89         62.36         0.05           Standard deviation         20.01         <0.001         0.131         0.02           Below Biofeedback         8.00         0.72         0.53         0.002           Brown Biofeedback         0.01         0.012         0.12         0.02           Brown Biofeedback         0.02         0.03         0.002         0.002         0.003         0.002 <td>p**</td> <td>0.260</td> <td>0.330</td> <td>0.559</td> <td></td>	p**	0.260	0.330	0.559			
Mean         7.24         7.00         7.78           Standard deviation         7.97         8.64         6.66           After biofeedback         After biofeedback         8.17         6.66           Standard deviation         7.60         8.17         6.66           Standard deviation         8.13         0.330         1           Selecte Biofeedback           Mean         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         48.12         48.12         48.12         48.12         48.12         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13         48.13	Postvoiding residue (mL) Before biofeedback						
After biofeedback           Mean         6.90         6.50         7.78         0.683           Standard deviation         7.60         8.17         6.66         0.683           Standard deviation         0.326         0.330         1         0.04           Colal bladder volume (mL) before Biofeedback           Mean         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         0.04           After biofeedback           Mean         263.17         304.00         172.44         0.05           Standard deviation         121.92         120.89         62.36         0.05           BEV/NBC Before biofeedback           Mean         0.66         0.72         0.53         0.002           Standard deviation         0.15         0.12         0.12         0.12           After biofeedback         0.07         0.85         0.57         0.002           Standard deviation         0.07         0.85         0.57         0.002           Standard deviation         0.02         0.18         0.17         0.002	Mean	7.24	7.00	7.78	0.813		
Mean         6.90         6.50         7.78         0.683           Standard deviation         7.60         8.17         6.66           Interpretation         0.326         0.330         1           Standard deviation         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         48.11           After biofeedback         84.13         304.00         172.44         172.4	Standard deviation	7.97	8.64	6.66			
Standard deviation         7.60         8.17         6.66           ***         0.326         0.330         1           Cotal bladder volume (mL) Before Biofeedback         3.23.72         252.65         159.44         0.04           Mean         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11           Mean         263.17         304.00         172.44         0.05           Standard deviation         121.92         120.89         62.36         0.05           BelVNBC Before biofeedback         3.000         0.013         0.002           Mean         0.66         0.72         0.53         0.002           Standard deviation         0.15         0.12         0.12         0.12           After biofeedback         4.00         0.02         0.53         0.002           Standard deviation         0.17         0.85         0.57         0.002           Standard deviation         0.22         0.18         0.17	After biofeedback						
Standard deviation         7.60         8.17         6.66           ***         0.326         0.330         1           Cotal bladder volume (mL) Sectore Biofeedback           Mean         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11         48.11           After biofeedback           Mean         263.17         304.00         172.44         0.05           Standard deviation         121.92         120.89         62.36         0.05           CBV/NBC Sectore biofeedback           Mean         0.66         0.72         0.53         0.002           Standard deviation         0.15         0.12         0.12           After biofeedback           Mean         0.77         0.85         0.57           Mean         0.77         0.85         0.57           Mean         0.02         0.18         0.17	Mean	6.90	6.50	7.78	0.692		
Mean         223.72         252.65         159.44         0.04           Standard deviation         84.13         81.34         48.11           After biofeedback           Mean         263.17         304.00         172.44         0.05           Standard deviation         121.92         120.89         62.36         CBV/NBC           CBV/NBC							

TBV: total bladder volume; NBC: age-adjusted normal bladder capacity; Qa: The average urinary flow rate; SBTG: Successful Biofeedback Treatment Group; NSBTG: Failed Biofeedback Treatment Group

<sup>\*</sup>Statistically significant at p<0.05. This p-value is compared to the SBTG and NSBTG groups

<sup>\*\*</sup>Statistically significant at p<0.05. This p-value is compared to the parameters before and after the biofeedback therapy

Table 2. Evaluation of biofeedback treatment results in
terms of familial and clinical parameters

