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Treatment Outcomes of Combined Solifenacin and Desmopressin Therapy Compared with Desmopressin Monotherapy in Children with Primary Monosymptomatic Nocturnal Enuresis: A Prospective Cohort Study

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Abstract: ***Background:*** Primary monosymptomatic nocturnal enuresis (PMNE) is a common pediatric condition that adversely affects children's psychological well-being, quality of life, and family functioning. Although desmopressin is recommended as first-line pharmacological therapy, treatment response is often incomplete and relapse is common. Combination therapy with solifenacin and desmopressin may improve treatment outcomes by targeting multiple pathophysiological mechanisms. ***Objective:*** To compare the treatment outcomes of combined solifenacin and desmopressin therapy with desmopressin monotherapy in children with primary monosymptomatic nocturnal enuresis. ***Methods:*** This prospective cohort study was conducted at the Department of Pediatric Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan, between June 2023 and December 2023. A total of 100 children aged 5–14 years diagnosed with PMNE were enrolled and allocated into two treatment groups: desmopressin monotherapy (n = 50) and combined solifenacin plus desmopressin therapy (n = 50). Participants were followed for 12 weeks. The primary outcome was treatment response according to International Children's Continence Society criteria. Secondary outcomes included changes in weekly wet nights, time to clinical improvement, medication adherence, parent satisfaction, and adverse events. ***Results:*** Children receiving combination therapy demonstrated significantly greater clinical improvement than those receiving desmopressin monotherapy. Combination therapy resulted in significantly fewer wet nights at Weeks 4, 8, and 12, a greater percentage reduction in nocturnal enuretic episodes, higher complete response rates, and shorter time to clinical improvement (all $P < 0.001$). Medication adherence and parent satisfaction were also significantly higher in the combination therapy group (both $P < 0.001$). The frequency of adverse events, treatment discontinuation, and follow-up completion did not differ significantly between the treatment groups ($P > 0.05$). ***Conclusion:*** Combined solifenacin and desmopressin therapy was associated with superior clinical effectiveness compared with desmopressin monotherapy while maintaining an acceptable safety profile in children with PMNE. These findings support consideration of combination therapy as a therapeutic option for appropriately selected children, particularly those who are unlikely to achieve satisfactory symptom control with desmopressin monotherapy. Larger multicenter randomized studies with longer follow-up are warranted to confirm these findings.

Keywords: Primary monosymptomatic nocturnal enuresis; desmopressin; solifenacin; combination therapy; pediatric urology; prospective cohort study, neonatal soft-tissue mass.

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INTRODUCTION

Primary monosymptomatic nocturnal enuresis (PMNE), defined as intermittent nocturnal urinary incontinence during sleep in children aged five years or older in the absence of daytime lower urinary tract symptoms or bladder dysfunction, is one of the most common pediatric urological disorders. Although the condition demonstrates a spontaneous annual remission rate of approximately 15%, PMNE continues to affect a substantial proportion of school-aged children and adolescents, making it an important public health concern. Beyond the physical symptom of nocturnal bedwetting, PMNE exerts considerable psychosocial consequences, including reduced self-esteem, embarrassment, anxiety, impaired social functioning, and diminished health-related quality of life. These effects frequently extend to parents and caregivers, contributing to emotional stress, disrupted family routines, increased healthcare utilization, and additional financial burden. Given its high prevalence and significant impact on children and their families, timely diagnosis and effective treatment remain essential components of pediatric clinical practice (1,2).

The pathophysiology of PMNE is multifactorial and reflects the interaction of several physiological mechanisms. The principal contributors include nocturnal polyuria resulting from inadequate nocturnal secretion of arginine vasopressin, reduced functional bladder capacity, nocturnal detrusor overactivity, impaired arousal from sleep despite bladder fullness, and delayed maturation of the central nervous system pathways involved in bladder control. Genetic susceptibility and sleep-related factors have also been implicated in disease development. Consequently, contemporary management emphasizes individualized treatment according to the predominant underlying mechanism. Standard treatment includes education and reassurance, behavioral and lifestyle modification, fluid management, treatment of constipation where appropriate, enuresis alarm therapy, and pharmacological intervention. Among pharmacological options, desmopressin, a synthetic analogue of arginine vasopressin, is recommended as a first-line therapy, particularly for children with nocturnal polyuria. By reducing nocturnal urine production through enhanced renal water reabsorption, desmopressin rapidly decreases the frequency of wet nights and provides symptomatic relief for many patients. However, a considerable proportion of children demonstrate only partial response or fail to achieve complete dryness, and relapse following treatment discontinuation remains a well-recognized limitation of desmopressin monotherapy (1,3,7).

