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DIFFERENTIATED APPROACH TO THE DIAGNOSIS AND TREATMENT OF MONOSYMPTOMATIC NOCTURNAL ENURESIS IN CHILDREN

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ABSTRACT

Background: Monosymptomatic nocturnal enuresis (MNE) is a common developmental disorder characterized by intermittent urinary incontinence during sleep in children aged five years or older in the absence of clinically relevant daytime lower urinary tract symptoms. Although spontaneous remission occurs in a proportion of affected children, persistent enuresis may adversely influence emotional well-being, self-esteem, family functioning, and social participation. The heterogeneous pathophysiology of MNE explains why a uniform therapeutic strategy frequently produces suboptimal results. **Objective:** To evaluate contemporary approaches to the diagnosis and management of monosymptomatic nocturnal enuresis and to formulate a differentiated diagnostic and therapeutic algorithm based on the predominant pathophysiological phenotype, clinical characteristics, and treatment response. **Materials and Methods:** A structured narrative review of contemporary scientific literature and international recommendations concerning MNE in children was performed. Particular attention was paid to publications addressing nocturnal polyuria, functional bladder capacity, arousal mechanisms, voiding diaries, enuresis alarms, desmopressin therapy, combination treatment, treatment resistance, and clinically relevant comorbidities. Current recommendations of the International Children's Continence Society (ICCS), European Association of Urology/European Society for Paediatric Urology (EAU/ESPU), and recent evidence-based reviews were incorporated. **Results:** Current evidence supports differentiation of children with MNE according to the predominant mechanism: nocturnal polyuria, reduced nocturnal or functional bladder capacity, impaired arousal from sleep, or a mixed phenotype. Desmopressin is particularly appropriate when nocturnal polyuria predominates, whereas alarm therapy provides an etiologically rational option in children with adequate family motivation and may offer superior sustained response after treatment discontinuation. Children with mixed phenotypes or incomplete response to monotherapy may benefit from combination therapy. Constipation, sleep-disordered breathing, psychological difficulties, poor adherence, and previously unrecognized daytime lower urinary tract symptoms should be actively investigated in treatment-resistant cases. **Conclusion:** MNE should not be regarded as a homogeneous clinical condition. Phenotype-oriented assessment based on careful history, voiding diaries, nocturnal urine production, functional bladder capacity, comorbidity screening, and previous therapeutic response can facilitate individualized treatment selection. A differentiated strategy may improve therapeutic efficacy, reduce unnecessary pharmacological exposure, and enhance long-term adherence.

KEYWORDS: monosymptomatic nocturnal enuresis; children; nocturnal polyuria; desmopressin; enuresis alarm; bladder capacity; individualized treatment; paediatric urology.

INTRODUCTION

Nocturnal enuresis remains one of the most prevalent elimination disorders encountered in paediatric practice. According to contemporary terminology, enuresis refers to intermittent urinary incontinence occurring during sleep in a child who has reached an age at which nocturnal bladder control would normally be expected. Monosymptomatic nocturnal enuresis is distinguished from non-monosymptomatic enuresis by the absence of clinically significant daytime lower urinary tract symptoms.[1,2]

The prevalence of enuresis decreases progressively with age as a result of spontaneous maturation. Nevertheless, a clinically relevant proportion of children continue to experience nocturnal wetting during school age and adolescence. Persistence of the disorder may substantially affect psychosocial functioning. Children may avoid sleepovers, school excursions, camps, and other activities involving overnight stays. Feelings of embarrassment and reduced self-esteem may develop, while parents may experience frustration, sleep disruption, and increased household burden.[3,4]

MNE was historically interpreted mainly as delayed maturation of nocturnal bladder control. Current evidence, however, indicates a considerably more complex pathophysiological model. Three mechanisms are particularly important: insufficient nocturnal secretion or action of arginine vasopressin resulting in excessive nocturnal urine production; reduced functional or nocturnal bladder capacity; and impaired arousal in response to bladder filling during sleep.[1,5] These mechanisms can occur independently or coexist in the same child.

