

Review Article

Nocturnal enuresis: etiology, management and the impact on different age groups

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ABSTRACT

Nocturnal enuresis or night time incontinence is a common condition that usually affects children and can be associated with significant psychological effects on the affected child if left untreated. It can be defined as night time wetting of the bed that usually occurs in children that are ≥ 5 years old. In this literature review, the aim was to discuss the etiology and management of nocturnal enuresis and the impact of the condition on the different age groups. Management of the underlying comorbidities, taking care of the overactive bladder and dealing with the potential psychological conditions might be the main key factors to nocturnal enuresis. Many pharmacological and non-pharmacological approaches have been proposed for these patients. However, the success rates of applying behavioral management approaches have been reported to be the highest as compared to other approaches. Early interventions should be applied for children that have multiple risk factors or with parents that once suffered from the condition as genetics were reported in the literature to have a significant role in the development of nocturnal enuresis. Pharmacological therapies have also been reported as effective modalities in resistant cases and desmopressin was reported to achieve a 100% success rate if used with alarm therapy. However, clinicians should care for the potential adverse events when approaching the pharmacological modalities.

Keywords: Nocturnal enuresis, Pediatrics, Management, Epidemiology, Etiology

INTRODUCTION

Nocturnal enuresis or night time incontinence is a common condition that usually affects children and can be associated with significant psychological effects on the

affected child if left untreated. It can be defined as night time wetting of the bed that usually occurs in children that are ≥ 5 years old.¹ A previous report estimated that the prevalence of nocturnal enuresis is 8% as estimated in 9.5 year aged children who suffer from night time

bedwetting ≥ 2 times weekly.² Moreover, previous studies have demonstrated the impact of genetic involvement on the severity of nocturnal enuresis as it has been estimated that children with parenteral nocturnal enuresis usually suffer from a 3.5 times more severe condition than others.³ Evidence also shows that gender is a significant predictor for the prevalence of nocturnal enuresis, which was indicated by a previous United States investigation has showed that the prevalence of the condition was 2.51% in females and 6.21% in male participants in children that ranged between 8 and 11 years old.⁴ Sureshkumar et al also concluded that male children with nocturnal enuresis usually have a more severe condition than females.⁵ In this literature review, the aim was to discuss the etiology and management of nocturnal enuresis and the impact of the condition on the different age groups.

METHODS

A systematic search was conducted to identify relevant studies in the following databases: PubMed, Medline, Web of Science, Embase, Google Scholar and Scopus. The following search terms were used (urethral stricture) and (recurrence) and (post or after) and (urological treatment or urological outcome). The reference lists were manually searched to identify additional relevant studies meeting inclusion criteria. No restrictions were applied.

DISCUSSION

Etiology

It has been reported that the etiology of nocturnal enuresis is multifactorial with a reported genetic involvement, in addition to the potential presence of immaturity of the central nervous system connections in the affected children that are usually responsible for bladder control.⁶ Although the genetic component has been previously validated by studies in the literature to strongly take part in the development of nocturnal enuresis with no specific genes were reported.⁶ However, it was evidenced that children usually inherit the condition in an autosomal dominant pattern and an estimated penetrance of 90% for these children.⁷ In this context, previous estimates also reported that children that have one parent that previously suffered from nocturnal enuresis usually have a chance of 44% to develop nocturnal enuresis and the rate increases up to 77% when both parents are affected.^{7,8} It is worth noting that the previously reported psychiatric or psychological factors as direct etiologies of the condition are now considered as a result of the development of nocturnal enuresis or present co-morbidities with the condition.⁹ Moreover, many other conditions were also reported to co-exist with nocturnal enuresis as cystitis, urethral obstruction, diabetes insipidus, constipation, ectopic ureter, small bladder capacity, disorders of sleep disruption and overactive bladder.^{10,11}

