A comprehensive review of adult enuresis

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Abstract

Nocturnal enuresis (NE) is a combined symptom of nocturia and urinary incontinence. In this review, we aim to summarize the current literature on NE in terms of its definition, diagnosis, and management. Recommended diagnostic evaluation of NE includes a focused history and physical examination, urinalysis, and when indicated, ultrasound examination, flow rate, urine volume chart, urodynamics, and cystoscopy. Therapeutic options include lifestyle modification and medications (i.e., desmopressin and anticholinergics).

Introduction

Gaining the ability to hold urine through the night is one of the developmental neuro-motor skills of a functioning bladder.[1] Nocturnal enuresis (NE) is considered a physiological finding in children less than five years of age, but is considered abnormal in adults.[1] The International Continence Society (ICS) definition for NE is any unintended voiding during night-time sleep.[2] This definition lacks duration and frequency. In the current literature, NE has been defined as one episode of nocturnal incontinence per six months or more[3] at least one time per week[4] or one per month.[5]

Regardless of underlying pathology, patients with NE experience discordance between bladder compliance, sphincter efficiency, and urine production overnight and often lack of awareness of a sensation to void. Many adults afflicted with NE are affected psychologically. The aim of this article is to further understand the definition, diagnosis, and management of NE.

Classification

There are two types of adult enuresis classifications (Table 1).[1,2,6-8] NE can be classified chronologically (i.e., primary vs. secondary) or by symptomology (i.e., associated with lower urinary tract symptons[LUTS] or not).

Epidemiology

Prevalence

In adults, the prevalence of NE has been reported as 2–3%.[9-11] In females with voiding dysfunction and patients in nursing homes, the prevalence is higher, 23%[12] and 39%,[13] respectively. In special populations, such as patients with Down syndrome, the prevalence is 17.2%.[14-16]

Clinical course

The most common form of NE is persistent (PPNE; never dry for more than six months) followed by recurrent (PRNE; dry for more than six months before adulthood recurrence) then secondary (SNE).[1] In general, NE is associated with a higher number of episodes overall and is less likely to resolve if diagnosed as an adult compared to childhood diagnosis.[9-11] It is unclear if progression of NE into adulthood is dependent on the severity of childhood presentation or if adult NE arises de novo due to different physiological mechanisms.

Risk factors

Neurologic disease, psychiatric medications, and sleep apnea syndrome are risk factors for NE.[6,12,17,18] Smoking,[12] obesity,[17] decreased physical activity, and hypertension[18] are risk factors specifically identified in women. In men, benign prostatic hyperplasia and outlet obstruction are significantly associated with higher prevalence of secondary NE.[6] Interestingly, NE in childhood does not increase enuresis risk in adulthood.[19]

Psychosocial consideration

There is a significantly higher incidence of anxiety, depression, chronic fatigue, and lower self-esteem in adults with

Table 1. Adult enuresis classification

	Primary NE (PNE) (positive history in childhood)		Secondary nocturnal enuresis (SNE) (no evidence of NE in childhood)
Chronologic classification	Persistent (PPNE) (never dry for more than six months)	Recurrent (PRNE) (dry for more than six months before adulthood recurrence)	
Symptomatic classification	Monosymptomatic NE (the only symptom is NE)	Polysymptomatic NE (NE with other LUTS)	

LUTS: lower urinary tract symptoms; NE: nocturnal enuresis.

NE as compared to the general population.[6,15] Significant impact on psychosocial well-being has been noted in Western countries,[2] Middle East countries,[5] and Southeast countries.[9] The relationship between psychological conditions and NE is complex. It is not fully established if these conditions result from NE or exacerbate NE.

Physiology

Pathophysiological mechanisms of nocturnal continence are outlined in Fig. 1. Briefly, through the night, a normal adult bladder can reach to volumes of 300–400 cc without needing to void due to bladder compliance and a closed outlet. Glomerular filtration typically decreases by 30% during the night and water reabsorption increases through the action of arginine-vasopressin. Thus, urine production decreases significantly.[20] When one experiences increased volume of bladder to more than 300–400 cc, a central mechanism awakens the person before unintentional voiding occurs.[12]

Etiology

Etiologies of adult enuresis are classified as detrusor disorders, outlet issues, nocturnal diuresis, and increased sleep arousal threshold (Table 2).