Consequently, two children with apparently identical frequencies of bedwetting may have fundamentally different physiological disturbances. One child may produce an abnormally large volume of urine during the night despite relatively normal bladder storage capacity, whereas another may have normal nocturnal urine production but insufficient bladder capacity to maintain continence until morning. In a third child, both abnormalities may coexist.

This heterogeneity has direct therapeutic implications. Desmopressin reduces nocturnal urine production and is therefore particularly logical in patients with nocturnal polyuria. Enuresis alarms, by contrast, aim to modify the relationship between bladder filling and arousal and may provide more durable improvement in appropriately selected and motivated families.[1,6] Failure to recognize the dominant mechanism may therefore contribute to treatment failure.

The purpose of the present review was to systematize current evidence regarding the diagnosis and management of MNE in children and to propose a differentiated clinical approach in which diagnostic findings guide the selection and sequencing of treatment.

MATERIALS AND METHODS

The present study was designed as a structured narrative review focused on contemporary diagnostic and therapeutic approaches to monosymptomatic nocturnal enuresis in paediatric patients.

Relevant publications were identified through searches of PubMed/MEDLINE and major international guideline resources. Priority was given to publications mainly from 2020–2026, while earlier landmark consensus and standardization documents were included when necessary to define terminology or fundamental diagnostic principles.

Search concepts included combinations of the following terms: *monosymptomatic nocturnal enuresis*, *nocturnal enuresis*, *children*, *nocturnal polyuria*, *functional bladder capacity*, *maximum voided volume*, *desmopressin*, *enuresis alarm*, *voiding diary*, *treatment-resistant enuresis*, *constipation*, and *sleep-disordered breathing*.

Guidelines, consensus statements, systematic reviews, meta-analyses, randomized or controlled clinical studies, and clinically relevant observational studies were considered. Particular attention was given to the updated ICCS recommendations and EAU/ESPU guidance.[1,2]

The analysed evidence was organized into five domains

1. diagnostic confirmation of monosymptomatic enuresis;
2. identification of the predominant pathophysiological phenotype;
3. selection of first-line therapy;
4. assessment of treatment response and reasons for treatment failure;
5. management of refractory or recurrent MNE.

The differentiated approach was constructed on the assumption that therapeutic selection should reflect the physiological abnormality most likely to maintain nocturnal wetting rather than bedwetting frequency alone.

RESULTS AND DISCUSSION

1. Diagnostic Confirmation of Monosymptomatic Nocturnal Enuresis

The first and most important diagnostic step is to determine whether the child genuinely has monosymptomatic disease. MNE should be differentiated from conditions associated with daytime urgency, increased or decreased voiding frequency, daytime incontinence, holding manoeuvres, interrupted voiding, straining, weak urinary stream, or a sensation of incomplete emptying.[1,2]

The distinction is clinically important because children with non-monosymptomatic enuresis may have underlying lower urinary tract dysfunction requiring a different diagnostic and therapeutic strategy.

History taking should establish the frequency and duration of nocturnal wetting, previous periods of dryness, timing and approximate volume of nocturnal episodes, daytime voiding behaviour, bowel habits, fluid intake, sleep characteristics, snoring, medication use, developmental history, and family history of enuresis.[1,3]

Primary MNE is generally characterized by the absence of a prolonged previous period of nocturnal continence.

Secondary enuresis refers to recurrence after a substantial period of dryness and warrants particular attention to potential psychological, metabolic, neurological, urinary, and sleep-related precipitating factors.

Physical examination is usually normal in uncomplicated MNE but remains important for excluding clinically relevant abnormalities. Growth parameters, blood pressure when appropriate, abdominal examination for faecal masses or bladder distension, inspection of the lumbosacral region, external genital examination when indicated, and a basic neurological assessment may identify features requiring additional investigation.[2,3]

Routine extensive laboratory or imaging investigations are generally unnecessary in a child with a typical history of primary MNE and a normal physical examination. Urinalysis may be appropriate when diabetes mellitus, urinary tract infection, renal disease, or another urinary abnormality is suspected.[3]

Thus, the principle of diagnostic proportionality should be followed: uncomplicated MNE requires focused assessment rather than indiscriminate testing, while atypical symptoms should prompt targeted investigations.