Evidence in the current literature shows that many causes and mechanisms are involved in the development of nocturnal enuresis. Among the proposed mechanisms, three have been reported to be the most common to cause nocturnal enuresis. Figure 1 summarizes the common mechanisms of nocturnal enuresis. These mechanisms include overactivity of the bladder, excessive production of nocturnal urine and the potential failure that some individuals might have as a response to full bladder sensations and feelings during bedtime.¹²⁻¹⁴ All of the aforementioned mechanisms have been previously reported by adequate investigations, however, none of these theories can explain the mechanism and etiology of nocturnal enuresis among all the affected children and the etiology remains variable across the different patients. Besides, previous studies have demonstrated that the excessive production of nocturnal urine and the development of nocturnal enuresis in children is probably attributable to the pathological presence of abnormally elevated plasma levels of vasopressin.¹⁵⁻¹⁷ It has also been reported that some children might suffer from bladder overactivity. Nevertheless, it has also been reported that these patients usually present with other daytime clinical symptoms related to the bladder such as frequency, incontinence and urgency. This was indicated in a previous investigation by Yeung et al that reported that in patients with overactive bladder, the ambulatory cytometric analysis of these patients showed that overactivity can be a direct etiology behind nocturnal enuresis that is resistant to the standard management modalities.¹⁸ Recent evidence from previous studies also suggests the potential involvement of the central nervous system in the development of nocturnal enuresis. Suggestions have pointed out that, according to the parents of the affected children, these patients usually suffer from deep sleeping, although some of them might also suffer from regular sleep disruptions. The latter theory was indicated in a previous investigation that showed that some children that suffered from nocturnal enuresis had night time sleeping disruption which was compensated by more frequent sleeping during the day.¹⁹ In previous animal investigations, it was also reported that the observed absence of response in the physiologic inhibitory signals to the bladder might result secondary to sleep disruption in the included animals.²⁰ Additionally, a previous investigation also reported that the development of nocturnal enuresis might be attributable to the same cause in patients that suffer from obstructive sleep apnea.²¹

Management approaches

The management of the condition is mainly dependent on treating the underlying etiology and dealing with the right associated mechanism. Moreover, careful and adequate monitoring of the case would achieve favorable outcomes. After the underlying etiology and associated morbidities were identified, early management of these etiologies should be carried out as early as possible, preferably before the age of six years old.⁶ Many

treatment modalities have been previously described in the literature and the key to successful management lies within the appropriate evaluation of the case.²² Moreover, it should be noted that the management procedure also requires the integration of the patients and their families to achieve adequate interventions and enhance the prognosis.⁶ Dealing with underlying morbidities like constipation and/or psychological associated disorders with nocturnal enuresis should be firstly managed because evidence from previous studies in the literature reports that successful management and enhanced prognosis of these cases is significantly dependant on the appropriate dealing with such disorders that may be involved in the pathophysiology of nocturnal enuresis.^{9,23,24} Behavioral modifications should be the initial management modality which is achieved by restricting the administration of fluids and dairy before bedtime by 2 and 4 hours, respectively to prevent osmotic diuresis and voiding of water before sleep.⁸ Another therapeutic approach that was also previously reported in the literature includes the alarm system, which was also previously indicated to have a slightly higher significant favorable effect over the administration of desmopressin.⁶ Evidence from previous studies shows that the estimated successful management rates for using alarm therapy are as high as 70%. Furthermore, although the administration of the modality requires sticking to a strict daily regimen and longer periods of administration, it has been reported with significantly lower relapse rates of nocturnal enuresis after stopping the administration of the modality when compared to the pharmacological modalities.⁸ The conditioned response has been reported to be the main mechanism by which the modality works.²⁵ This is simply achieved by making children wear their pants normally instead of diapers and waking them up to go to the bathroom at night when the alarm goes off.⁸ It has been reported among studies in the literature that this management modality best suits older patients with nocturnal enuresis who are more eager and motivated to

achieve dryness and those patients that suffer from monosymptomatic nocturnal enuresis.^{8,26} Alarm therapy can be considered successful when the patient finally does not use the alarm to wake up at night to urinate and successful and adequate management usually takes up to 3-4 months in many cases.⁸ Pharmacological management modalities can also be used as adjuvant therapeutic approaches until the main etiology naturally fades away and is not considered curative.⁸ These modalities should be considered in cases where behavioral management modalities fail to manage the case or in case of adequate evaluation of the underlying etiology which requires the administration of a certain pharmacological therapy. Among the reported pharmacological therapies, desmopressin is a common management modality with reported high successful rates by acting through reducing the production of urine.^{8,27} Previous investigations have suggested that desmopressin and alarm therapy should be approached simultaneously with reported 100% success rates.^{7,8,28} This management modality is advisable and is associated with fewer adverse events; however, fluid intake should be timely done to avoid the development of hyponatremia.²⁹ Moreover, the administration of desmopressin is absolutely contraindicated in case of the presence of underlying comorbidities that might cause metabolic abnormalities and relatively as an intranasal formulation in case of water intoxication.^{8,29} Anticholinergic agents as oxybutynin have also been previously suggested to be used as adjuvant modalities to desmopressin in resistant cases. Nevertheless, it should be noted that they are associated with many adverse events and tolterodine is not even approved by the FDA in pediatric patients.^{8,29} Other pharmacological modalities include the administration of tricyclic antidepressants as imipramine, which are usually suitable for older patients with reduced response to the aforementioned management modalities. Adverse events of the modality might include dryness after discontinuing the treatment and some ECG changes which require patients to be closely monitored after drug intake.^{8,28,29}

