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# Comparison of Desmopressin Withdrawal Strategies on Relapse Rates in Children with Monosymptomatic Nocturnal Enuresis

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**Abstract**

**Introduction:** Desmopressin is a well-established first-line therapy for monosymptomatic nocturnal enuresis (MNE). Although it provides a rapid and effective response in most patients, relapse following drug discontinuation remains a major clinical challenge. The optimal strategy for discontinuing desmopressin to minimize relapse has not yet been clearly defined. Relapse after desmopressin withdrawal is a major source of frustration for both families and clinicians, emphasizing the need for optimized discontinuation strategies.

**Materials and Methods:** This multicenter retrospective study evaluated children with MNE who achieved a full response to desmopressin therapy. Based on the method of treatment cessation, patients were categorized into three groups: abrupt cessation, dose reduction, and time-extended tapering. Relapse was defined as the recurrence of more than one wet night per month within 12 weeks after discontinuation. Demographic and clinical characteristics, as well as relapse rates, were compared among the groups using appropriate statistical tests.

**Results:** A total of 286 children were included. Baseline characteristics such as age, gender, and pre-treatment wet-night frequency were comparable among groups. Relapse occurred most frequently in the abrupt cessation group, while structured withdrawal methods, including dose reduction and gradual tapering, were associated with lower relapse rates. Relapse rates were significantly higher after abrupt cessation compared with both structured protocols, highlighting the clinical relevance of planned withdrawal schedules.

**Conclusion:** In children with MNE who respond completely to desmopressin, structured withdrawal strategies appear to improve treatment durability and reduce relapse compared with abrupt discontinuation. Implementing gradual or time-extended discontinuation schedules may help sustain therapeutic success. These findings underline the importance of individualized treatment planning and patient education during the discontinuation phase to sustain long-term dryness and improve quality of life.

**Key words:** Enuresis; desmopressin; recurrence; drug tapering.

## Introduction

Monosymptomatic nocturnal enuresis (MNE) refers to involuntary urination during sleep that occurs intermittently and without any associated daytime lower urinary tract symptoms. Its prevalence is approximately 5–10% at age seven and decreases to 1–2% in adolescence, with a consistent male predominance (1). With an annual spontaneous remission rate of approximately 15% across age groups, MNE often resolves over time without intervention (2). Nocturnal enuresis is associated with emotional, social, and familial stress, and is linked to reduced quality of life in affected children compared to their peers (3, 4). Initial management focuses on regulating daytime fluid intake and limiting fluids before bedtime, though bladder diaries and basic advice alone have limited effectiveness in early NE treatment (5). If initial supportive measures are insufficient, first-line treatment options include enuresis alarms and desmopressin. Although alarms offer higher cure rates, desmopressin is often preferred due to its convenience, safety profile, and low incidence of side effects (6). Desmopressin therapy provides a rapid and effective response in most patients; however, relapse remains a significant issue, occurring in up to 83% of cases (7). It remains uncertain whether implementing a structured withdrawal strategy, such as gradually tapering the dose or following a planned discontinuation schedule, can effectively reduce the high relapse rates observed after desmopressin treatment (8, 9). In this study, we aimed to evaluate the effectiveness of different desmopressin withdrawal strategies in order to better understand their impact on treatment outcomes and relapse rates.

## Materials and Methods

This retrospective multicenter study was conducted to evaluate the impact of different desmopressin withdrawal strategies on relapse

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rates in children diagnosed with MNE. Medical records were reviewed from two urology centers, one specializing in pediatric urology and the other in general urology practice, for patients treated between January 2023 and January 2025.

**Definition and patient evaluation:** MNE was defined in accordance with ICCS criteria as nighttime bedwetting in children over five years of age, without daytime urinary symptoms such as urgency, frequency, incontinence, voiding postponement, infrequent voiding, dysuria, or a weak stream. All patients underwent a comprehensive evaluation, including medical history, physical examination, urinalysis, a two-day bladder diary, and assessment of bowel habits using the Bristol Stool Form Scale. Ultrasonography, uroflowmetry, and laboratory tests were performed only in patients who did not respond to initial treatment. All received standard urotherapy, which consisted of education on healthy voiding habits, lifestyle recommendations, and constipation management.

**Treatment and inclusion criteria:** Patients who did not respond adequately to urotherapy and opted for pharmacologic treatment were initiated on oral desmopressin melt at a dose of 120 µg/day. If there was insufficient response after two weeks, the dose was increased to 240 µg/day. Patients were followed every two weeks during the first month and monthly thereafter.

