INVITED ARTICLE

NOCTURNAL ENURESIS

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ABSTRACT

Nocturnal enuresis is a treatable condition. It is defined as functional urinary incontinence during sleep beyond the age (arbitrarily taken to be) of 6 years old at which control should be established. Although it is a physically benign condition, it is unfortunately associated with emotional-behavioural disturbances and developmental delays. Diagnosis is usually straight-forward, and based mainly on history and physical examination. Often, only a microscopic examination of urine is required to exclude urinary tract infection. Treatment begins with a baseline recording of the frequency of enuresis. This is incorporated into motivational therapy which consists of counselling , enhancement of self-responsibility and self-efficacy with positive reinforcement for success. Failing which, enuretic alarm provides the single most effective mode of treatment. However, it suffers from poor compliance. Medication is usually used on an as-needed basis because most relapse after cessation of treatment. Imipramine is the most well-studied and commonly used medication but suffers from potential toxicity. Desmopressin, on the other hand, has few adverse side-effects and is just as effective as imipramine. Its main drawback is its cost.

Keywords: enuresis, nightwetting, bedwetting, children

SINGAPORE MED J 1994; Vol 35: 198-200

Definition

Nocturnal enuresis is defined as functional urinary incontinence during sleep beyond the age at which control should be established. It can be sub-divided into primary and secondary type. Primary nocturnal enuresis occurs when the patient has never been dry for extended period. In contrast, in secondary nocturnal enuresis there is a past history of a continuous dry period of six months to a year. Nocturnal enuresis is also variously known as enuresis, non-organic enuresis (ICD-10)[1], or functional enuresis (DSM-3-R)[2].

Clinical features

Nocturnal enuresis commonly presents at the age of 7 to 11. The parents usually initiate the referral, and they often blame the child for what they perceive as wilful wetting of the bed, even when there is a positive family history of the same condition. No other urinary symptoms are usually present, although occasionally there may also be complaints of urinary frequency, urgency and dysuria. Prior to the referral, the parents may have tried a variety of methods to treat the enuresis themselves, like fluid restriction, waking up the child to pass urine, teasing the child, and even physical punishment. The latter often results in a deteriorating parent-child relationship and psychiatric morbidity which are often compounded by the concurrent presence of developmental delays and educational difficulties[3].

Differential diagnoses

Diagnosis of nocturnal enuresis is often quite straight-forward, and is based mainly on the history and physical examination. However, a number of conditions need to be excluded.

1) Medical conditions, like diabetes mellitus and diabetes insipidus, may present with polyuria so that the volume of urine produced may exceed the functional volume of the bladder and hence resulting in voiding of the urine while asleep. However, there will also be polydipsia and other symptoms indicative of the primary medical condition.

2) Seizure occurring at night may present with urinary incontinence. The diagnosis may be suspected if the patient has a history of seizure or if seizure is observed during sleep.

3) Neurogenic bladder (eg from spina bifida and spine injuries) can have urinary incontinence at night. But, the diagnosis is not easily missed as there will also be day-time urinary incontinence and neurological deficits.

4) Urinary infection presenting with nocturnal urinary incontinence, often has other symptoms like urinary frequency, dysuria, and foul smelling urine.

5) Others: ectopic ureter, constipation[4], sleep apnoea, severe psychosocial stress.

Natural history of nocturnal enuresis

Urinary incontinence during sleep is a normal phenomenon in early childhood. With increasing age, the child gradually develops control over his bladder resulting in a 15% spontaneous resolution of nocturnal enuresis per year. Nocturnal enuresis affects about 10% of 6-year-olds, 3% of 12-year-olds, and 2% of 15-year-olds. The prevalence in adults is unknown. Although some studies suggest that urinary incontinence during sleep after age 4 is qualitatively abnormal, specific treatment is usually started only after age 6.

Postulated causes of nocturnal enuresis

The exact aetiology of nocturnal enuresis is unknown. It may be a heterogeneous group of conditions, each with a different mix of aetiological factors. The aetiological factors are:

1) *Genetics*

Nocturnal enuresis usually runs in families. Indeed, 70% have a positive family history in a first degree relative and the concordance in identical twins is 68% and non-identical twins is 36% (Balkwin 1973)[5].

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2) *Small bladdder capacity*
A small bladder capacity may fail to accommodate the amount of urine produced throughout the night. Studies have shown that in some but not all enuretics, the functional bladder capacity is indeed smaller than normal. But this does not detract from the fact that the sensations of a full bladder have failed to rouse the patients from their sleep which would have happened in a normal person.

3) *Nocturnal diuresis*
Related to the idea of a small bladder capacity is the disturbed urinary circadian rhythm with decreased nocturnal vasopressin production in some enuretics[6]. This results in nocturnal diuresis which overloads the storage capacity of the bladder and serves as the basis for treating enuretics with desmopressin which is an analog of vasopressin.

4) *Urinary tract abnormalities*
Anterior urethral valves, meatal stenosis, or bladder neck obstruction are found in a small proportion of those referred for urological assessment. However, these are probably coincidental findings as correction of the abnormalities does not result in a cure of nocturnal enuresis.

5) *Lower urinary tract infection*
This is five times more common in the enuretics than in the normal population. The infection may be aetiologically significant in the genesis of nocturnal enuresis. But, the converse may also be true. That is, the infection is secondary to the poor genital hygiene which results from nocturnal enuresis. Interestingly, treatment of the infection often alleviates the nocturnal enuresis.

