Nocturnal Enuresis: A Novel Concept on its Pathogenesis and Treatment

October 10, 2010
By OBGYN.net Staff [1]

Urinary continence depends on two main factors, one inherent, and one acquired.

View the accompanying educational tutorial: Nocturnal Enuresis: An Update on the Pathogenesis and Treatment

Introduction

Urinary continence depends on two main factors, one inherent, and one acquired.

1) The inherent factor is the presence of an intact and strong internal urethral sphincter, which is a collageno-muscular tissue cylinder that extends from the urinary bladder neck to the perineal membrane in both sexes, males, and females.

2) The acquired factor, (second stage of micturition) is an acquired behavior gained by learning and training in early childhood, how to maintain a high alpha sympathetic tone at the internal urethral sphincter keeping it closed all the time till voiding is needed and/or desired.

Failure to gain that acquired behavior, complete failure, or partial failure, will lead to diurnal/nocturnal enuresis, or nocturnal enuresis, respectively.

There is usually, as well, lack of nor-epinephrine in the nervous system, which explains why those patients fall rapidly into deep sleep.

Treatment is by giving alpha-sympathomemtics, e.g. ephedrine hydrochloride tablets. Ephedrine HCL is an alpha-sympathomemtic which has dual action, it acts on the receptors as agonist, and in addition, it stimulates the alpha nerve endings to secrete nor-epinephrine.

Nocturnal Enuresis: A Novel Concept on its Pathogenesis and Treatment

Nocturnal enuresis means uncontrolled urination at night after the age of 5 years in girls and 6 years in boys.

It is more frequent in boys than girls, a ratio of 2:1 reflecting developmental variations.

Enuretics have been divided into: primary and secondary, this depends on whether continence has ever been achieved.

About 10% of all patients suffering from enuresis also wet in the daytime.

There is a strong familial aspect to enuresis:
If both parents have a history of enuresis, there is an approximately 75% chance that 1 or more of their children will be enuretic.

If one parent had enuresis there is about a 40% chance that a child in that family will be enuretic.

If neither parent was enuretic, the risk decreases to 15%.
In the infant, micturition occurs spontaneously as a spinal cord reflex.

The young infant sleeps for almost 60% of the day, and approximately 40% of the voids occur during sleep. (1)

**Pathogenesis:**

Nocturnal Enuresis is a multifactor condition, the theoretical causes include:

1) Premature training  
2) Insufficient training  
3) Emotional disturbance  
4) Alteration in circadian antidiuretic hormone, (ADH) secretion  
5) Sleep disturbances  
6) And / or a delay in adequate neuromuscular bladder control. (1-7)

Rarely physical lesions may be found in enurtics, such as:

1) Spina bifida, manifesta, or occulta.

Obstructive lesion of the distal urinary outflow tract, such as:

2) Urethral valve or urethral stenosis.  
3) Urinary tract infection.  
4) Diabetes Mellitus.  
5) Diabetes insipidus.  
6) Chronic renal disease.  
7) Nervous system dysfunction.

In infancy micturition is controlled at the spinal cord level, with little influence from the higher centers; thus when the bladder is full it will spontaneously empty with no thought for the time and place.

Under normal circumstances bladder training starts in most children between the age of 18 and 24 months, and is usually completed by the age of 3-4 years.

Accidents of bed wetting should be tolerated until the age of 5 years in girls, and 6 in boys.

Accordingly, treatment of nocturnal enuresis is to treat organic causes if found; if no organic lesion is the cause, several many trials of treatment by drugs, alarm devices, behavioral therapy, and even psychiatric support and treatment were tried without good results.

**Classic treatment by drugs is one of:**

1) Imiprmine hydrochloride, (Tofranil).  
2) Desmopressin acetate, (Minirin) nasal spray or tablets.
3) Anticholinergic drugs e.g., emeponium bromide (Cetiprin).

Recently, in 1996 we put forward a new concept, based on evidence explaining the act of micturition and urinary continence. (8, 9)

**Micturition can be divided into 2 stages:**

- **Stage-I:** in Infancy before bladder training.
- **Stage-II:** is the acquired stage of micturition. It is acquired in childhood by learning and training; (the stage where the mother trained her child, how to control voiding).

**The Second stage of micturition, (how to control):**

It is an acquired behavior gained by learning and training in early childhood how to maintain a high alpha sympathetic tone (thoracic 10 to lumbar 2) at the internal urethral sphincter, thus keeping it closed all the time until voiding is needed and/or desired.

**Urinary continence depends on two main factors:** (9-17) *One inherent, and **One acquired.

1) *the inherent factor:

Is the presence of an intact and strong internal urethral sphincter.

The internal sphincter is a collageno--muscular tissue cylinder that extends from the bladder neck down to the perineal membrane.