2. The Role of the Voiding Diary in a Differentiated Approach

One of the most clinically valuable tools for phenotyping MNE is the bladder or voiding diary. A properly completed diary provides objective information that cannot reliably be obtained from retrospective parental reporting.

Daytime recordings can document voiding frequency and individual voided volumes, while overnight measurements can estimate nocturnal urine production. Maximum voided volume provides an approximate measure of functional bladder capacity and can be interpreted relative to age-appropriate expected bladder capacity.[1,5]

The diary can therefore distinguish two clinically important patterns.

Phenotype A – predominant nocturnal polyuria.

The child produces an excessive quantity of urine during the night while functional bladder capacity is relatively preserved.

Phenotype B – reduced functional bladder capacity.

Nocturnal urine production may be within the expected range, but the bladder cannot reliably store the generated volume throughout the night.

A third group demonstrates both abnormalities and can be considered a mixed phenotype.

This classification is clinically meaningful because it connects diagnosis directly with therapeutic selection rather than merely assigning a descriptive diagnosis of "bedwetting."

3. Nocturnal Polyuria and Desmopressin-Responsive MNE

In healthy children, nocturnal vasopressin activity contributes to reduced urine production during sleep. In a subgroup of children with MNE, this physiological nocturnal reduction is insufficient, resulting in nocturnal urine production that exceeds functional bladder storage capacity.[1,5]

For these patients, desmopressin represents a rational first-line pharmacological intervention. Desmopressin is a synthetic analogue of vasopressin with pronounced antidiuretic activity. By reducing nocturnal urine formation, it decreases the probability that bladder capacity will be exceeded during sleep.[1,7]

Desmopressin can produce rapid clinical improvement and is particularly useful when immediate dryness is desired, including during school trips, camps, holidays, and sleepovers.[3]

Recent systematic evidence confirms that desmopressin can increase the number of dry nights during active treatment compared with placebo, although certainty for some outcomes remains limited.[7]

The principal limitation is recurrence after treatment withdrawal. Desmopressin controls the physiological imbalance while the medication is active but does not necessarily induce permanent maturation of nocturnal bladder control. Therefore, therapeutic success during treatment and permanent cure after withdrawal should be regarded as distinct outcomes.

Safety is also dependent on appropriate administration. Families must receive clear instructions regarding evening fluid restriction because excessive fluid intake combined with the antidiuretic effect of desmopressin increases the risk of water retention and hyponatraemia.[1,3]

A differentiated strategy therefore identifies desmopressin as particularly suitable for children with.

- documented or strongly suspected nocturnal polyuria;
- relatively preserved functional bladder capacity;
- a need for rapid symptom control;
- sufficient ability to follow fluid-restriction instructions;
- preference for pharmacological rather than alarm-based therapy.

4. Reduced Functional Bladder Capacity and Alarm Therapy

Another important MNE phenotype is characterized by insufficient functional bladder capacity relative to overnight urine production.

Alarm therapy is one of the principal first-line interventions recommended for MNE.[1–3, 12, 13] The

device detects moisture at the beginning of urination and activates an acoustic or vibratory signal. Initially, parents may need to awaken the child when the alarm is triggered. Repeated association between bladder filling, voiding, and awakening is intended to modify the arousal response and ultimately promote independent awakening or nocturnal bladder control.

Alarm therapy differs fundamentally from desmopressin because its objective is not simply to suppress wet nights during active treatment. Instead, it promotes behavioural and neurophysiological adaptation. This may explain why sustained dryness following treatment withdrawal can be more favourable with alarm therapy than with pharmacological suppression alone.[7,8]

The main limitation is adherence. Alarm therapy requires considerable commitment from both the child and family and typically needs to be continued consistently for several weeks. Families should therefore be informed that immediate success is not expected.

Alarm therapy is especially appropriate for children and families who are strongly motivated and able to adhere consistently to the treatment protocol. This therapeutic approach may be particularly beneficial when nocturnal polyuria is absent or does not represent the predominant pathophysiological mechanism, especially in children with relatively reduced functional bladder capacity. Successful implementation requires active family participation and a willingness to respond consistently to the alarm during the treatment period. Alarm therapy is therefore particularly suitable when achieving sustained long-term nocturnal continence is considered a greater priority than obtaining rapid short-term dryness.