Only patients who achieved a full response, defined as complete absence of wet nights during the final month of desmopressin therapy, after at least three months of continuous treatment were included in the analysis.

**Additional inclusion criteria were:**

- Age ≥5 years,
- Diagnosis of MNE with at least two wet nights per week prior to treatment,
- Availability of follow-up data for at least 12 weeks after desmopressin cessation.

**Exclusion criteria included:**

- Non-monosymptomatic nocturnal enuresis,
- Neurological or structural urological abnormalities,
- Prior use of alarm therapy or any pharmacologic agents, including anticholinergic medications, within the last three months,
- Incomplete treatment or follow-up documentation.

**Withdrawal strategies and study groups:** Based on medical records, patients were retrospectively assigned to one of the following three groups depending on how desmopressin therapy was discontinued

- Group 1: Abrupt Cessation – Immediate discontinuation without tapering.
- Group 2: Dose Reduction – Desmopressin dose was reduced by 50% for two weeks before cessation.
- Group 3: Time-Extended Tapering – The full effective dose was continued every other night for two weeks, followed by every third night for another two weeks prior to cessation.

The withdrawal method was determined by the treating physician as part of routine clinical care. No randomization was performed.

**Outcome assessment:** All patients were followed for 12 weeks following desmopressin discontinuation. Relapse was defined as the occurrence of more than one wet night per month during the follow-up period. Data regarding relapse were obtained from follow-up visit notes and, when available, bladder diaries.

**Ethical approval:** This retrospective study received ethical approval from the Pamukkale University Non-Interventional Clinical Research Ethics Committee (Approval No: E-60116787-020-622655). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Statistical analysis:** Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation for normally distributed data or as median with interquartile ranges for non-normally distributed data. Categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro–Wilk test. Based on the distribution of the data, comparisons between groups were conducted using one-way ANOVA for normally distributed variables and the Kruskal–Wallis test for non-normally distributed variables. For categorical variables, Chi-square or Fisher's exact test was applied, as appropriate. All p-values were reported with three decimal places, and a p-value less than 0.050 was considered statistically significant.

## Results

A total of 1826 children who presented with nocturnal enuresis between January 2023 and January 2025 were retrospectively screened. Of these, 847 were excluded due to non-monosymptomatic nocturnal enuresis (NMNE), 236 had previously received desmopressin or

alarm therapy, 292 had incomplete medical records or insufficient follow-up, and 165 were excluded due to underlying neurological conditions or structural anomalies affecting the urinary system. Following these exclusions, 552 patients with MNE were initiated on desmopressin therapy. Among them, 110 patients (19.9%) were non-responders, 156 patients

**Table 1:** Baseline Characteristics of the Study Groups

| Variable | Abrupt (n=122) | Dose Reduction (n=89) | Tapered (n=75) | p-value |
|---|---|---|---|---|
| Age (median [min–max]) | 7.5 [5-15] | 8.0 [5-15] | 8.0 [5-14] | 0.546* |
| Pre-treatment wet nights (median [min–max]) | 6.0 [4-7] | 6.0 [4-7] | 6.0 [3-7] | 0.258* |
| Male (n) | 71 (58.2%) | 56 (62.9%) | 47 (62.7%) | 0.732** |
| Female (n) | 51 (41.8%) | 33 (37.1%) | 28 (37.3%) | |

**p*:** Kruskal–Wallis test was used for comparing continuous variables due to non-normal distribution (as confirmed by the Shapiro–Wilk test), ***p***:** Chi-square test was used for comparison of categorical variables

**Table 2:** Post-treatment Outcomes and Relapse Rates

| Variable | Abrupt (n=122) | Dose Reduction (n=89) | Tapered (n=75) | p-value |
|---|---|---|---|---|
| Wet nights at 1st month (median [min–max]) | 2.0 [0-3] | 2.0 [0-3] | 2.0 [0-3] | 0.635* |
| Wet nights at 2nd month (median [min–max]) | 1.0 [0-3] | 1.0 [0-2] | 1.0 [0-3] | 0.922* |
| Relapse rate (%) | 55.7 | 42.7 | 38.7 | 0.039** |

**p*:** Kruskal–Wallis test was used for comparing continuous variables due to non-normal distribution (as confirmed by the Shapiro–Wilk test), ***p***:** Chi-square test was used for comparison of categorical variables

(28.3%) exhibited a partial response, and 286 patients (51.8%) achieved a full response. Only patients with a full response were included in the final comparative analysis. A total of 286 children who showed a full response to desmopressin treatment were included in the analysis. Based on the method of treatment cessation, patients were categorized into three groups: Group 1 (abrupt withdrawal, n = 122), Group 2 (dose reduction, n = 89), and Group 3 (tapered withdrawal, n = 75).