Multifactorial NE is common and can complicate clinical diagnosis. For example, diuretic use can increase nocturnal urine output and concurrent sedative use can increase sleep arousal threshold. Similarly, psychiatric medications, such as olanzapine, clozapine, quetiapine,[2,6] and risperidone[21-23] can cause enuresis by several mechanisms, including increased arousal threshold, increased urine production, and decreased sphincter tone.[6] Injured urinary sphincter during radical pelvic surgeries and concomitant polyuria caused by their continent pouch,[6] as well as abnormal bladder and sphincter function and nocturnal polyuria in spinal cord injury[2,6] are other examples of multifactorial NE.

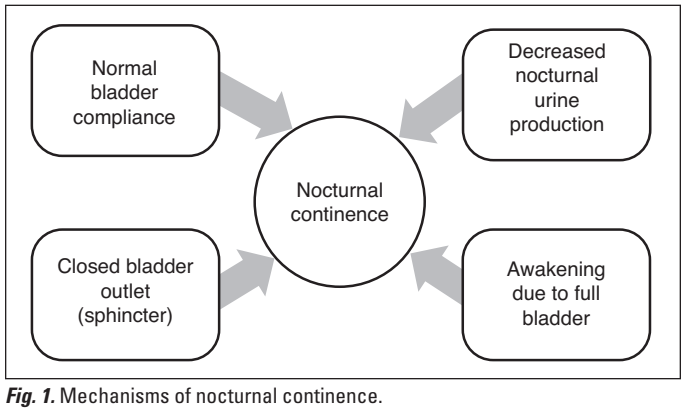

Fig. 1. Mechanisms of nocturnal continence.

Table 2. Etiologies of adult enuresis

Etiology	Subtype	Disease
Detrusor disorder	Detrusor over activity[12]	Neurogenic bladder Idiopathic detrusor overactivity[1,6]
	Detrusor hypo-compliance[12]	Scarred bladder Chronic infection[1,6]
Outlet issues	Outlet obstruction[12]	Neurogenic bladder, BPH, urethral stricture
	Outlet incompetence[12]	Neurogenic bladder Iatrogenic sphincter apparatus injury Antipsychotics
Nocturnal diuresis	Renal disorder[12,20]	Chronic renal disorder Renal medullary concentration disorder (hemolytic disorders)[4] Diuretics Nephrogenic diabetes insipidus
	Central disorder	Obstructive sleep apnea syndrome*[2,6] Chronic liver disease[12,20] Elderly[12] Central diabetes insipidus
Sleep arousal threshold disorder[18]	Sleep disorder	Primary sleep disorder Elderly Alcohol, sedatives, antipsychotics
	Reduced bladder sensation	Diabetes neuropathy

*Obstructive sleep apnea (OSA) syndrome increases secretion of atrio-natrioretic peptide during sleep and this results in nocturnal polyuria.[2,6] BPH: benign prostatic hyperplasia.

Assessment

Initial presentation of NE is typically managed by primary care physicians. Further workup by a urologist is advised for adults presenting with complex or prolonged bothersome NE.[6] Suggested urological evaluation is detailed in Table 3.

Details of assessment in adult enuresis are depicted in Fig. 2.

Management

Psychosocial stress and bothersome NE episodes typically prompt treatment. First-line treatment options include lifestyle modifications, behavioral therapy, and medical therapy. Other interventions, such as surgical intervention, neuromodulation, and botulinum toxin injection to bladder