Recognition of the heterogeneous pathophysiology of PMNE has stimulated increasing interest in combination pharmacotherapy targeting multiple mechanisms simultaneously. Solifenacin, a selective muscarinic M3 receptor antagonist, improves bladder storage by inhibiting involuntary detrusor contractions and increasing functional bladder capacity. Although primarily indicated for overactive bladder, it may also benefit children with PMNE in whom reduced nocturnal bladder capacity contributes to persistent symptoms. The combination of solifenacin with desmopressin is therefore biologically plausible because it simultaneously addresses nocturnal polyuria and impaired bladder storage function. Emerging evidence from randomized clinical trials and systematic reviews suggests that combination therapy may result in higher complete response rates, fewer wet nights, and greater overall treatment success than desmopressin alone without a significant increase in adverse events. Nevertheless, variations in study populations, treatment protocols, outcome definitions, and follow-up periods have resulted in inconsistent findings, and the overall evidence remains insufficient to establish combination therapy as the preferred initial pharmacological approach for all children with PMNE (3–6,10).

Despite encouraging evidence supporting combined therapy, important gaps remain in the current literature. Many published studies have involved relatively small sample sizes, retrospective designs, or heterogeneous patient populations, limiting the generalizability of their findings. Furthermore, prospective comparative studies evaluating the effectiveness of combined solifenacin and desmopressin therapy against desmopressin

monotherapy remain limited, particularly in resource-limited settings where treatment decisions must balance efficacy, safety, and cost. Additional prospective evidence is therefore required to clarify the comparative effectiveness of these treatment strategies, optimize patient selection, and strengthen the evidence base informing clinical practice guidelines. Such evidence may contribute to improved therapeutic outcomes and facilitate more individualized management of children with PMNE.

METHODOLOGY

This prospective cohort study was conducted to compare the treatment outcomes of combined solifenacin and desmopressin therapy with desmopressin monotherapy in children diagnosed with primary monosymptomatic nocturnal enuresis (PMNE). The study was carried out at the Department of Pediatric Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan, over a seven-month period from June 2023 to December 2023. A prospective observational design was selected to enable systematic follow-up of children receiving routine clinical treatment and to evaluate comparative therapeutic outcomes in a real-world clinical setting.

Children aged 5–14 years presenting to the pediatric urology outpatient department with PMNE were screened for eligibility. The diagnosis of PMNE was established according to the criteria of the International Children's Continence Society (ICCS), defined as intermittent nocturnal urinary incontinence occurring in children aged five years or older in the absence of daytime lower urinary tract symptoms or underlying bladder dysfunction. Eligible participants were required to have experienced at least two wet nights per week during the preceding three months and to have received no pharmacological treatment for nocturnal enuresis within the previous three months. Children with secondary nocturnal enuresis, non-monosymptomatic nocturnal enuresis accompanied by daytime urinary symptoms, congenital urinary tract anomalies, neurogenic bladder, active urinary tract infection, diabetes mellitus, diabetes insipidus, chronic kidney disease, constipation requiring medical treatment, known hypersensitivity to desmopressin or solifenacin, or neurological and developmental disorders affecting bladder function were excluded from the study.

A total of 100 eligible children were enrolled using a consecutive non-probability sampling technique. All patients fulfilling the eligibility criteria during the study period were invited to participate after written informed consent had been obtained from their parents or legal guardians. Participants were allocated

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into two cohorts according to the treatment prescribed by the attending pediatric urologist as part of routine clinical practice. Fifty children received combined solifenacin and desmopressin therapy, while the remaining fifty received desmopressin monotherapy. As this was an observational cohort study, treatment allocation was based on clinical decision-making rather than randomization.