In contrast, families experiencing substantial sleep disruption, psychosocial stress, or poor adherence may find alarm therapy difficult to sustain.

5. Mixed Phenotype and Combination Treatment

Not all patients can be classified as having isolated nocturnal polyuria or isolated reduced bladder capacity. A substantial proportion demonstrate overlapping pathophysiological abnormalities.

For example, a child may produce excessive nocturnal urine and simultaneously have a relatively low functional bladder capacity. In such circumstances, correction of only one mechanism may be insufficient.

This observation provides the physiological rationale for combined desmopressin and alarm therapy in selected children.[1,2] Desmopressin reduces the nocturnal urinary load, whereas the alarm simultaneously addresses the arousal/continence response.

Combination therapy may therefore be considered in children in whom nocturnal polyuria coexists with reduced functional bladder capacity, particularly when a single first-line treatment has resulted in only partial improvement. This approach may also be beneficial when a rapid reduction in the frequency of wet nights is desired while the longer-term conditioning effects of alarm therapy are being established. Successful implementation of combined treatment, however, depends on the ability of the child and family to maintain adequate and consistent adherence to both therapeutic interventions.

However, combination therapy should not automatically replace carefully selected monotherapy. Treatment complexity may reduce adherence, and unnecessary medication should be avoided when a single mechanism clearly predominates.

6. Impaired Arousal and Sleep-Related Factors

Difficulty awakening from sleep has long been recognized as a characteristic feature of many children with enuresis. The problem should not be simplistically interpreted as “deep sleep.” Rather, the relevant abnormality appears to involve inadequate integration of bladder afferent signals with central arousal mechanisms.[1,5]

Sleep history should therefore form part of routine assessment.

Particular attention should be given to snoring, mouth breathing, witnessed apnoea, restless sleep, daytime sleepiness, morning headache, and adenotonsillar hypertrophy. Sleep-disordered breathing and obstructive sleep apnoea may coexist with enuresis and should be addressed when clinically suspected.[3]

Recognition of sleep pathology is particularly important in children apparently resistant to conventional enuresis therapy because treatment of an underlying sleep disorder may contribute to improvement of nocturnal continence.

7. Constipation as a Modifier of Treatment Response

Constipation is a frequent and clinically relevant comorbidity in children presenting with urinary disorders. Rectal distension may influence bladder storage and emptying through anatomical, neurological, and functional interactions.

The possibility of constipation should therefore be actively investigated rather than relying solely on the child's or parent's statement that bowel movements are “normal.” Stool frequency, painful defecation, hard stools, faecal retention, large-diameter stools, and faecal incontinence should be assessed systematically.[3]

Unrecognized constipation may contribute to apparent treatment resistance. Accordingly, bowel dysfunction should be adequately treated when present before the child is classified as having refractory MNE.

8. Behavioural Measures and Standard Urotherapy

Basic behavioural recommendations remain an essential component of management irrespective of the selected active treatment.[1–3,12–15]

Children should be encouraged to maintain adequate fluid intake during the earlier part of the day rather than chronically restricting fluids. Excessive drinking close to bedtime should be avoided, particularly during desmopressin treatment. Regular daytime voiding and voiding immediately before sleep are advisable.[1–3]

Caffeinated beverages in the evening should be minimized. Families should also avoid punitive measures.

Reward systems, when used, should focus on behaviours under the child's control—for example, completing a diary, voiding before bed, correctly using the alarm, or following the fluid schedule—rather than rewarding a dry night itself.

This distinction is psychologically important because involuntary nocturnal urination is not an intentional behaviour.

9. Treatment-Resistant Monosymptomatic Enuresis

The term “treatment resistance” should be applied cautiously. Before concluding that first-line therapy has failed, clinicians should reconsider the original diagnosis.

Before treatment resistance is established, several clinically relevant factors should be carefully reassessed. It is essential to confirm that the condition is truly monosymptomatic and that the prescribed treatment has been implemented correctly and consistently. Nocturnal urine production and functional bladder capacity should be objectively evaluated whenever possible, while constipation should be adequately excluded or treated. Particular attention should also be paid to symptoms suggestive of sleep-disordered breathing. In children receiving desmopressin, the timing of administration, adherence to recommended fluid restriction, and overall compliance should be reviewed. Similarly, the duration and consistency of alarm therapy, including active parental participation, should be assessed. Finally, psychological, behavioural, and family-related factors that may interfere with treatment adherence or contribute to an inadequate therapeutic response should be taken into consideration.

