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Desmopressin, Alarm, or Both? Evaluating Efficacy and Relapse in Children with Primary Monosymptomatic Nocturnal Enuresis

Primer Monosemptomatik Enürezis Nokturna'da Alarm Cihazı, Desmopressin ve Kombinasyon Tedavisinin Etkinliğinin Karşılaştırılması

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ABSTRACT

Background: Monosymptomatic nocturnal enuresis (MNE) is a common pediatric condition that affects a child's self-esteem and daily family life. Both enuresis alarm and desmopressin are recommended as first-line treatment options, but their comparative effectiveness and relapse rates remain subjects of discussion.

Aim: This study aimed to compare the short-term treatment outcomes and relapse rates of desmopressin, alarm therapy, and combination therapy in children with primary MNE.

Materials and Methods: This retrospective two-center study included 202 children diagnosed with MNE between September 2022 and January 2025. Patients were grouped into desmopressin monotherapy (n=124), alarm therapy (n=45), and combination therapy (n=33). Demographic data, treatment responses, and relapse rates were evaluated.

Results: Complete response rates were 39.5% for desmopressin, 42.2% for alarm therapy, and 63.6% for the combination group. Relapse occurred in 48.4% of the desmopressin group, 33.3% of the alarm group, and 30.3% of the combination group. Although the combination group showed higher response rates and lower relapse rates, these differences were not statistically significant (p>0.05).

Conclusion: Desmopressin, alarm therapy, and their combination are effective options for the treatment of primary MNE. Combination therapy may provide added benefit in selected patients, but no clear superiority was demonstrated in this study. Treatment plans should consider individual factors such as nocturnal urine output and family compliance.

Keywords: Monosymptomatic nocturnal enuresis, Desmopressin, Enuresis alarm

ÖZET

Giriş: Monosemptomatik noktürnal enürezis (MNE), çocuklarda özgüven ve aile düzenini olumsuz etkileyen yaygın bir durumdur. Enürezis alarmı ve desmopressin birinci basamak tedavi seçenekleri arasında yer almakta, ancak etkinlik ve nüks oranları hâlâ tartışılmaktadır.

Amaç: Bu çalışmanın amacı, primer MNE tanılı çocuklarda desmopressin, alarm tedavisi ve kombine tedavinin kısa dönem tedavi sonuçları ile nüks oranlarını karşılaştırmaktır.

Gereç ve Yöntem: Bu retrospektif iki merkezli çalışmaya, Eylül 2022 ile Ocak 2025 tarihleri arasında MNE tanısı alan 202 çocuk dahil edildi. Hastalar desmopressin monoterapisi (n=124), alarm tedavisi (n=45) ve kombine tedavi (n=33) gruplarına ayrıldı. Demografik veriler, tedavi yanıtları ve nüks oranları değerlendirildi.

Bulgular: Tam yanıt oranları desmopressin grubunda %39,5, alarm grubunda %42,2 ve kombine grupta %63,6 idi. Nüks oranı desmopressin grubunda %48,4, alarm grubunda %33,3 ve kombine grupta %30,3 olarak saptandı. Kombine tedavi sayısal olarak daha iyi sonuç verse de fark istatistiksel olarak anlamlı değildi (p>0,05).

Sonuç: Primer MNE tedavisinde desmopressin, alarm tedavisi ve kombine tedavi etkili seçeneklerdir. Kombine tedavi bazı hastalarda ek fayda sağlayabilir, ancak bu çalışmada belirgin bir üstünlük göstermemiştir. Tedavi planı, bireysel faktörler ve aile uyumu göz önünde bulundurularak yapılmalıdır.

Anahtar kelimeler: Monosemptomatik noktürnal enürezis, Desmopressin, Enürezis alarmı

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Introduction

Monosymptomatic nocturnal enuresis (MNE) is one of the most common pediatric urological conditions, characterized by involuntary bedwetting during sleep in children without other lower urinary tract symptoms(1). This condition can considerably impair a child's psychosocial well-being, self-esteem, and daily family life(2).

The International Children's Continence Society (ICCS) recommends both enuresis alarm therapy and desmopressin as first-line treatment options for MNE(2). Alarm devices aim to condition the child's arousal response to bladder filling, thereby training the child to wake up and void when necessary(3). Desmopressin, a synthetic analog of vasopressin, reduces nocturnal urine production by increasing renal water reabsorption(4). Despite their proven efficacy, each option has its limitations: alarm therapy requires strong family motivation and consistent compliance, whereas desmopressin is associated with higher relapse rates after treatment discontinuation(5).

Recent randomized controlled trials and meta-analyses have compared these modalities individually and have also begun to explore their combined use (5, 6). Some studies suggest that combination therapy may offer added benefits in children with high nocturnal urine production or poor response to single treatment(7).

