

Management of primary nocturnal enuresis



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BACKGROUND

Primary nocturnal enuresis is the involuntary discharge of urine at night by children old enough to be expected to have bladder control. Enuresis is considered primary when bladder control has never been attained and secondary when incontinence reoccurs after at least six months of continence.

Children should not be labelled enuretic unless regular (more than twice per week) wetting persists beyond the age of five years. Primary nocturnal enuresis is more common in boys. Bedwetting is found in 10% to 15% of five-year-old children and 6% to 8% of eight-year-old children, and it declines to 1% to 2% by 15 years of age.

Primary nocturnal enuresis should be regarded as a variation in the development of normal bladder control. It may be associated with deep sleep patterns. Emotional and behavioural problems are not causative factors, although they may influence treatment outcome (1,2).

METHOD OF DATA COLLECTION AND SYNTHESIS

The present statement was last revised in 2002. A PubMed search was conducted for articles published since 1999 to ensure appropriate overlap with the previous review. The search was conducted using the search term 'Enuresis', and was limited to 'Clinical Trials', 'Randomized Controlled Trials' and 'Meta-Analyses'. In addition, relevant systematic reviews from the Cochrane database were identified, as were relevant references from identified articles. A single reviewer appraised the quality of the articles. Articles about therapy were appraised by using the method of Sackett et al (3) and systematic reviews were appraised by using the method of Oxman et al (4).

GENERAL MEASURES

A thorough history and physical examination are essential. A family history of enuresis is often present. Recent studies have identified a gene for enuresis on chromosome 13q (5). For primary nocturnal enuresis, when the

history and physical examination are completely reassuring, the low pretest probability of a true-positive result on urinalysis may obviate the need for any routine tests at all, given the potential to generate false-positive results. Judicious, rather than routine, tests for primary nocturnal enuresis are most appropriate.

Enuresis that persists beyond the age of eight to 10 years may be associated with a poor self-concept or other psychological problems (6,7). Reassurance, support, and avoidance of punishment and humiliation are important to maintain the child's self-esteem and minimize parental frustrations. Parents may seek medical opinion simply for reassurance. It is important to communicate openly with the child and parents. Enuresis should only be treated with pharmacotherapy and/or alarms in cases where it poses a significant problem for the child (strength of recommendation – B, level of evidence – III [see Appendix for key to strength of recommendations and level of evidence]).

Commonly recommended strategies for parents to help their child achieve continence include the following (8):

- Clarify the goal of getting up at night and using the toilet.
- Assure the child's access to the toilet.
- Avoid caffeine-containing foods and excessive fluids before bedtime.
- Have the child empty the bladder at bedtime.
- Take the child out of diapers (training pants may be acceptable).
- Include the child in morning cleanup in a nonpunitive manner.
- Preserve the child's self-esteem.

SPECIFIC TREATMENT MEASURES

Alarm devices in the management of nocturnal enuresis
In 1907, Pfaundler invented the first alarm device for the management of nocturnal enuresis. Since then, studies

have shown the benefit of these devices (9,10). The purpose of the enuresis alarm is to teach the child to respond to a full bladder while asleep. The alarm goes off when the child starts to void. It may teach the child to wake up to the alarm and then, by approximation, transfer the waking to the sensation of a full bladder.

The miniature alarm systems are lightweight, portable, worn on the body and run on miniature batteries. Sensitive to a few drops of urine, they give a very prompt alarm response, and young children can operate them without difficulty. There are no 'buzzer burns' or shocks, which were associated with the older bell and pad alarms (1).

The success of the alarm depends on the child being motivated, and on the willingness of both the child and the parents to be awakened. Although occasionally effective in children as young as five years, the alarms are most effective in children older than seven or eight years. Initially, the child may continue to sleep deeply through the buzzer, requiring the parents to wake the child and alert him or her to the bedwetting episode.

Therapeutic trials of the alarm system should be continued for three to four months. It may take up to one to two months to see an improvement. Often, the initial improvement is a decrease in urine output rather than a totally dry night. Use of the alarm system is continued until there have been 14 consecutive dry nights. At this point, some authors (6) recommend an 'overlearning': the child is encouraged to drink extra fluid (eg, two glasses of water) to 'overcondition' the bladder. This overlearning is continued until the patient has achieved seven dry nights in a row (6). Among the children who relapse, some may be treated successfully with a repeat of the original alarm program (11). If a relapse occurs, the treatment may be repeated, with a success rate similar to that of the initial course of therapy. There are a number of alarms readily available in the \$80 range. Because they tend to 'wear out' after two to three patients, it is more practical for parents to purchase a new alarm for their child. Commercial companies advertise systems at a very high cost. The public should be forewarned before purchasing these systems.