Baseline characteristics, including age, gender, and the number of pre-treatment wet nights, were comparable across the three groups. Since the Shapiro–Wilk test demonstrated non-normal distributions for all continuous variables, including age, pre-treatment, and post-treatment wet nights ($p < 0.050$), the Kruskal–Wallis test was used for between-group comparisons. The median age was 7.5 years in Group 1 and 8.0 years in both Group 2 and Group 3 ($p = 0.546$). The median number of wet nights prior to treatment was 6.0 across all groups ($p = 0.258$). Male predominance was observed in each group (58.2%, 62.9%, and 62.7%, respectively; $p = 0.732$, Chi-square test). These baseline characteristics are summarized in Table 1. Post-treatment outcomes were likewise similar. The median number of wet nights during the first and second months after desmopressin discontinuation did not significantly differ among groups (1st month: $p = 0.635$; 2nd month: $p = 0.922$; Kruskal–Wallis test). These findings are presented in Table 2. Relapse was observed in 55.7% of patients in Group 1 (68/122), 42.7% in Group 2 (38/89), and 38.7% in Group 3 (29/75). A statistically significant difference was found among the three groups in terms of relapse rates ($p = 0.039$, Chi-square test), with the highest relapse rate occurring in the abrupt withdrawal group. Relapse data are also detailed in Table 2. To further investigate the differences between individual withdrawal strategies, post-hoc pairwise comparisons were performed. Relapse rates were significantly higher in the abrupt cessation group compared to the tapered withdrawal group (55.7% vs. 38.7%, $p = 0.020$). The difference between the

abrupt cessation group and the dose reduction group also reached statistical significance (55.7% vs. 42.7%, $p$ = 0.041). No significant difference was observed between the dose reduction and tapered withdrawal groups (42.7% vs. 38.7%, $p$ = 0.601).

## Discussion

In this multicenter retrospective study, we found that the method of desmopressin withdrawal significantly affected relapse rates in children with MNE who had initially achieved full response. The abrupt cessation group had the highest relapse rate (55.7%), while more structured tapering strategies, such as dose reduction and time-extended tapering, were associated with lower relapse rates (42.7% and 38.7%, respectively). These findings suggest that a gradual or stepwise discontinuation of desmopressin may reduce the likelihood of symptom recurrence compared to abrupt withdrawal. Our findings are in line with those of Gökçe et al., who conducted a multicenter randomized controlled study that contrasted two regimented tapering schedules for desmopressin against both abrupt discontinuation and a placebo arm (10). They reported significantly lower relapse rates in both structured withdrawal groups (39.1% and 42.4%) compared to abrupt cessation (55.3%) and placebo (53.1%) after 12 weeks of follow-up. Notably, their study identified non-structured withdrawal as an independent risk factor for relapse. Similarly, in our study, the relapse rate was highest in the abrupt cessation group (55.7%) and lower in groups with structured discontinuation strategies (42.7% and 38.7%). Unlike their study, which included placebo and utilized a randomized design, our study was retrospective in nature but included a comparable number of patients and withdrawal protocols. Despite methodological differences, both studies support the implementation of structured withdrawal methods to reduce relapse following successful desmopressin therapy. A meta-analysis by Chua et al., which synthesized findings from four randomized controlled trials, evaluated whether organized desmopressin tapering protocols improve outcomes in pediatric enuresis(8). Their pooled analysis revealed that structured withdrawal was significantly more effective than abrupt cessation in maintaining a relapse-free status, with dose-dependent tapering demonstrating the most favorable outcomes. Although the studies included in their analysis were conducted in controlled research settings, their conclusions align with our findings. In our study, relapse rates were also lower in both the dose-reduction and time-extended tapering groups compared to the abrupt withdrawal group. While our design was retrospective and observational in nature, the consistency between our results and the meta-analytic data supports the generalizability of structured withdrawal strategies. While our study focused on the relapse rates within a 12-week period after desmopressin withdrawal, future research could benefit from longer follow-up durations to assess the sustainability of treatment success over time. The relevance of extended monitoring is supported by studies such as that of Alkış et al., who demonstrated that childhood voiding dysfunction may be associated with urinary symptoms in adulthood, including overactive bladder(11). These findings emphasize the importance of long-term evaluation in pediatric populations with lower urinary tract symptoms and suggest that structured treatment and withdrawal approaches may have implications beyond the immediate post-treatment phase. A retrospective study by İssi and Biçakcı, which included 447 children treated with oral desmopressin lyophilisate, reported similar relapse rates between patients who stopped treatment abruptly (42.5%) and those who underwent a structured discontinuation protocol (41.1%) after one month of follow-up(9). While their results differ from ours, this may be partly explained by differences in study design and population characteristics. Notably, our study focused specifically on children who achieved full response prior to withdrawal, allowing for a more targeted assessment of relapse patterns in a clearly defined subgroup. Despite some variability in methodology, both studies contribute valuable insights into the clinical management of desmopressin discontinuation in children with MNE. Previous studies investigating desmopressin withdrawal strategies have reported conflicting results, and there is still no clear consensus on the optimal approach. While some studies have found no significant advantage of structured tapering, others have demonstrated its benefit in reducing relapse. In this context, our findings contribute to the growing body of evidence by suggesting that both gradual dose reduction and time-extended withdrawal may be preferable to abrupt cessation. These approaches may help lower the risk of relapse in children who respond fully to desmopressin and could be considered in routine clinical practice.

