

ENURESIS

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KEY WORDS: Enuresis, epidemiology, aetiology, Treatment.

INTRODUCTION

The term enuresis refers to the inappropriate and involuntary passage of urine by a child who has reached an age at which bladder control is expected i.e. after 5 years of age^{1,5}. The voiding occurs at a socially unacceptable time or place according to 1998 International Children's Continence Society⁴. The prevalence rate is about 8% at the age of 6 years and 4% at the age of 10 years⁵. It may be nocturnal (nighttime) or diurnal (daytime) enuresis^{1,2}, but for practical purposes, the term enuresis is generally refers to nocturnal enuresis. Enuresis is a common worldwide problem among school age children. The aetiology is mostly multi-factorial and non-organic^{1,3,9}. Organic causes contribute to less than 10% of nocturnal enuresis^{2,10-24}. However, it can cause significant distress and impairment of self-esteem. Punitive measures are not therefore helpful and may be effect of the problem on the patient and the parents' attitude^{2,3,32}. Spontaneous remission may occur without treatment. Unfortunately health problem is not given adequate attention by the public and health professionals. In this review, the aetiological causes, Epidemiology and treatment options available for enuresis are reviewed.

Definitions:

Nocturnal Enuresis^{2,3,5,10}. This is also called bed wetting or sleep enuresis. The individual who has achieved daytime bladder control while awake urinates while asleep. It may be primary (PNE) or secondary (SNE) type. In PNE, the child has not achieved nighttime bladder control. From infancy for uninterrupted period of 6months, while in SNE (acquired or onset enuresis), bedwetting occurs after a period of dryness (at least 6 months). Diurnal Enuresis: is daytime wetting that occurs in child who is awake. It is avoiding dysfunction not related to neurological abnormalities. Physiology of micturition^{3,3}. Micturition is fundamentally a spinal reflex modulated by high brain centers. The reflex is integrated in the sacral portion of the spinal cord. The threshold is adjusted by the activity of the facilitatory (pons and posterior hypothalamus) and inhibitory centers (midbrain)^{3,3}. During voiding, the perineal muscles and external sphincter are relaxed; the detrusor muscles contract. Voluntary voiding involves relaxation of the muscles of the pelvic floor, and this may cause a special tug on the detrusor muscle to initiate contraction of the bladder. Development of Bladder control Children achieve bladder control at different ages because arousal response to bladder distension develops with age. Daytime continence is achieve earlier than nighttime continence^{2,3,5}.

It involves several skills such as awareness of urgency, ability to initiate urination and to inhibit urination while awake or asleep^{2,4}. Daytime continence is achieved by 12 - 24 months, while nocturnal continence is achieved a little latter, between 2¹/₂ and 3¹/₂ yrs². At 2¹/₂ yrs, 90% of girls and 80% of boys indicate the need to micturate during the day. Seventy - five percent and 98% of children achieve nocturnal continence at the age of 3¹/₂ and 5 years respectively. The girls acquire nighttime dryness earlier than boys. In Baltimore, U.S.A, 45% of girls aged 2 - 3 years and only 3% of boys were dry at night^{1,8}. As a result it has been argued for epidemiologic surveys that it might be better to reserve the strict diagnostic term of NE to girls over the age of five years and boys over the age of six years^{3,4}.

Epidemiology of enuresis

Nocturnal enuresis is a common worldwide problem among school age children 1 - 5. It is common in the first few years after toilet training is achieved. The frequency is at least 2 episodes/month in younger children of 5 - 7 years and at least 1/month for older children. The prevalence varies in countries and steadily declines with age^{1,5}. The incidence is slightly higher in the USA compared to some European countries^{1,2,4,5,8,9}. In Nigeria, Famuyiwa noted a prevalence rate of 25% of PNE among school children in Lagos³. Primary nocturnal enuresis is more prevalent than the secondary type at approximate ratios of 10:^{11,2}. Diurnal enuresis is less common than bedwetting (NE). While 2/3 of patients with daytime wetting as the main problem with NE, only 10-15% of patients with NE have DE^{2,5}. DE is more common in boys. There is a strong association between diurnal enuresis and urgency, incontinence (urge, stress, giggle and vaginal) and pollakuria (extreme frequency)^{2,5,21}. Bedwetting is more common in the first-born children, in the lower socioeconomic classes and those who had suffered a social or psychological stress in the first 4 years of life^{1,8,20}. Up to age 11 years, the incidence is 2-3 times more in boys, after which it equalizes or is weighted towards females^{3,5}.