Nevertheless, despite increasing evidence, data comparing these treatment approaches in routine clinical practice are still relatively limited. Therefore, this retrospective two-center study was designed to examine and compare the short-term effectiveness, relapse rates, and treatment adherence of alarm therapy, desmopressin monotherapy, and their combination in children with primary MNE. It is expected that combined therapy may provide higher treatment success and lower relapse rates than monotherapy alone, offering additional insight for clinical decision-making.

Methods

Study Design and Ethics

This retrospective, two-center cohort study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local Non-Interventional Clinical Research Ethics Committee (Approval No: E-60116787-020-622659).

Patient Selection

Medical records of pediatric patients diagnosed with primary MNE were retrospectively reviewed. Eligible patients were those who attended the urology and pediatric urology outpatient clinics of two tertiary centers between September 2022 and January 2025.

Inclusion criteria were:

- Age ≥5 years,
- Diagnosis of MNE according to ICCS criteria,
- At least two wet nights per week before treatment,
- No prior pharmacological or surgical treatment for enuresis.

Children with non-monosymptomatic enuresis, daytime urinary tract symptoms, neurological or anatomical urinary tract abnormalities, urinary tract infections, or incomplete records were excluded.

Treatment Allocation

Patients were categorized into three groups based on their documented treatment strategy:

1. **Alarm Therapy Group:** Managed with enuresis alarm alone, with family guidance on daily use and device maintenance.
2. **Desmopressin Group:** Treated with oral desmopressin melt at standard pediatric doses (120 µg/day, adjusted if needed).
3. **Combination Group:** Received both alarm therapy and desmopressin melt concurrently, either as initial treatment or after insufficient response to monotherapy.

All patients received standard urotherapy advice, including healthy voiding habits, evening fluid restriction after dinner, and constipation management.

Table 1. Demographic and Clinical Characteristics

Variable	Desmopressin (n=124)	Alarm (n=45)	Combined (n=33)	p-value
Age (years), median [min–max]	9 [5–16]	10 [5–15]	9 [5–15]	0.458*
Baseline wet nights/week, median [min–max]	6 [3–7]	6 [4–7]	6 [4–7]	0.873*
Post-treatment wet nights/week, median [min–max]	2 [0–7]	2 [0–6]	1 [0–6]	0.061*
Male (n, %)	71 (57.3%)	25 (55.6%)	21 (63.6%)	0.753**
Family history of enuresis (n, %)	49 (39.5%)	19 (42.2%)	12 (36.4%)	0.872**

P*: P-values calculated using Kruskal-Wallis test for continuous variables

p**: P-values calculated using Chi-square test for categorical variables

Data Collection and Definitions

Demographic data (age, sex), baseline frequency of wet nights, family history of enuresis, and bladder diary records were extracted. Treatment duration, adherence notes, treatment response, and any relapse were documented.

Treatment response was defined according to ICCS standards as:

- *Complete Response:* Total dryness during follow-up.
- *Partial Response:* ≥50% reduction in wet nights per week compared to baseline.
- *No Response:* <50% reduction.

Relapse was defined as the recurrence of more than one wet night per month after treatment discontinuation or initial dryness.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA), consistent with our previous methodology. Continuous variables were reported as mean ± standard deviation or median with interquartile ranges, based on distribution. Normality was tested using the Kolmogorov–Smirnov test. Between-group comparisons were made using one-way ANOVA or the Kruskal–Wallis test for continuous variables and chi-square or Fisher's exact test for categorical variables. A p-value of <0.05 was considered statistically significant.

Results

A total of 202 children with monosymptomatic nocturnal enuresis (MNE) were included in the study. Of these, 124 received desmopressin monotherapy, 45 received alarm therapy, and 33 received combined therapy. The mean age was 9.26 ± 2.49 years in the desmopressin group, 9.78 ± 2.58 years in the alarm group, and 9.30 ± 2.66 years in the combined group (p=0.458). The male proportion was 57.3% for desmopressin, 55.6% for alarm, and 63.6% for combined therapy (p=0.753). A positive family history of enuresis was present in 39.5%, 42.2%, and 36.4% of the desmopressin, alarm, and combined groups, respectively (p=0.872). The demographic and clinical characteristics of the study groups are summarized in Table 1. The median follow-up duration was 3 months (range 3–6) in the desmopressin group, 3 months (range 3–5) in the alarm group, and 3 months (range 3–6) in the combined therapy group. There was no statistically significant difference between the groups (p = 0.642).

The baseline mean number of wet nights per week was 5.90 ± 0.94 in the desmopressin group, 5.87 ± 0.97 in the alarm group, and 5.82 ± 0.95 in the combined group (p=0.873). After treatment, the mean number of wet nights per week decreased to 1.94 ± 1.82 for desmopressin, 1.76 ± 1.75 for alarm, and 1.12 ± 1.65 for combined therapy (p=0.061).