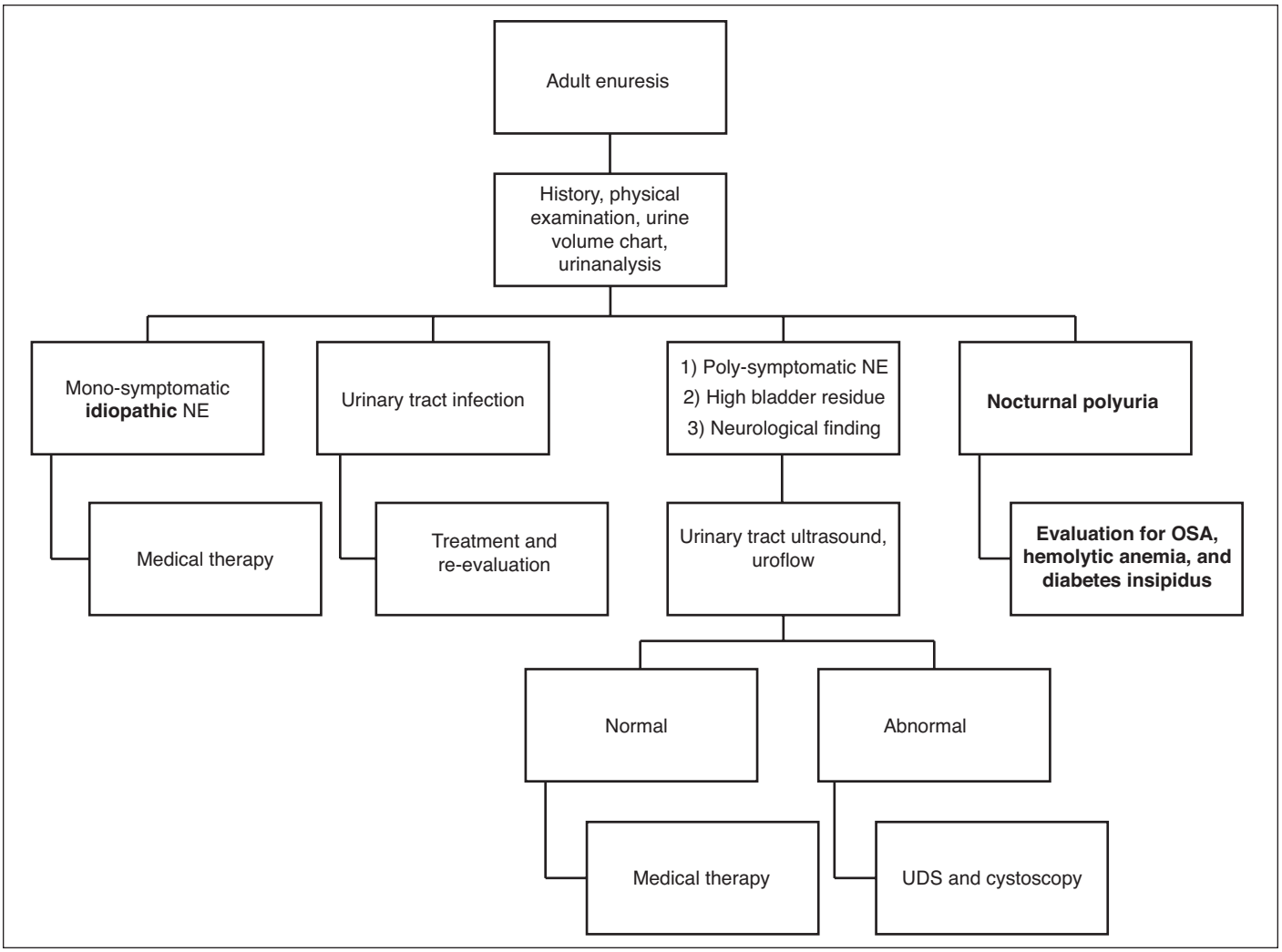

Fig.2. Assessment in adult enuresis. NE: nocturnal enuresis; OSA: obstructive sleep apnea; UDS: urodynamic study.

Table 3. Adult enuresis assessment

Type of assessments	Indication	Assessment	Details and findings
Essential assessments	In all patients	History	Lower urinary tract symptoms, past medical and surgical history and medications[1]
		Physical examination	Focused neurological examination, digital rectal examination and bulbocavernous reflex[1]
		Urinalysis	To rule out urinary tract infection[1]
Optional assessments	In patients with inadequate results with essential assessments	Urine flow rate (uroflow)	To screen silent obstruction or hypocontractile bladder[2]
		Frequency volume chart	To reveal daytime hidden symptoms, nocturnal polyuria, and maximum functional bladder capacity[6,24]
		Ultrasound of upper and lower urinary tract and post voiding residue	To evaluate upper tract damages and lower tract efficiency in urine elimination[2]
		Urodynamic study	Findings in SNE detrusor over activity, hypo-compliant bladder and silent bladder outlet obstruction[2] Urodynamic studies have less value in PNE[6,11]
		Cystoscopy	In cases with bladder outlet obstruction, posterior urethral valve and urethral stricture have been the most common findings (6.7%)[11]

PNE: primary nocturnal enuresis; SNE: secondary nocturnal enuresis.

have been used in some patients but are typically reserved as second-line modalities.