Children assigned to the monotherapy cohort received oral desmopressin at an initial dose of 0.2 mg once daily at bedtime, with dose escalation to 0.4 mg after two weeks if clinically indicated because of an inadequate response. Participants in the combination therapy cohort received the same desmopressin regimen together with oral solifenacin 5 mg once daily. Treatment was continued for 12 weeks in both groups. In addition to pharmacological therapy, all participants received standardized urotherapy, including counseling regarding appropriate fluid intake, restriction of excessive evening fluids, avoidance of caffeinated beverages, regular daytime voiding, complete bladder emptying before bedtime, and management of constipation when indicated. Parents and caregivers were instructed regarding medication administration and were asked to maintain a daily bladder diary documenting treatment adherence and the frequency of nocturnal enuretic episodes throughout the study period.

Baseline evaluation included detailed demographic information, medical history, family history of nocturnal enuresis, duration and severity of symptoms, previous treatment history, physical examination, and routine urinalysis to exclude urinary tract infection. Additional laboratory or radiological investigations were performed whenever clinically indicated to exclude underlying pathological conditions. Participants were followed at four, eight, and twelve weeks after treatment initiation. At each follow-up visit, bladder diaries were reviewed, treatment adherence was assessed, adverse drug reactions were documented, and treatment response was recorded using standardized case report forms by trained pediatric urology residents under the supervision of consultant pediatric urologists.

The primary outcome measure was treatment

response at 12 weeks, assessed according to the reduction in the number of wet nights per week compared with baseline. Treatment response was categorized according to ICCS recommendations as complete response (100% reduction in wet nights), partial response (50–99% reduction), or non-response (less than 50% reduction). Secondary outcome measures included the mean reduction in wet nights per week, time to initial clinical improvement, treatment adherence, frequency of adverse drug reactions, and treatment discontinuation resulting from medication-related adverse events.

The principal independent variable was treatment modality, categorized as combined solifenacin and desmopressin therapy or desmopressin monotherapy. Dependent variables included treatment response, reduction in wet nights, complete response rate, partial response rate, treatment adherence, and adverse events. Additional demographic and clinical variables including age, sex, duration of symptoms, baseline frequency of nocturnal enuresis, family history, body mass index, and previous behavioral interventions were recorded because of their potential influence on treatment outcomes.

To ensure data quality, all investigators received standardized training before commencement of the study. Data were collected using predesigned case report forms, reviewed at each follow-up visit for completeness and accuracy, and entered into a secure electronic database. Double-checking of data entry and routine data cleaning were performed before statistical analysis. Participant confidentiality was maintained by assigning unique study identification numbers and storing all records in password-protected electronic files accessible only to the research team. Incomplete records were verified against the original case report forms, and analyses were performed using complete-case data when missing information was minimal.

Ethical approval for the study was obtained from the Institutional Review Board of the Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar. Written informed consent was obtained from the parents or legal guardians of all participants prior to enrollment. Confidentiality and anonymity were maintained throughout the study, and all research procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and applicable institutional ethical guidelines.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed data were summarized as mean ± standard deviation, whereas non-normally distributed variables were presented as median with interquartile range. Categorical variables were expressed as frequencies and percentages. Baseline characteristics between the two treatment groups were compared using the independent-samples t test or the Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Treatment outcomes were compared using the chi-square test for categorical variables and the independent-samples t test for continuous variables. Multivariable logistic regression analysis was planned to evaluate the independent association between treatment modality and complete response after adjustment for potential confounding variables, including age, sex, baseline enuresis frequency, and family history. Adjusted odds ratios with 95% confidence intervals were calculated, and a two-tailed p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 children diagnosed with primary monosymptomatic nocturnal enuresis were enrolled in this prospective cohort study, with 50 participants receiving desmopressin monotherapy and 50 receiving combined solifenacin and desmopressin therapy. All participants met the eligibility criteria and were included in the final analysis. Follow-up was completed by 96 participants (96.0%), while four participants (4.0%) were lost to follow-up.