**Study limitations:** Several limitations should be considered when interpreting the results of this study. First, its retrospective design may have

resulted in selection and reporting bias, as the analysis was based on previously documented clinical records rather than on data collected through a standardized prospective protocol. Second, the lack of randomization in group assignment limits the ability to control for potential confounding variables, as withdrawal strategies were determined by treating physicians during routine care. Third, although the study included a relatively large and multicenter sample, the follow-up period was limited to 12 weeks, which may not fully capture long-term relapse rates. Lastly, variations in follow-up practices between centers and the absence of standardized relapse assessment tools could affect the consistency of outcome evaluation.

## Conclusion

In children with MNE who respond fully to desmopressin, the method of treatment withdrawal appears to influence treatment success. Our findings suggest that structured discontinuation strategies, such as gradual dose reduction or time-extended tapering, may be more effective than abrupt cessation. Incorporating these approaches into clinical practice may help improve treatment outcomes and reduce the risk of recurrence.

**Ethical approval:** This retrospective study was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (Approval No: E-60116787-020-622655). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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**Author contributions:** AA: Conceptualization, study design, data interpretation, manuscript writing, supervision. MCK: Data collection, statistical analysis, literature review, manuscript editing.

## References

1. Butler RJ, Golding J, Northstone K. Nocturnal enuresis at 7.5 years old: prevalence and analysis of clinical signs. BJU Int 2005;96(3):404-10.
2. Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the International Children's Continence Society. Neurourol Urodyn 2016;35(4):471-481.
3. Rangel RA, Seabra CR, Ferrarez C, Soares JL, Choi M, Cotta RG, et al. Quality of life in enuretic children. Int Braz J Urol 2021;47(3):535-541.
4. Collis D, Kennedy-Behr A, Kearney L. The impact of bowel and bladder problems on children's quality of life and their parents: A scoping review. Child Care Health Dev 2019;45(1):1-14.
5. Caldwell PH, Nankivell G, Sureshkumar P. Simple behavioural interventions for nocturnal enuresis in children. Cochrane Database Syst Rev 2013(7):Cd003637.
6. Nevéus T, Fonseca E, Franco I, Kawauchi A, Kovacevic L, Nieuwhof-Leppink A, et al. Management and treatment of nocturnal enuresis-an updated standardization document from the International Children's Continence Society. J Pediatr Urol 2020;16(1):10-19.
7. Monda JM, Husmann DA. Primary nocturnal enuresis: a comparison among observation, imipramine, desmopressin acetate and bed-wetting alarm systems. J Urol 1995;154(2 Pt 2):745-748.
8. Chua ME, Silangcruz JM, Chang SJ, Williams K, Saunders M, Lopes RI, et al. Desmopressin Withdrawal Strategy for Pediatric Enuresis: A Meta-analysis. Pediatrics 2016;138(1):e20160495.
9. Issi Y, Biçakci U. Does desmopressin withdrawal strategy affect relapse rates in monosymptomatic enuresis treatment? Eur J Pediatr 2021;180(5):1453-1457.
10. Gökçe M, Hajıyev P, Süer E, Kibar Y, Sılay MS, Gürocak S, et al. Does structured withdrawal of desmopressin improve relapse rates in patients with monosymptomatic enuresis? J Urol 2014;192(2):530-534.
11. Alkis O, Baser A, Özlülerden Y, Zumrutbas A, Aybek Z, Ölçücü M. Factors Facilitating the Emergence of Overactive Bladder in Adults With Childhood Voiding Disorder. Yeni Üroloji Dergisi. 2020;15(3):189-193.