Lifestyle modification

Caffeine and sedative avoidance are suggested, as they alter sleep cycle function. Alcohol avoidance is suggested due to its effect as a diuretic. Weight reduction can be advantageous through its effects of improving sleep apnea syndrome. Regular physical activity is another potential ways to decrease episodes of NE.[13,18]

Behavioral therapy

Although there is data to support timed voiding every two hours and alarm systems for NE in children[24] there is no data in young adults. Furthermore, timed voiding has a limited role in elderly patients with NE due to decreased adaptive conditioning skills and effect on sleep disturbances.[13,24] Unfortunately, compliance with enuresis alarm systems is low in the adult population, with a high withdrawal rate;[4,6] however, when desmopressin failed to control enuresis, adding an alarm system has been reported to increase the response rate by 33%.[2]

Adapted dry behavioral therapy (ADBT) is a cognitive behavioral and prompted voiding therapy that includes close observation during sleep, waking up frequently during the night (every hour), alarm use, and day-time timed voiding. Although it is effective, high cost and time commitment commonly deter its use.[25]

Despite successful results in children, behavioral therapy is not as effective in adults.[6] In selected adult cases (infrequent bed wetting, normal sonography, and cystometric capacity greater than 300 cc), it may have a contributive role.[25]

Specific treatments

First-line therapy after lifestyle changes and behavioral therapy includes treating identifiable pathologies (Fig. 3). In addition to specific therapy, any psychiatric contributors, such as depression and anxiety, should be addressed as well.[15]

Medical therapy

In patients with NE with no defined etiology, medical therapy is first-line. There are two classes of medications with supportive evidence: desmopressin and anticholinergics.