Baseline Characteristics

The baseline demographic and clinical characteristics of the study participants are presented in Table 1. The mean age was comparable between the desmopressin monotherapy and combination therapy groups (9.22 ± 2.83 vs. 9.42 ± 2.88 years, $p = 0.727$). Although males predominated in both groups, the difference in sex distribution was not statistically significant (64.0% vs. 82.0%, $p = 0.072$). No statistically significant differences were observed between the groups regarding weight, height, body mass index, duration of enuresis, age at onset, baseline frequency of wet nights, family history of enuresis, previous treatment, constipation, deep sleeping, or snoring (all $p > 0.05$), indicating that the two cohorts were comparable before treatment initiation.

Table 1. Baseline Demographic and Clinical Characteristics of Children with Primary Monosymptomatic Nocturnal Enuresis According to Treatment Group.

Variable	Desmopressin Monotherapy (n = 50)	Combination Therapy (n = 50)	P-value
Age (years), Mean ± SD	9.22 ± 2.83	9.42 ± 2.88	0.727
Male, n (%)	32 (64.0)	41 (82.0)	0.072
Weight (kg), Mean ± SD	30.49 ± 8.04	30.03 ± 8.12	0.776
Height (cm), Mean ± SD	131.08 ± 14.75	132.38 ± 14.41	0.657
Body Mass Index (kg/m²), Mean ± SD	17.42 ± 1.64	16.79 ± 1.77	0.070
Duration of Enuresis (years), Mean ± SD	3.70 ± 1.11	3.82 ± 1.13	0.607
Age at Onset (years), Mean ± SD	5.53 ± 2.90	5.64 ± 2.78	0.850
Baseline Wet Nights per Week, Mean ± SD	5.76 ± 1.12	5.72 ± 1.13	0.859
Family History of Enuresis, n (%)	20 (40.0)	16 (32.0)	0.532
Previous Treatment, n (%)			0.965
Behavioral Therapy	16 (32.0)	17 (34.0)	
Alarm Therapy	21 (42.0)	21 (42.0)	
No Previous Treatment	13 (26.0)	12 (24.0)	
Constipation, n (%)	2 (4.0)	4 (8.0)	0.674
Deep Sleeper, n (%)	28 (56.0)	29 (58.0)	1.000
Sleep Disturbance/Snoring, n (%)	13 (26.0)	13 (26.0)	1.000

Treatment Outcomes

Treatment outcomes following 12 weeks of therapy are summarized in **Table 2**. Children treated with combined solifenacin and desmopressin therapy demonstrated significantly greater improvement than those receiving desmopressin monotherapy. The mean number of wet nights per week was significantly lower in the combination therapy group at Week 4 (3.46 ± 1.18 vs. 4.58 ± 1.32, $p < 0.001$), Week 8 (1.64 ± 1.09 vs. 3.22 ± 1.41, $p < 0.001$), and Week 12 (0.62 ± 0.81 vs. 2.10 ± 1.36, $p < 0.001$). Similarly, the mean percentage reduction in wet nights was significantly greater among children receiving combination therapy (88.7% ± 18.6%) than among those receiving desmopressin monotherapy (63.4% ± 22.8%, $p < 0.001$). The combination therapy group also experienced a shorter mean time to clinical improvement (3.9 ± 1.4 weeks vs. 5.8 ± 1.7 weeks, $p < 0.001$).

Table 2. Comparison of Treatment Outcomes Between Desmopressin Monotherapy and Combined Solifenacin + Desmopressin Therapy

Outcome Variable	Desmopressin Monotherapy (n = 50)	Combination Therapy (n = 50)	P-value
Wet nights/week at Week 4, Mean ± SD	4.58 ± 1.32	3.46 ± 1.18	<0.001
Wet nights/week at Week 8, Mean ± SD	3.22 ± 1.41	1.64 ± 1.09	<0.001
Wet nights/week at Week 12, Mean ± SD	2.10 ± 1.36	0.62 ± 0.81	<0.001
Percentage Reduction in Wet Nights (%), Mean ± SD	63.4 ± 22.8	88.7 ± 18.6	<0.001
Time to Clinical Improvement (weeks), Mean ± SD	5.8 ± 1.7	3.9 ± 1.4	<0.001
Treatment Response, n (%)			<0.001
Complete Response	4 (8.0)	13 (26.0)	
Partial Response	22 (44.0)	35 (70.0)	
Non-response	24 (48.0)	2 (4.0)	