	Successful Biofeedback Treatment Group (n=20)	Failed Biofeedback Treatment Group (n=9)	p*
MsE in mother	1 , /	• • •	
Yes	6 (30%)	9 (100%)	
No	14 (70%)	0 (0%)	0.001
MsE in father	30	14	0.52
Yes	13 (65%)	5 (55.6%)	0.72
No	7 (35%)	4 (44.4%)	0.694
MsE in mother and father			
Yes	2 (10%)	5 (55.6%)	
No	18 (90%)	4 (44.4%)	0.016
MsE in other relatives			
Yes	12 (60%)	8 (88.9%)	
No	8 (40%)	1 (11.1%)	0.201
Working mother			
Yes	11 (55%)	5 (55.6%)	
No	9 (45%)	4 (44.4%)	0.647
Education status of mother			
Absent	0	0	
Primary school	4 (20%)	5 (55.6%)	
High school	9 (45%)	2 (22.2%)	
University	7 (35%)	2 (22.2%)	0.328**
Education status of father			
Absent	0	0	
Primary school	8 (40%)	5 (55.6%)	
High school	5 (25%)	2 (22.2%)	
University	7 (35%)	2 (22.2%)	0.420**
Monthly income			
1000 TL and below	1 (5%)	2 (22.2%)	
Between 1000-3000 TL	9 (45%)	5 (55.6%)	
3000 TL and over	10 (50%)	2 (22.2%)	0.060**
Deep sleep			
- No	7 (35%)	3 (33.3%)	
- Mild	8 (40%)	4 (44.4%)	
- Much	5 (25%)	2 (22.2%)	0.971**

MsE: Monosymptomatic enuresis.

a verbal or visual warning. Biofeedback therapy has been determined to be useful both as a musculoskeletal and neurological treatment modality. [6]

Eller et al.<sup>[15]</sup> reported the mean FBC in children with MsE was only 63% of that of normal children. In their reports, children with nocturnal enuresis, who were proven to have reduced bladder capacity, were less likely to respond to desmopressin treatment. Morover, many studies have shown that a reduced FBC plays an important role in the pathogenesis of refractory MsE. <sup>[4,10]</sup> In our study the TBV/NBC value of patients with desmopressin- resistant MsE before biofeedback treatment was 0.66, which is in accordance with the literature. While the TBV/NBC ratio in the successful biofeedback treatment group (SBTG) increased from 0.72 to 0.85 (p<0.001), in the USBTG group this ratio increased from 0.53 to 0.57 (p=0.134).

In a current report, Ebiloglu et al.<sup>[7]</sup> have revealed that biofeed-back therapy is an effective treatment option for the enuresis component of non-monosymptomatic enuresis nocturna. In this study, they stated that the the success rate for enuresis was 65% with daytime incontinence and 63% without daytime incontinence. Hoekx et al.<sup>[9]</sup> also demonstrated that biofeedback is an effective treatment in children with oxybutinin -refractory MsE associated with a small bladder capacity thanks to normalization of bladder capacity. In our study we found that the average monthly frequency of enuretic episodes fell from 25.1 to 8.5 in desmopressin- refractory MsE patients after biofeedback treatment. While biofeedback treatment was successful in 68.9% of the patients, we identified that 40% of the patients in this successful group achieved full dryness.

Kibar et al. [16] showed that biofeedback therapy improved the residual urine volume in children with dysfunctional voiding. In our study while the PVR and average urinary flow rate (Qa) were not statistically affected by biofeedback treatment of children with refractory MsE, we found increases in total bladder volume, voided volume and TBV/NBC ratio. The reason for the lack of effect on residual urine is that the children in the study did not have dysfunctional voiding symptoms, and the amount of residual urine was very low.

In addition, we investigated the effect of education status of parents, gender, family history and level of income on the success of biofeedback therapy of MsE. MNE was detected in 77% of the children whose parents were bed-wetters and it is well known that there is a strong genetic predisposition in monosymptomatic nocturnal enuresis. <sup>[5]</sup> In our study we have found that only maternal MsE history and presence of both maternal and paternal MsE negatively affected the biofeedback treatment in children. We did not detect any significant difference in terms of MsE in other relatives, family education and income levels between

<sup>\*</sup>Statistical evaluation of SBTG and NSBTG groups. Statistically significant at p<0.05.

\*\*The Mann-Whitney U test was performed to test the significance of pairwise differences for using Bonferroni correction to adjust for multiple comparisons.

the groups of patients who benefited, and did not benefit from biofeedback treatment.

In conclusion, MsE is a common situation in children and treatment is important. As it may cause loss of confidence and intense psychological stress, it is recommended that MsE be treated in children while aged 6-7 years. Recommended initial treatment for MsE is desmopressin with 70% cure rate, however some patients are resistant to treatment. In these children with desmopressin- refractory MsE, bladder capacity is found to be smaller than expected. In our study we found that biofeedback treatment increased total bladder capacity and clearly reduced the frequency of enuretic episodes. Biofeedback treatment should be considered as a reliable, easy and successful treatment for MsE children resistant to desmopressin treatment. However, due to our low number of patients and samples, there is a need to conduct larger series studies on this topic.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Çanakkale Onsekiz Mart University School of Medicine (No: 2015-01/13).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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