Pathophysiology

In Nocturnal enuresis, there ate inability to waken in response to signals from a full bladder, relative nocturnal polyuria due to insufficient vasopressin (AVP) release during nocturnal sleep and reduced functional bladder capacity especially in demopression non-responders^{5,21}. In Diurnal enuresis, there is delayed maturation of the cortical mechanism that allows voluntary control of micturition reflex, bladder instability and lack of co-ordination between the contraction of the detrusor muscles and relaxation of the sphincter (dyssnergia).

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Aetiology

They are multifactorial, and most times the specific cause is unknown. Ninety-seven percent or more of PNE are non organic^{1,3,9}. The factors implicated include: Genetic factors: Heredity is one of the most important factors contributing to enuresis^{5,1,3}. While only 15% and 77% of children bedwet when one or both parents bed wet respectively⁵. The probability increases with a higher frequency as the closeness with a history of enuresis increases. Recent evidence points to the involvement, in some cases, of a single autosomal dominant gene with reduced penetrance. Linkage to chromosomes 8,12,13 9q) as been found^{5,1,3}. Monozygotic twins are twice more likely to bedwet compared to dizygotic twins. Bedwetting is associated with left-handedness (gene focus, chromosome 12)^{1,3}. Bladder dysfunction. Enuretics especially PNE, DE have functionally smaller bladder^{5,2,12,2}. The most frequent case is bladder instability, in which there is uninhibited contraction of detrusor muscles during filling and inability to suppress voluntary bladder contraction. It may also be due to urethral instability. This is characterized by urethral sphincter relaxation during bladder filling in the absence of detrusor contraction^{2,1}. The resting external urethral sphincter (EUS) activity is increased and fails to relax completely during voiding.

Disorder of sleep

According to a sleep study research conducted at the famous McGill University of Montreal Canada, enuresis is primarily due to sleep disorder^{1,5}. The enuretic cannot be awakened by the signal of full bladder at the deep sleep stage. A higher incidence of defective arousal mechanisms and sleep related breathing disorders i.e. obstructive sleep apnea (OSA) have been found in children with PNE^{1,4,1,6}. Similarly, patients with (OSA) have increased urine output and increase atrial natriuretic peptides (ANP) at night^{1,7}.

Psychological stress^{1,5,1,8}

Stress and anxiety are common cause of SNE^{1,5,1,8}. Stressful events occurring early in childhood (3rd, 4th year) have been shown to be associated with enuresis later in life. The chance of enuresis is proportional to severity and number of stressful events². These stressful include separation from mother or parents, broken home through death or divorce, birth of young sibling, moving house, repeating a new term in school, prolonged hospital admission, accidents, surgery, social deprivation, sexual, physical abuse and child neglect and malnutrition. Although the stress may be transient, the symptoms of enuresis persist long enough generating, more anxiety, and creating a vicious cycle.

Psychiatric illness

Enuresis may be associated with some psychiatric disorder and vice versa^{1,9,2,0}. Behavioural disturbances are common in children with DE, particularly the boys. They include attention-deficit hyperactivity disorder, autism and antisocial behaviours such as faecal soiling. Behavioural and psychosocial disorders are more prevalent in SNE compared to those with PNE, who are usually better adjusted socially.

Organic causes

Organic disorder are less common causes of enuresis. SNE is more likely to be associated with an organic cause than PNE².