Based on the International Children's Continence Society response criteria, complete response was achieved by 13 (26.0%) children in the combination therapy group compared with 4 (8.0%) in the monotherapy group. Partial

response was observed in 35 (70.0%) and 22 (44.0%) participants, respectively, whereas non-response occurred in only 2 (4.0%) children receiving combination therapy compared with 24 (48.0%) children receiving desmopressin monotherapy ($p < 0.001$).

Treatment Adherence and Safety

Treatment adherence and safety outcomes are presented in **Table 3**. Children receiving combination therapy demonstrated significantly higher medication adherence than those receiving desmopressin monotherapy (93.8 ± 4.8% vs. 89.4 ± 5.6%, $p < 0.001$) and reported significantly fewer missed doses (5.2 ± 3.1 vs. 8.6 ± 4.5, $p < 0.001$). Parent satisfaction scores were also significantly higher in the combination therapy group (4.5 ± 0.7 vs. 3.2 ± 0.9, $p < 0.001$).

Table 3. Comparison of Treatment Adherence, Safety Profile, and Follow-up Outcomes Between the Two Treatment Groups

Variable	Desmopressin Monotherapy (n = 50)	Combination Therapy (n = 50)	P-value
Treatment adherence (%), Mean ± SD	89.4 ± 5.6	93.8 ± 4.8	<0.001
Missed doses, Mean ± SD	8.6 ± 4.5	5.2 ± 3.1	<0.001
Parent satisfaction score (1–5), Mean ± SD	3.2 ± 0.9	4.5 ± 0.7	<0.001
Adverse events, n (%)	4 (8.0)	7 (14.0)	0.337
Treatment discontinuation, n (%)	1 (2.0)	1 (2.0)	1.000
Follow-up completed, n (%)	47 (94.0)	49 (98.0)	0.617
Lost to follow-up, n (%)	3 (6.0)	1 (2.0)	0.617

Adverse events were uncommon in both treatment groups and did not differ significantly between participants receiving combination therapy and those receiving desmopressin monotherapy (14.0% vs. 8.0%, $p = 0.337$). Treatment discontinuation was rare, occurring in one participant in each group (2.0%, $p = 1.000$). Follow-up completion exceeded 90% in both treatment groups, with no statistically significant difference observed between groups (98.0% vs. 94.0%, $p = 0.617$).

Multivariable Logistic Regression Analysis

The results of the multivariable logistic regression analysis are presented in **Table 4**. After adjustment for age, sex, duration of enuresis, baseline frequency of wet nights, family history of enuresis, deep sleeping, and treatment adherence, combined solifenacin and desmopressin therapy remained independently associated with a significantly greater likelihood of achieving complete treatment response compared with desmopressin monotherapy (adjusted odds ratio [AOR] = 4.89; 95% confidence interval [CI]: 1.42–16.86; $p = 0.012$). Higher treatment adherence was also independently associated with complete response (AOR = 1.09; 95% CI: 1.02–1.17; $p = 0.014$). None of the remaining demographic or clinical variables demonstrated statistically significant independent associations with treatment success.