This reassessment is crucial because apparent pharmacological resistance may actually represent inappropriate phenotype selection or poor treatment implementation.

Recent clinical studies continue to demonstrate phenotypic differences between MNE and non-monosymptomatic forms and emphasize the importance of identifying clinical characteristics associated with treatment response.[9]

For persistent refractory cases, referral to a paediatric urologist, paediatric nephrologist, or specialized continence service should be considered. Additional evaluation may then be individualized according to clinical findings.

10. Proposed Differentiated Clinical Algorithm

Current international practice demonstrates considerable variability in the diagnostic evaluation and therapeutic management of nocturnal enuresis, further emphasizing the need for standardized and phenotype-oriented clinical decision-making.[10,11]

Stage 1: Confirm the diagnosis.

Establish age ≥5 years, nocturnal urinary incontinence, and absence of clinically relevant daytime lower urinary tract symptoms.

Stage 2: Identify complicating factors.

Screen for constipation, urinary infection when clinically suspected, diabetes-related symptoms, neurological abnormalities, developmental difficulties, psychosocial stressors, and sleep-disordered breathing.

Stage 3: Characterize the phenotype.

Use a voiding diary and nocturnal urine measurements when feasible to estimate functional bladder capacity and octurnal urine production.

Stage 4: Select treatment according to phenotype

Treatment should be selected according to the predominant clinical and pathophysiological phenotype. In children with predominant nocturnal polyuria, desmopressin is generally considered the most appropriate first-line pharmacological option. When reduced functional bladder capacity is the principal finding and both the child and family are sufficiently motivated, enuresis alarm therapy may be preferred. In patients presenting with a mixed phenotype, particularly when nocturnal polyuria coexists with reduced functional bladder capacity, combined treatment with an enuresis alarm and desmopressin may be considered. If clinically significant constipation is identified, appropriate management of bowel dysfunction should be incorporated into the therapeutic strategy. Children with symptoms suggestive of sleep-disordered breathing should undergo appropriate sleep-related and/or otorhinolaryngological assessment. Furthermore, the identification of previously unrecognized daytime lower urinary tract symptoms (LUTS) requires reconsideration of the initial diagnosis, as these patients should be reclassified and managed according to the principles applicable to non-monosymptomatic enuresis.

Stage 5: Evaluate response and adherence.
Treatment response should be assessed using objective changes in the number of wet nights rather than subjective impressions alone.

Stage 6: Reassess non-responders.
Before escalating therapy, reconsider phenotype, adherence, hidden comorbidities, and the original classification.
This model transforms the management of MNE from a trial-and-error approach into a mechanism-oriented clinical strategy.

CONCLUSION

Monosymptomatic nocturnal enuresis is a heterogeneous condition rather than a single uniform disorder. Although affected children share the clinical manifestation of involuntary nocturnal urination, the underlying physiological mechanisms may differ substantially.

The contemporary diagnostic approach should therefore extend beyond confirmation of bedwetting and attempt to identify the dominant pathophysiological phenotype. Assessment of nocturnal urine production, functional bladder capacity, voiding behaviour, arousal characteristics, bowel function, sleep-related symptoms, and treatment adherence provides the foundation for individualized management.

Children with predominant nocturnal polyuria are particularly suitable candidates for desmopressin therapy, whereas alarm treatment represents an important first-line option when a durable response is desired and the child and family can maintain adequate adherence. Mixed phenotypes may require combination treatment. Persistent treatment failure should prompt reassessment for hidden daytime lower urinary tract symptoms, constipation, sleep disorders, inadequate adherence, or incorrect initial phenotyping.

Thus, a differentiated approach to MNE provides a rational bridge between pathophysiology and clinical decision-making. Individualized treatment selection may improve response rates, reduce unnecessary therapeutic escalation, increase family satisfaction, and potentially improve long-term outcomes.

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