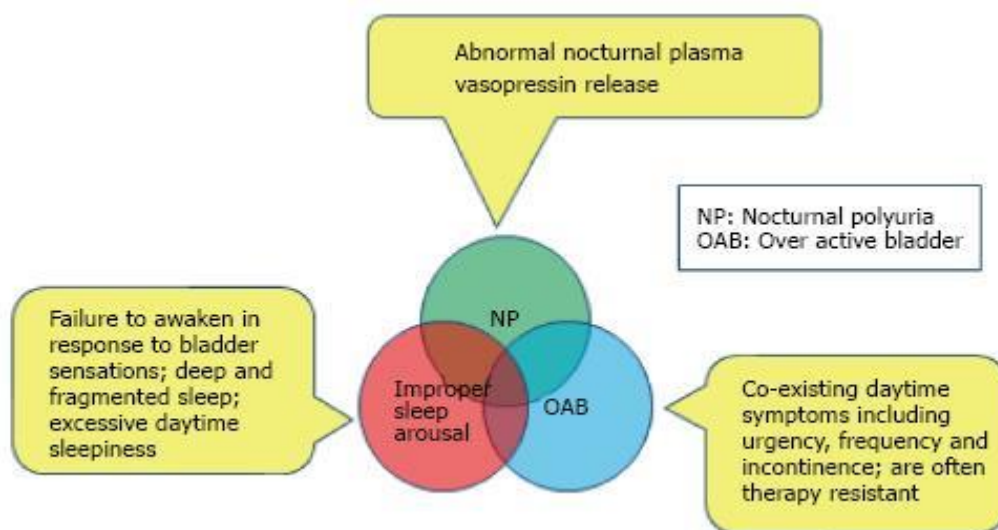


Figure 1: Common mechanisms of nocturnal enuresis.³⁰

Impact on different age groups and prognosis

Previous investigations have demonstrated that the condition usually resolves over time, even without any medical interference and management. As previously reported, it has been estimated that around 15% of patients with nocturnal enuresis acquire continence every year.⁸ However, it has also been previously reported that the affected patients usually suffer from many conditions that should be considered to manage even when the condition fades away. It has been demonstrated that many social, emotional and physical abuse issues might be an obstacle for some patients that require further assistance. The current evidence also supports that the highest success management rates are associated with the administration of desmopressin and imipramine, in addition to approaching the patients with alarm therapy. However, it has also been reported that despite the hopeful management responses among patients, many patients around 20% will continue to suffer from nocturnal enuresis as adults. The persistence and failure of management of nocturnal enuresis can lead to a series of complications that have been frequently reported in the literature to affect the different age groups and their families. High degrees of stress, mood problems, low self-esteem and other issues that are related to the quality of life of the affected patients and their families have been reported in studies in the literature.^{6,7,9,26} Moreover, the persistence of the disorder can also affect the patient's ability to engage and socialize with other individuals and participate in normal daily activities. On the other hand, previous investigations also showed that if the condition was effectively managed by adequate approaches, the quality of life and the observed complications have been previously reported to enhance over time.⁹ Moreover, it has been previously suggested that medical consultation and referral to a specialist are still needed. This is strongly recommended in cases that suffer from non-monosymptomatic enuresis as it has been reported that the standard management modality is not useful with these patients. Previous investigations recommended that if the patients do not respond to the standard management modality after three months from initiating the treatment, referral to a specialist should be considered for these patients to achieve the best management.²⁸

CONCLUSION

In this literature review, it has discussed the different etiological factors and management modalities that are currently described for nocturnal enuresis among studies in the literature. Management of the underlying comorbidities, taking care of the overactive bladder and dealing with the potential psychological conditions might be the main key factors to nocturnal enuresis. Many pharmacological and non-pharmacological approaches have been proposed for these patients. However, the success rates of applying behavioural management approaches have been reported to be the highest as compared to other approaches. Early interventions should

be applied for children that have multiple risk factors or with parents that once suffered from the condition.

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