They include urinary tract infections (UTI) and some other urinary tract abnormalities^{11,1,22,32,4}. Enuresis is the presenting symptom in 15% of children with nocturnal enuresis have a high incidence of UTI (5 - 10%)^{2,1}. Girls seem to be particularly prone to infection induced enuresis. About 50% of the girls over the age of 5 years with daytime wetting were found to have UTI¹¹. UTI is a more common feature of DE than NE. Urinary tract abnormalities such as congenital or acquired minor urethral obstruction of the bladder neck (meatal stenosis, small bladder calculi and anterior urethral valve) may cause enuresis, due to resultant hypertrophy and irritability of the bladder, with overflow incontinence^{1,2}. Ectopic ureter, pelvic masses, such as presacral teratoma, hydrocolpos, or faecal impaction, which compress the bladder, may also cause daytime wetting with incontinence. Others include Diabetes mellitus diabetes insipidus, and chronic renal failure by causing polyuria, hyperthyroidism and seizure disorders (epilepsy)^{2,1,2}. Poorly adjusted sickle cell disease may also cause enuresis due to urinary concentrating defect as well as stress of frequent hospital admissions.

Diagnosis

This requires a detailed medical history, comprehensive physical examination, and examination of the urine among other investigations^{1,5,1,2}. **History:** The parents and child need to be interviewed separately to achieve the necessary opportunity to obtain history of worries and stress in the family. Specific questions should be asked systematically to establish the type of enuresis (PNE, SNE, DE) and the possible causes (s) such as sleep pattern, snoring (OSA), fluid intake, psychiatric disturbances, dysuria, polyuria, polydipsia, urgency, constipation, pollakiuria. Family history of enuresis and previous treatment (s) including use of herbs, orthodox interventions and punitive measures should be explored.

Physical examination: The examination is unlikely to reveal any abnormality, particularly if the history is unexceptional. However, it is therapeutic and reassuring to all parties. Through general and systemic examinations including anthropometrics measurements (height, weight and growth velocity) for suspected chronic renal failure, neurological and rectal examinations. Blood pressure measurement is necessary.

Investigations: Various diagnostic tests may be performed to determine the cause of enuresis^{1,2,1,22,1}. However, in view of the natural tendency for the condition to improve with age, the extent of investigations should be carefully considered. The only obligatory investigation is urine examination. Urinary tract infection should be excluded in all patients, but additional investigations are warranted unless there are accompanying symptoms. Anatomical/physiological assessments of the urinary system using abdominal ultrasound, micturating cystometry, sphincter electron myography, and uroflometry may be done in suspected urinary tract abnormalities. Spinal x-ray, magnetic resonance imaging, myelography and computerized tomography scan are done in few cases^{1,22,1}.

Treatment

The goals of treatment are to reduce the social and psychological impact of enuresis, and also eliminate the cause

(S)^{1-5, 22, 1}. The therapeutic approach depends on the age of the patient, the effect on the problem on the patient and the parents' attitude.

Behavioural modifications:

Behavioural modifications are not very effective in controlling enuresis when used alone. Psychotherapy is helpful in SNE because of the numerous psychosocial problems associated with it^{5, 12}. The parents and child should be reassured that the condition might be self-limiting. The use of gifts as rewards for dry nights, chart and stars (Placebo) are effective in 10% of enuresis^{5, 6, 12}. Punishments are not entertained because they adversely affect the psychological development of the child. Studies have shown then lifting and periodically waking the child onto potty does not train the child^{2, 5, 23, 6}. Interval training is effective for daytime urinary frequency. The child is encouraged to void every 30 minutes, while increasing the interval by half an hour until the child can manage longer intervals of 3 or 4 hours. Restriction of fluids late in the day and voiding before bedtime may be helpful^{3, 23, 6}. Alarm therapy (Audio or vibratory): Enuresis alarms are the most popular form of conditioning therapy. It is recognized in UK as the only therapy capable of effecting a long term 'cure' of enuresis^{5, 2, 12, 5, 2, 7}. It is the safest, most successful and cost effective method of curing enuresis. They are known by many titles: "bell and pad", "buzzer alarm", "bed buzzer", and "conditioning therapy". There are two main types of wearable moisture sensor alarms in use for nocturnal enuresis. In one a detector mechanism such as mesh or foil pads are connected to an alarm buzzed placed by the bed, out of the child's reach. The other uses a wet-detector strip attached to the child's pants and connected to an alarm worn on the child's wrist or shoulder. The mechanism is triggered by voided urine completing the electrical circuit, and then the alarm goes. A noncontingent buzzer, which rings at intervals of 1-2 hours, is used for daytime wetting. Alarms are most successful for older co-operative children above 7 years of age⁸, although, parental and child motivation is required. The success rate is 70-85% with dryness achieved within 4-12 weeks. The different devices available are WET - STOP, Malem or ULTIMATE Bedwetting Alarm, Ferris Audio MULTITONE, Vibrawake ALARM WITH INTEGRAL VIBRATION (Model DPI, DP2, SMI-M)^{2, 6, 2, 7}. Alarm system is more efficient than pharmacological treatments in NE but unfortunately they are not available in our environment.