According to ICCS criteria, the complete response rate was 39.5% for desmopressin, 42.2% for alarm, and 63.6% for combined therapy. The partial response rate was 32.3%, 33.3%, and 18.2%, respectively. Non-response rates were 28.2% for desmopressin, 24.4% for alarm, and 18.2% for combined therapy (p=0.168).

Table 2. Treatment Response and Relapse

Outcome	Desmopressin (n=124)	Alarm (n=45)	Combined (n=33)	p-value
Complete Response (n, %)	49 (39.5%)	19 (42.2%)	21 (63.6%)	0.168*
Partial Response (n, %)	40 (32.3%)	15 (33.3%)	6 (18.2%)	
No Response (n, %)	35 (28.2%)	11 (24.4%)	6 (18.2%)	
Relapse (n, %)	60 (48.4%)	15 (33.3%)	10 (30.3%)	0.070*

P*: P-values calculated using Chi-square test for categorical variables

Relapse was observed in 48.4% of patients in the desmopressin group, 33.3% in the alarm group, and 30.3% in the combined therapy group (p=0.070). Treatment response and relapse rates are presented in Table 2.

Discussion

In this retrospective two-center study, we compared the treatment outcomes of desmopressin monotherapy, enuresis alarm therapy, and their combination in children with primary MNE. Our results showed that although the combined therapy group demonstrated numerically higher complete response rates and lower relapse rates compared to either monotherapy, these differences did not reach statistical significance. Similarly, while the relapse rate appeared lower for combined therapy than for desmopressin alone, this difference also failed to show a significant statistical effect. These findings indicate that the combined therapy did not demonstrate the strong benefit that might have been expected, highlighting the need for careful patient selection and realistic treatment expectations.

Several previous studies have similarly reported that while combination therapy intuitively seems promising due to its ability to target both the physiological (nocturnal polyuria) and behavioral (arousal training) components of enuresis, its superiority over monotherapy is not always evident in practice(7, 8). Randomized controlled trials and meta-analyses have shown that alarm therapy alone can achieve sustained dryness when families are well motivated(5, 9), whereas desmopressin provides rapid symptom relief but is associated with higher relapse rates when withdrawn abruptly(5). In this context, our results align with reports suggesting that adding desmopressin to alarm therapy does not consistently produce a statistically significant improvement in treatment success or relapse prevention, especially when alarm therapy is implemented effectively as a first-line intervention.

One possible explanation for the lack of a clear statistical advantage of combined therapy in our study may be related to the absence of detailed subgroup analyses rather than insufficient data collection. Although voiding diaries were routinely used to assess nocturnal urine output and bladder function, our study did not include separate analyses for children with specific risk factors such as pronounced nocturnal polyuria or reduced bladder capacity, which have been shown to influence response to desmopressin-based regimens(7, 8). Moreover, adherence to alarm use and family motivation, which are known to impact alarm therapy outcomes, were not quantitatively evaluated in our cohort(6, 9). These aspects may partly explain why the expected benefit of combination therapy did not clearly emerge and underline the importance of individualized treatment planning based on patient-specific characteristics.

Taken together, our findings support the view that all three treatment modalities, desmopressin, alarm therapy and their combination, are effective options for managing primary MNE and may be selected according to individual patient needs and family circumstances. Alarm therapy can be a good choice in families who are highly motivated and able to maintain consistent device use, while desmopressin may be preferable for children needing rapid symptom control, especially in the presence of nocturnal polyuria(7, 9). For patients with an insufficient response to either monotherapy, combined treatment remains a reasonable alternative, although its benefit may not

be as pronounced as expected in all cases(6, 10, 11). Future prospective studies with larger sample sizes and clear subgroup analyses are needed to better define which children benefit most from each approach.

This study has several limitations that should be acknowledged. First, its retrospective design may carry inherent biases related to data completeness and treatment documentation. Second, although voiding diaries were used for initial assessment, detailed subgroup analyses based on nocturnal polyuria or bladder capacity could not be performed due to the retrospective nature of the dataset. Third, treatment adherence and family motivation, which are known to influence outcomes especially in alarm therapy, were not quantitatively measured. Finally, the relatively small size of the combined therapy group may have limited the statistical power to detect significant differences. These factors should be considered when interpreting our results and highlight the need for future prospective studies with more rigorous subgroup evaluation.

Conclusion

This study adds to the existing evidence by demonstrating that although combined therapy may provide additional benefit for selected children with primary MNE, it did not show clear superiority over monotherapy in this cohort. Clinicians should carefully consider individual factors such as nocturnal urine production, bladder capacity, and family motivation when planning treatment. Well-designed prospective studies are still needed to clarify optimal patient selection and to identify the most effective sequencing or combination of available treatment options.

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Ethical Statement: This study was approved by the Non-Interventional Clinical Research Ethics Committee of Pamukkale University (Approval No: E-60116787-020-622659, Date: 10.12.2024). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest Statement: The named authors have no conflict of interest, financial orotherwise.

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