Parents should also be forewarned that alarm therapy also requires a commitment from other siblings because the alarms are sufficiently loud that often all members of the household are wakened when the alarm goes off. Alarms are impractical for 'sleepovers' and camp. Other therapies may be more appropriate for such settings.

Two systematic overviews (12,13) have recently been published based on meta-analyses of studies examining the long-term cure rate with alarm devices. Each of these meta-analyses analyzed available data about dropouts in a methodologically appropriate way. In each overview, the length of follow-up and the criteria for reporting success varied among reviewed articles, but the studies were analyzed with uniform criteria.

Both of these systematic overviews concluded that the actual cure rate of primary nocturnal enuresis using alarm

devices is just under 50% (significantly lower than previously found) (12,13). In one of these overviews (from the Cochrane collaborative [12]), it was noted that although less than 50% of the children in the group receiving alarm therapy remained dry, almost none of the children in the groups that did not receive the alarm therapy remained dry at the end of the studies. The Canadian Paediatric Society recommends the use of alarm devices for older, motivated children from motivated families for whom more simple measures are unsuccessful (strength of recommendation – A, level of evidence – I).

Pharmacological therapy

Desmopressin acetate: Desmopressin acetate has been studied for use in enuresis since the 1970s. It is a synthetic analogue of antidiuretic hormone (ADH) (14).

Nørgaard and Rittig's studies from Denmark (15) showed that in some children, enuresis occurred randomly throughout the sleep cycle. The enuretic children had an altered pattern of ADH secretion compared with control patients. The control patients had an elevation of ADH levels at night, while the enuretic children had a constant level of ADH throughout a 24 h period. Therefore, it appears that in some children with nocturnal enuresis, high volumes of urine are produced at night, with subsequent overflow of the bladder. The rationale that follows from Nørgaard's study is that desmopressin acetate could be used as a hormonal replacement therapy for children with enuresis.

Moffatt et al (16) reviewed 18 randomized clinical trials with desmopressin acetate. Their review showed that one-quarter of the subjects became completely dry. A systematic overview (17) based on a meta-analysis from the Cochrane collaborative concluded that the use of desmopressin acetate resulted in one to two fewer wet nights per week compared with placebo and twice the likelihood of becoming completely dry during treatment. Cure rates after treatment was discontinued were not substantially greater than with placebo (17). Potential side effects, usually mild, are headache and abdominal pain, as well as stuffiness and epistaxis for the nasal preparation. Although there have been case reports of water intoxication (17), of the 752 subjects reviewed by Moffatt et al (16), there were no cases of water intoxication.

The expense of this medication needs to be factored into decisions about therapy. The dose range for the nasal spray is 10 µg to 40 µg. In tablet form (100 µg or 200 µg tablets), desmopressin acetate may be prescribed at doses from 200 µg to 600 µg and has the same degree of safety as the spray. The tablet preparation may be more effective for some children because potential difficulties with absorption specific to the spray (eg, stuffy nose and allergic rhinitis) are eliminated.

Desmopressin acetate should be used with extreme caution in children having problems with osmoregulation or fluid balance, or in children with cystic fibrosis,

and the nasal preparation may be ineffective in children with symptomatic allergic rhinitis or viral rhinitis.

Desmopressin acetate's greatest value may be for short-term treatment, in settings such as camp or sleepovers, rather than as an attempt at a cure (17) (strength of recommendation – A, level of evidence – I).

Imipramine hydrochloride: Imipramine hydrochloride is a tricyclic antidepressant whose mode of action in the treatment of enuresis is unclear. The antiuretic response is often immediate. The recommended starting dose is 25 mg for children six to 12 years of age and 50 mg for those older than 12 years. The dose is given 1 h to 2 h before bedtime. The maximal effect is noted within the first week of treatment, but a two-week therapeutic trial should be undertaken before adjusting the dose. At that time, the dose may be increased gradually to a maximum of 50 mg in children six to 12 years of age and 75 mg for those older than 12 years. An increase beyond this amount does not enhance therapeutic response but may significantly increase the potential for drug toxicity.