2) **the acquired factor: (Second stage of micturition)

It is an acquired behavior gained by learning and training in early childhood how to maintain a high alpha sympathetic tone, (T10-L2), at the internal urethral sphincter, thus keeping it closed all the time until voiding is needed or desired.

Functional disturbance, and/or Structural damage, of the internal urethral sphincter will lead to Urinary incontinence. (17)

Functional disturbance, there is 3 possibilities:

1) Failure to gain the acquired behavior of having high alpha sympathetic tone, completely, or partially will lead to Nocturnal Enuresis, (with or without diurnal enuresis).

2) Sympathetic over activity, e.g., caused by pain e.g. episiotomy; spinal cord lesions e.g. disseminated sclerosis, or systemic lupus erythematosus, causing pelvic parasympathetic paralysis and sparing the thoraco-lumbar sympathetic system will lead to Retention of urine, Overflow incontinence.

3) Sympathetic failure e.g., severe fear, deep anesthesia, drugs,(alpha sympathetic blockers) will lead to transient urinary incontinence.

Failure to gain the acquired high alpha-sympathetic tone (T10-L2) will leave micturition as a spinal cord reflex, as in early infancy and the full bladder will empty spontaneously. (= complete failure.)

This condition is rather rare; enuresis will be by both day and night. This accounts for about 10% of all enuretics.
More frequently there is a partial gain of alpha-sympathetic tone, which will be sufficient for good control and urinary continence during the daytime but it will fail during sleep.

There may be no sleep disturbance, but falling asleep will cause loss of the rather weak control over the internal urethral sphincter, allowing uncontrolled emptying of the bladder. (Nocturnal Enuresis = Partial failure. This accounts for 90% of all the enuretics.

The treatment, therefore, will be giving alpha-sympathomimetics and not anti-cholenergics.

Giving an alpha-sympathomimetic drug e.g., ephedrine hydrochloride, this will increase the tone of the internal urethral sphincter, thereby preventing uncontrolled urination.

Ephedrine is a non-catechol amine sympathomimetic drug that has a dual action:

1) It acts on the sympathetic receptors, as a stimulant, (agonist).
2) It also stimulates the alpha nerve endings to induce production of nor-epinephrine.
3) Ephedrine may also stimulate the sleep centre, preventing rapid falling into deep sleep.

It is the second action, (stimulating the alpha-sympathetic nerve endings to produce nor-epinephrine), that cause complete cure after giving the drug for a period that varies from two to twelve weeks according to the age of the patient and the severity of the condition.

Occasionally, there is a concomitant stool incontinence, which requires longer period of treatment with the drug.

Dosage:

Ephedrine hydrochloride tablets, taken orally after meals 3 times daily for 1-2 weeks, (according to severity of the condition), followed twice daily for another 3-5 weeks. The evening dose must be taken at bed time, and not early after dinner, to avoid its analeptic effect.

The dose is 30 mg each time for those patients who are 10 years or younger, and is 60 mg each time for those patients who are older than 10 years.

There may be a remission while taking the medicine, this may be due to exhaustion of the nor-epinephrine stores at the nerve endings, and continuing taking the drug will produce cure of the illness.

At birth the parasympathetic system is the dominant division of the autonomic nervous system.

As one grows up, repeated everyday life stresses increase the sympathetic tone, which gradually takes the upper hand.

This explains the reports of an annual spontaneous cure rate of about 15% in those suffering nocturnal enuresis. (18)

However nocturnal enuresis may persist into adolescence and adult life.

Side effects of ephedrine, as:

1) cardio-vascular stimulation will be minimum effects because of the young age of the patients with their healthy, elastic, high capacity and highly adaptable compliant vessels and heart.

Other side effects, as:

2) Nervous system stimulation, an analeptic effect, is an advantage as those patients are usually deep sleepers. However, it can be avoided by giving the evening dose at bed time.
Other minor side effects include:

3) Anorexia and upper abdominal discomfort usually disappears after few days spontaneously.

4) Occasional slight frontal headache can be relieved by simple analgesics.

References:

11) Abd el Karim M. El Hemaly, Ibrahim M Kandil, Mohamed M. Radwan Urethro-raphy a new technique for surgical management of Stress Urinary Incontinence
http://www.obgyn.net/urogynecology?page=urogyn/articles/new-tech-urethro
http://www.obgyn.net/urogynecology?page=urogyn/articles/urethroraphy-092804
http://www.obgyn.net/urogynecology?page=/English/pubs/features/presentations/El-Hemaly02/el-hemaly02-ss
17) Abd el Karim M. El Hemaly Urinary incontinence in gynecology, a review article http://www.obgyn.net/urogynecology?page=/urogyn/articles/abs-urinary_incontinence_gyn_ehemaly

**Source URL:**

**Links:**