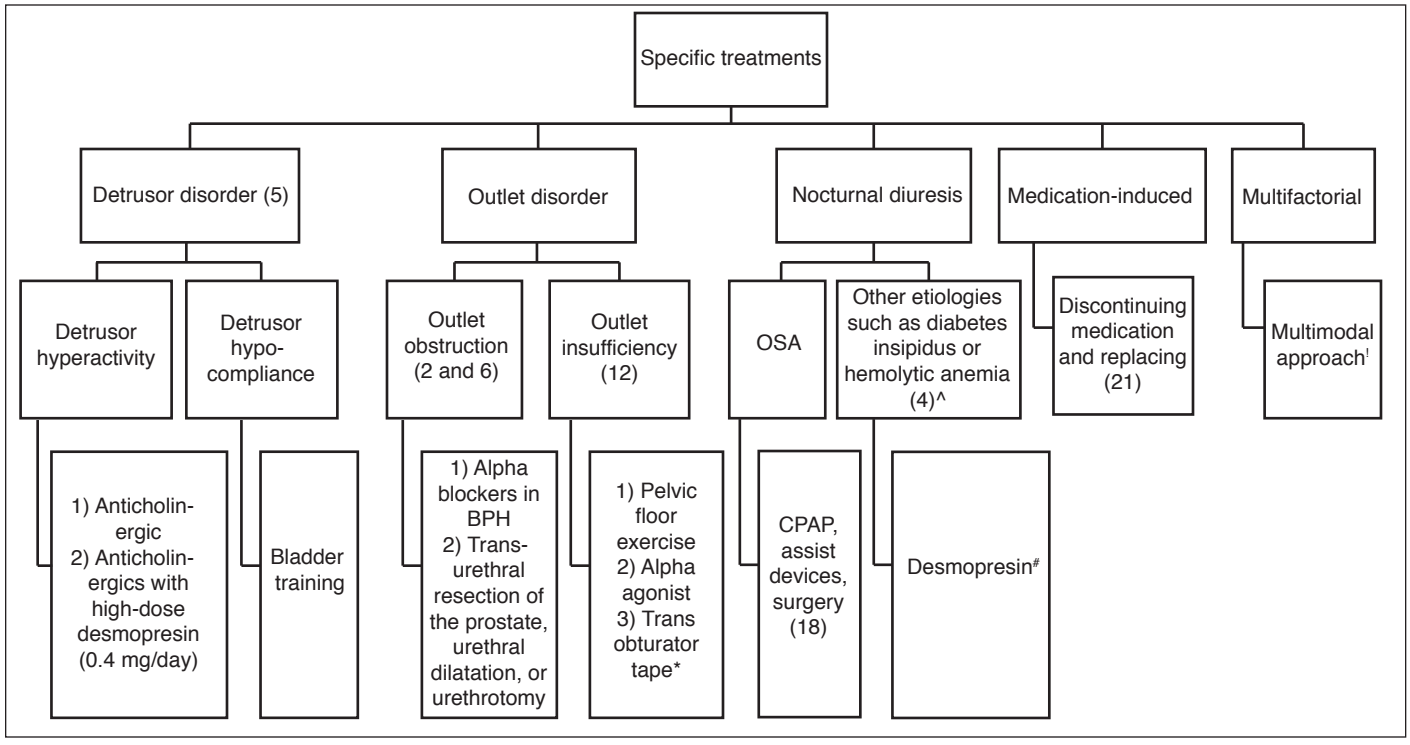

Fig. 3. Specific therapy for adult enuresis. *Possible explanation for decreasing nocturnal enuresis (NE) after mid-urethral sling placement is prevention of urinary leakage to proximal urethra and stress induced overactivity.[12] ^Higher severity of enuresis in hemolytic disorders is associated with increased admission; therefore, efforts to manage chronic disease may help manage and better treat NE. #Although in nocturnal diuresis due to overproduction, desmopressin is treatment of choice, one should be cautioned in patients with kidney and liver disease, water intoxication, and hyponatremia; these should also be individually addressed. !Multifactorial NE is difficult to treat and best controlled by multimodal approaches and addressing all contributing etiologies.[2,6] For example, empirically patients with spinal cord injury and neo-bladder after radical pelvic surgeries are managed by low-dose desmopressin, oxybutynin 5 mg three times a day, and catheterization before sleep.[2] BPH: benign prostatic hyerplasia; OSA: obstructive sleep apnea.