Table 4. Multivariable Logistic Regression Analysis of Factors Associated with Complete Treatment Response in Children with Primary Monosymptomatic Nocturnal Enuresis (N = 100)

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	P-value
Combination therapy (vs. Desmopressin monotherapy)	**4.89**	**1.42 – 16.86**	**0.012**
Age (per 1-year increase)	1.08	0.89 – 1.31	0.421
Male sex	1.27	0.45 – 3.57	0.648
Duration of enuresis (years)	0.86	0.65 – 1.15	0.314
Baseline wet nights/week	0.71	0.49 – 1.02	0.063
Family history of enuresis	0.82	0.31 – 2.16	0.687
Deep sleeper	0.89	0.33 – 2.41	0.819
Treatment adherence (%)	1.09	1.02 – 1.17	0.014

DISCUSSION

The present prospective cohort study demonstrated that combined solifenacin and desmopressin therapy was associated with superior clinical outcomes compared with desmopressin monotherapy in children with primary monosymptomatic nocturnal enuresis (PMNE). Children receiving combination therapy experienced significantly greater reductions in nocturnal enuretic episodes, higher complete treatment response rates, earlier clinical improvement, and better medication adherence and parent satisfaction. Importantly, these improved outcomes were achieved without a significant increase in adverse events or treatment discontinuation. These findings are clinically relevant because successful management of PMNE extends beyond reducing bedwetting episodes to improving psychological well-being, self-esteem, social functioning, and family quality of life.

The findings of the present study are consistent with accumulating evidence supporting combination pharmacotherapy for PMNE. Ahmad and Minallah reported significantly higher treatment success and complete response rates among children receiving combined solifenacin and desmopressin therapy compared with desmopressin alone, without a clinically meaningful increase in adverse events (12). Similarly, Ghanavati et al. demonstrated that both solifenacin–desmopressin and tolterodine–desmopressin combinations achieved greater reductions in wet nights and higher response rates than desmopressin monotherapy while maintaining acceptable tolerability (13). The present findings closely parallel these randomized clinical trials, reinforcing the concept that simultaneously targeting multiple pathophysiological mechanisms provides greater therapeutic benefit than treating nocturnal polyuria alone.

Additional support is provided by the randomized clinical trial conducted by Cho et al., who demonstrated that adding an anticholinergic agent to desmopressin significantly improved treatment outcomes while increasing functional bladder capacity (14). These findings are particularly important because reduced nocturnal bladder capacity has been recognized as a major contributor to persistent symptoms in many children with PMNE. Furthermore, a network meta-analysis by Song et al. concluded that combination therapy involving desmopressin and anticholinergic agents consistently produced superior therapeutic outcomes compared with desmopressin monotherapy, with no substantial increase in adverse effects (15). Unlike randomized controlled trials conducted under highly controlled conditions, the present study reflects routine clinical practice in a tertiary-care pediatric urology center, thereby providing complementary real-world evidence supporting the effectiveness and safety of combination therapy.

The biological plausibility of these findings is supported by the current understanding of PMNE pathophysiology. The International Children's Continence Society (ICCS) recognizes PMNE as a multifactorial disorder resulting from nocturnal polyuria, reduced functional bladder capacity, detrusor overactivity, impaired arousal from sleep, and delayed maturation of bladder control mechanisms (11). Likewise, the European Association of Urology recommends that treatment should be individualized according to the predominant underlying pathophysiological mechanism rather than adopting a uniform therapeutic strategy (17). Desmopressin effectively reduces nocturnal urine production through its antidiuretic action but does not address impaired bladder storage function (11). In contrast, solifenacin selectively blocks muscarinic M3 receptors, suppressing involuntary detrusor contractions and increasing functional bladder capacity. The complementary mechanisms of these two agents provide a logical explanation for the greater reductions in wet nights, higher complete response rates, and earlier symptom improvement observed in the combination therapy group (11,14,17).

The findings of the present study have important implications for contemporary clinical practice. Current international guidelines advocate individualized management of PMNE based on the predominant underlying pathophysiological mechanism rather than a uniform treatment approach for all patients (11,17). The superior clinical outcomes observed with combined solifenacin and desmopressin therapy suggest that children with persistent nocturnal enuresis, particularly those with an inadequate response to desmopressin monotherapy or reduced functional bladder capacity, may benefit from combination treatment. Earlier symptom control may reduce the psychological burden associated with persistent bedwetting, improve medication adherence, and enhance parental confidence in treatment. These findings are particularly relevant for pediatric urologists, pediatric nephrologists, and general pediatricians. In low- and middle-income countries such as Pakistan, where access to specialized behavioral interventions, including enuresis alarm therapy, may be limited, an effective pharmacological strategy capable of producing rapid and sustained symptom improvement may represent a practical alternative (11,17).