6) *Maturational delay*
Enuretics are twice as likely as other children to exhibit motor and speech developmental delays, slow growth, and neurological soft signs like fine and gross motor clumsiness, and perceptual dysfunction, suggesting that nocturnal enuresis may be due to a delay in maturation[7,8].

7) *Psychiatric disorders*
By and large, parents are intolerant of nocturnal enuresis, and more than half of the enuretics are distressed by their condition. Indeed, nocturnal enuresis is associated with psychiatric disorders although not to any specific pattern of emotional-behavioural disturbance. But, it is still not clear whether this relationship is causal, reactive, or just coincidental. The enuresis may be a manifestation of some psychiatric disorder, psychiatric disorder may be secondary to the distress resulting from enuresis, or both enuresis and psychiatric disorder may arise from another common factor[3].

8) *Sleep disorder*
Although parents commonly observe that the enuretic child sleeps so deeply that he fails to wake up in response to bladder distension, sleep studies revealed that enuresis occurs at all stages of sleep and not predominantly at deep sleep only[9].

Investigation
The majority of enuretics present with only the symptom of wetting their beds and do not have any other organic signs and symptoms. Hence, often the only investigation needed would be microscopic examination of the urine for evidence of urinary tract infection. Further urological investigations are not helpful.

Treatment
Nocturnal enuresis distresses both the child and his family. Parents may blame their child for either being too lazy to wake up to pass urine at night or wilfully bedwetting to spite the parents especially when it occurs irregularly and seemingly remits with punishment. However, strong negative parental reaction is not just confined to the issue of wetting bed. It is often part of a more pervasive parenting skill deficit which may lead to child psychiatric disorders and learning difficulties, and family psychopathology and dysfunction. Hence, in the management of nocturnal enuresis, it is important that the clinician is alert to psychosocial issues as well as the medical aspect of the problem.

The various different treatment modalities are:

1) *Motivational therapy*
This consists of explaining the causes and prognosis of enuresis, discontinuing unhelpful practices, providing practical discussion on coping, providing emotional support, fostering positive relationship between the child and the parents, enhancing self-responsibility, self-efficacy and positive expectancy in the treatment of enuresis, and providing positive reinforcement for success. In practice, a star chart is often used. Here, the child is rewarded with a star sticker to paste onto a calendar immediately after each dry night. This record of the frequency of dry night also helps to monitor the improvement with this treatment.

Although only 25% are cured, with a relapse rate of 5%[10], 70% showed marked improvement[11].

2) *Conditioning therapy*
An enuretic alarm is triggered off when a sensor placed in the vicinity of the external genital comes into contact with urine. The objective is to convert the sensations of a full bladder from a signal to urinate to a signal to inhibit urination and awake. This is based on the behavioural principles of conditioning (both classical and instrumental conditioning). The alarm (unconditioned stimulus) is associated with bladder distension (conditioned stimulus) and is also an aversive consequence to bedwetting, both leading to the response of urinary inhibition and awakening[12].

This is the single most effective method with a cure rate of 75% and a relapse rate of 35%, but suffers from poor compliance as close cooperation and high motivation are required of the child and his family.

3) *Tricyclic antidepressants*
Tricyclic antidepressants (imipramine, amitriptyline, nortriptyline, desipramine) are found to be effective. The pharmacological mechanism of action is unknown; four are proposed ie antidepressant effect, antispasmodic and/or anticholinergic effect, alteration in arousal and sleep, and adrenergic neurotransmitter reuptake blockade.

Imipramine[13] is the most well studied drug for enuresis. The starting dose is 0.9-1.5 mg/kg orally 1-2 hours before bedtime, with 25 mg increment every week if no response occurs within this period. ECG assessment is required with doses over 3.5 mg/kg. Generally, high dose is discouraged because of its cardiotoxicity and the rather benign nature of the illness. Medication is maintained for about 3 months before tapering off. Should relapse occur, the medication can be increased again to the pre-relapse dose. However, more often than not, imipramine is used on an as-needed basis in situations where being dry is particularly important to the child such as sleepovers and camping.

The cure rate is about 30% with improvement in 85%. However, most relapse after cessation of treatment of a few months.

4) *Desmopressin*
Desmopressin intra-nasally 10-40 ug nightly is generally as effective as imipramine and has few adverse side-effects[14]. But, the cost of this medication is high.

5) *Others*
Numerous other methods have been used but they are either not

well studied or impractical for general clinical use. These include anticholinergics (propantheline), musculotropic agents (oxybutynin), dry bed training, bladder training (retention control training; sphincter control exercises), waking procedures[15], hypnotherapy, and special diet.

In summary, treatment often begins with motivational therapy because it is simple and helps to dispel any misconception of enuresis. Failing which, conditioning therapy is tried as this is the single most effective method of treatment. Family cooperation, however, is essential. Treatment with imipramine is the next choice. The drawbacks are its side-effects, toxicity, and the risk of accidental overdose.

Conclusion

Nocturnal enuresis is very treatable. Although it is essentially a physically benign condition, it is associated with educational, behavioural, and emotional problems. The adverse family reaction to enuresis often reflects an underlying strained parent-child relationship or poor parenting skills. Most nocturnal enuresis can be successfully managed by the general practitioners. Treatment should begin with a baseline recording of the frequency of enuresis, followed by motivational therapy, conditioning therapy, and pharmacotherapy (imipramine) in that order of preference generally.

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