Pharmacological treatment:

Drug therapy is limited to older children with no success to non-pharmacological treatment, those with urgent need to achieve dryness due to social reasons or in a child whose self-esteem is being eroded^{1-5, 7, 3, 2}. They include the following: Desmopressin acetate (DDAVP): it's an antidiuretic hormone and a synthetic analog of vasopressin. It increases distal tubular retention of filtrates, hence reduces nocturnal urine production. It facilitates arousal in human, increases motor activity and stabilizes unstable bladder in rats⁵. Response is more in patients with a family history of nocturnal enuresis (91% vs 71%) and a high nocturnal urine output^{2, 8}. It is effective in 50 - 80% of PNE. The route of administration is oral (0.2-0.6mg daily, at bedtime) or intra nasal spray (10-40mcg daily, at

bedtime). A high relapse rate is reported on discontinuation of the drug. Minor side effects noted include headache, mild abdominal cramp, nausea, nasal congestion, epistaxis and water intoxication if fluid is not restricted^{1-5, 7, 3, 2}. DDAVP offers better short term results than alarm system but the latter is significantly more efficient. Oxybutynin chloride (Levsin) and Tolterodine: These are anticholinergic drugs, that reduce unstable detrusor contractions and hence increase bladder capacity. They are found beneficial in bladder instability or bladder dysnergy causing DE, urinary frequency, urgency and incontinence. The daily dose is 2.5-5mg at bedtime. Side effects include blurred vision, constipation, dry mouth, facial flushing, and fluctuation in mood^{5, 7, 1, 2}. Imipramine (Tofranil): A tricyclic antidepressant; affects sleep arousal and premature contractions of the detrusor (Anticholinergic effect). It treats PNE in (10-60%) of cases. It has a high relapse rate after withdrawal (40-60%). Its use is limited to older children and adolescents, at a dose of 1-2.5mg/kg taken 1 to 2 hours before bed. Overdose can be fatal^{5, 7, 1, 2}. As a result WHO disapproves of its use for nocturnal enuresis^{1, 2}. Oral antibiotics (e.g Bactrim, amoxicillin, cephalosporins, trimethoprim, nitrofurantoin and nalidixic acid) are useful for urinary tract infections^{3, 7, 8}. The duration of treatment range from 5 - 7 days^{1, 7, 8}. Presence of vesicoureteric reflux will require low-dose prophylactic antibiotics (trimethoprim or nitrofurantoin at 1 - 2mg/kg) given only at night until resolution of reflux^{3, 8, 9}. Other treatments include hypnotherapy for detrusor instability, chiropractic with Gonstead adjustment of the spine for PNE^{2, 9, 3, 1}, surgery-including implantation of an artificial urinary sphincter in selected children with incontinence^{8, 2, 1}. Exercises (kegel) or Biofeedback training of pelvic muscles and clean intermittent self-catheterization (CISC), done 4-6 times in a day for older patients (above 7 years) with manual dexterity^{2, 1}.

PROGNOSIS

This depends on the cause. Some studies reported spontaneous cure rate of 15% year in NE, with an overall 70-80% success rate following adequate treatment in compliant patients^{5, 7}.

Acknowledgement

The author is highly indebted to Professor F Eke for advice and contributions and to Professor K E O Nkanginieme for correcting the manuscript.

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