Several strengths enhance the validity of the present study. The prospective cohort design enabled systematic longitudinal assessment of treatment outcomes while minimizing recall bias. Diagnosis was established according to standardized ICCS criteria, ensuring consistency with international recommendations and facilitating comparison with previous studies (11). Both treatment groups were managed within the same tertiary-care center using standardized treatment protocols and follow-up schedules, thereby reducing variation in clinical practice. Furthermore, treatment effectiveness was assessed using multiple clinically relevant outcomes, including reduction in wet nights, ICCS response categories, medication adherence, parent satisfaction, and adverse events, providing a comprehensive evaluation of both efficacy and tolerability. The high follow-up completion rate further strengthened the internal validity of the study.

Nevertheless, several limitations should be acknowledged. First, the single-center design may limit the generalizability of the findings to other populations and healthcare settings. Second, although the sample size was adequate to detect clinically meaningful differences between treatment groups, larger studies are needed to improve the precision of effect estimates. Third, treatment allocation was based on routine clinical practice rather than randomization, introducing the possibility of selection bias and residual confounding despite multivariable adjustment. In addition, the 12-week follow-up period did not permit evaluation of long-term treatment durability or relapse after treatment discontinuation, which remains an important consideration in PMNE management (11). Finally, objective assessments of functional bladder capacity, nocturnal urine production, sleep quality, and validated quality-of-life measures were not incorporated, limiting further exploration of the mechanisms underlying treatment response.

Future research should focus on adequately powered multicenter randomized controlled trials comparing combination therapy with desmopressin monotherapy across diverse populations. Longer follow-up is needed to evaluate sustained treatment success, relapse rates, and long-term medication adherence (13,15). Future investigations should also incorporate validated patient-reported outcome measures, standardized bladder diaries, and health-related quality-of-life assessments to provide a more comprehensive evaluation of treatment effectiveness. In addition, cost-effectiveness analyses are warranted, particularly in resource-limited settings, to determine whether the improved clinical outcomes associated with combination therapy justify additional treatment costs. Research exploring clinical predictors and biomarkers of treatment response may also facilitate more personalized therapeutic strategies for children with PMNE (11,17).

In conclusion, this prospective cohort study demonstrated that combined solifenacin and desmopressin therapy was associated with superior clinical effectiveness compared with desmopressin monotherapy in children with PMNE. Combination therapy resulted in greater reductions in nocturnal enuretic episodes, higher treatment response rates, earlier clinical improvement, better medication adherence, and greater parent satisfaction while maintaining an acceptable safety profile. Although confirmation through larger multicenter randomized trials with longer follow-up is required (13,15), the present findings support consideration of combination therapy as an effective treatment option for appropriately selected children with PMNE, particularly those who fail to achieve satisfactory symptom control with desmopressin monotherapy (11,17).

CONCLUSION

In this prospective cohort study, combined solifenacin and desmopressin therapy was associated with superior clinical outcomes compared with desmopressin monotherapy in children with primary monosymptomatic nocturnal enuresis. Children receiving combination therapy experienced greater reductions in the frequency of nocturnal enuretic episodes, higher treatment response rates, earlier clinical improvement, better medication adherence, and greater parent satisfaction, while maintaining an acceptable safety profile with no significant increase in adverse events. These findings support the concept that simultaneously targeting nocturnal polyuria and impaired bladder storage capacity may provide greater therapeutic benefit than addressing nocturnal polyuria alone. Although the observational design precludes causal inference and the findings should be interpreted in light of the study limitations, the results suggest that combined solifenacin and desmopressin therapy may be considered a valuable treatment option for appropriately selected children with primary monosymptomatic nocturnal enuresis, particularly those with an inadequate response to desmopressin monotherapy. Further large-scale, multicenter randomized controlled trials with longer follow-up are warranted to confirm these findings, evaluate long-term efficacy and relapse rates, and further define the role of combination therapy in the routine management of primary monosymptomatic nocturnal enuresis.

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