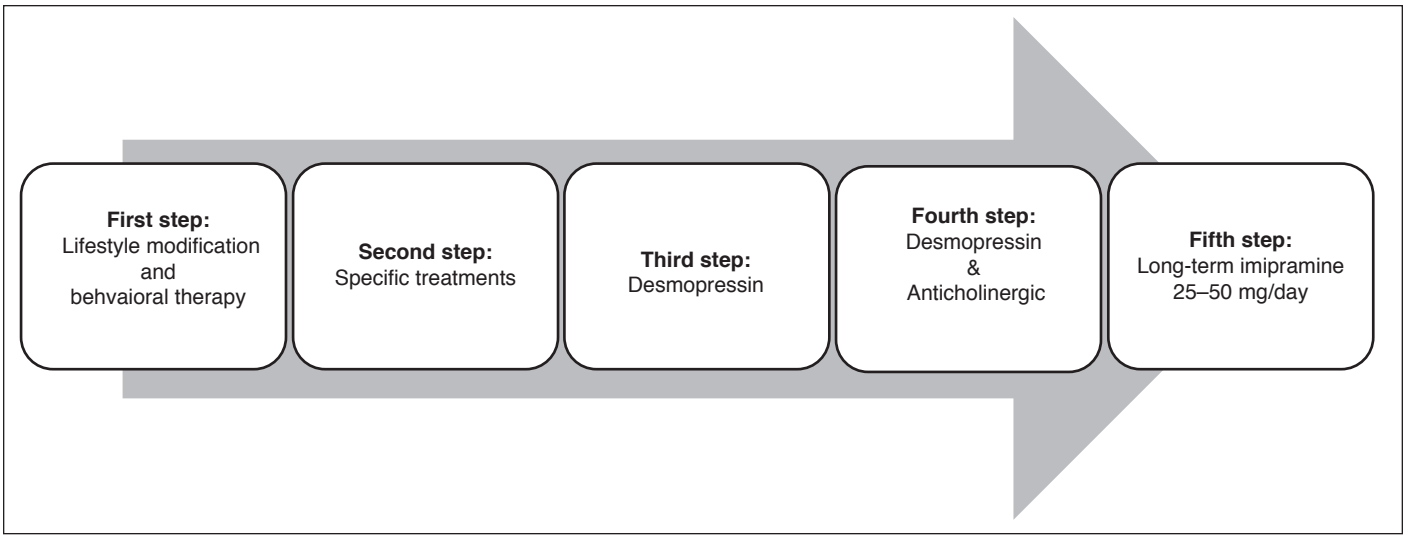

Fig. 4. Treatment steps for idiopathic nocturnal enuresis.

Desmopressin

Desmopressin has been accepted as first-line therapy of idiopathic adult NE.[2] Although some authors advocate to prescribe it only in the nocturnal polyuria variant of enuresis,[3] currently, it is the first treatment in adult NE with or without nocturnal polyuria.[2,5]

Most patients require at least 0.2–0.4 mg of desmopressin per night;[2,6] physicians should start at the low dose and titrate up. Patients with detrusor overactivity often require the higher dose (0.4 mg/day) to show any benefit.[5] Once the suitable dose is found, decreasing or withdrawing drug invariably causes symptom relapse and is, therefore, not recommended.[5] Informing the patient about needing long-term therapy and the likelihood of decreasing the dose, as well as safety of long-term usage of the drug should be highlighted during discussion before starting desmopressin.[3,5,26] Water intoxication and hyponatremia are dangerous and life-threatening complications. Fluid restriction from evening until morning is an efficient method to prevent these adverse effects. These complications are more common in the elderly. It is wise to verify serum sodium levels at short intervals in the first weeks of treatment.[26]

Anticholinergics

In desmopressin non-responders, an anticholinergic medication can be added. In general, there is good evidence for the safety of anticholinergics, with urinary retention being a very rare side effect, especially for the younger population with NE.[5] Imipramine as a peripheral anticholinergic and a drug with possible central effects has been shown to be effective in NE with polyuria. However, there are concerns about its cardiac adverse effects in elderly patients.[6] Watchful monitoring for urinary retention is important in patients using anticholinergics.

Combination therapy is a long-term and safe step in enuresis control. Discontinuation or decreasing dosage of drugs will often lead to symptom recurrence.[5] If desmopressin and an anticholinergic are not effective, imipramine 25–50 mg per day has demonstrated benefit, but is uncommonly prescribed by urologists due to need for ongoing close followup and poor compliance due to sexual side effects.[6]

The flow of treatment steps for idiopathic nocturnal enuresis is outlined in Fig.4.

Other treatments

Minimal data exists to support surgical intervention for mono-symptomatic NE.[12] Neuromodulation (peripheral and sacral) and botulinum toxin injection are capable of decreasing NE in patients with non-mono-symptomatic NE, however, there is no data supporting their use I mono-symptomatic NE.[2]

One randomized clinical study with 14 patients with refractory mono-symptomatic NE and abnormal detrusor function (overactivity and reduced compliance) in each group has reported significant improvement in the posterior tibial nerve stimulation arm in comparison to placebo.[27]

Conclusions

NE is a symptom of urinary tract disorder or systemic disease. It requires a standard evaluation consisting of history and physical exam, urinalysis, and when indicated, urinary ultrasonography, urine flow rate, frequency volume chart, urodynamic study, and cystoscopy. It is recommended that general practitioners refer adults with NE to a urologist for this workup because of its complexity.

There is minimal role for surgical intervention for this disease except in specific populations. However, many patients benefit from long-term desmopressin. Anticholinergics can

add benefit even in the absence of overactive bladder symptoms. The role of neuromodulation, onabotulinumtoxin A, and surgery are undefined in the literature. Behavioral techniques offer low-risk intervention, but their time commitment is considerable and they require a high degree of commitment on behalf of the patient to ensure compliance. Future studies should address these shortfalls in the literature to better manage adult patients with NE.

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This paper has been peer-reviewed.

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