The response rate during treatment is similar to that with desmopressin acetate, and the cure rate after treatment is similarly comparable with placebo (18). Minor side effects are common, and children should be monitored for personality changes, including emotional lability, irritability and anxiety. Other effects include disturbed sleep patterns, headaches and changes in appetite. Rare but serious side effects are convulsions, coma and cardiac arrhythmias from overdose. The possibility of accidental or deliberate overdose cannot be overstated and, therefore, even though imipramine hydrochloride is cheaper than desmopressin acetate, it should be used with extreme caution. Imipramine hydrochloride may be used as therapy for short-term treatment of nocturnal enuresis in distressed, older children if other treatments have been unsuccessful or are contraindicated, and if parents are judged to be reliable and are counselled about safe storage of the medication (strength of recommendation [in these special circumstances] – A, level of evidence – I).

Behavioural therapy

Simple behavioural therapy (such as reward systems or waking a child to void in the toilet ['lifting']) may be effective for some (19). Punishment and humiliation are to be avoided (7,20). Dry bed training, as described by Azrin and Thienes (21), is a more labour-intensive parent-awakening technique and may be slightly more effective in combination with alarm therapy than alarm therapy alone (22).

Studies examining simple behavioural therapies are too disparate in methodology to be analyzed using meta-analysis (19). Individual small trials cite fewer wet nights with reward systems (eg, 'star charts') and lifting. The potential for negative consequences of such therapy has not been carefully studied.

It may be difficult to convince a child that a wet night is nothing to be ashamed of when dry nights are rewarded. The failure to achieve dry nights leading to stars or stickers may contribute to poor self-esteem. Lifting is labour intensive and may contribute to frustration and conflict. The goal of treatment is largely to reduce problems with frustration, conflict and poor self-esteem and, thus, behavioural therapies for enuresis may do more harm than good.

In a systematic overview from the Cochrane collaborative (19), adverse outcomes of simple behavioural strategies for enuresis (when reported) leading to a high dropout rate were family strife, emotional problems, and failure of the treatment because it was too demanding of the children or their families (19). Given the limited data from small trials about the effectiveness of behavioural therapy for enuresis, particularly with respect to the potential for adverse effects, there is insufficient evidence to recommend routine use of behavioural therapy for primary nocturnal enuresis (strength of recommendation – I).

SUMMARY OF RECOMMENDATIONS

- Children for whom primary nocturnal enuresis is not distressing should not receive treatment. Parents should be reassured about their child's physical and emotional health and should be counselled about eliminating guilt, shame and punishment (strength of recommendation – B, level of evidence – III).
- A conditioning alarm system is the most efficacious therapy, but it will be successful in the long term in less than 50% of children. Alarms may be the most appropriate initial line of therapy for primary nocturnal enuresis for older children in highly motivated families (strength of recommendation – A, level of evidence – I).
- Pharmacological therapy with desmopressin acetate has a place in special situations, such as at camp and sleepovers, or when the alarm system is impractical or not effective (strength of recommendation – A, level of evidence – I). In difficult circumstances, imipramine hydrochloride may be used cautiously but requires careful explanation to reliable parents about the danger of overdose. Most children do not require imipramine hydrochloride.
- Treatment of primary nocturnal enuresis should be aimed at minimizing the emotional impact on the child. There is insufficient evidence about the good versus harm that behavioural therapies may exert in this regard. Reward systems and lifting should not be recommended without careful consideration of, and discussion with parents about, potential adverse effects (strength of recommendation – I).

APPENDIX: LEVELS OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

Levels of evidence behind selected management options and the strength of recommendations were graded using the methods of the Canadian Task Force on Preventive Health (23). The strength of a recommendation takes into account not only the level of evidence supporting a manoeuvre but also the value of potential benefits and risks of the manoeuvre. Thus, the grading of the strength of a recommendation is more subjective than the grading of the level of evidence behind a recommendation.

Level of evidence	Description
I	Evidence obtained from at least one properly randomized trial.
II-1	Evidence obtained from well-designed controlled trial without randomization.
II-2	Evidence obtained from well-designed cohort or case-controlled analytic studies, preferably from more than one centre or research group.
II-3	Evidence obtained from comparisons between times and places, with or without the intervention. Dramatic results in uncontrolled experiments could also be included in this category.
III	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.
Grade	Description
A	There is good evidence to recommend the clinical preventive action.
B	There is fair evidence to recommend the clinical preventive action.
C	The existing evidence is conflicting and does not allow a recommendation to be made for or against use of the clinical preventive action; however, other factors may influence decision-making.
D	There is fair evidence to recommend against the clinical preventive action.
E	There is good evidence to recommend against the clinical preventive action.
I	There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate.