NOCTURNAL ENURESIS IN CHILDREN

Gong Wei Kin, Yap Hui Kim

Nocturnal enuresis (NE) is a very common problem in childhood. Traditionally, there has been a lack of interest in this condition from the medical profession and the public, as it was perceived as part of “growing-up”. Unfortunately, when it persists beyond early childhood, it can be very stressful and distressing to the affected child as well as the family members. Recent advances in our understanding of the pathophysiology of NE have enabled us to design a management guideline for children with NE.

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- Incidence
- Pathophysiology
- Classification of NE
- Indications for treatment
- Clinical approach
- Treatment
DEFINITION

1) Nocturnal enuresis
   Involuntary voiding of urine during sleep of more than 3 times a week in healthy children above the age of 5 years.
   a. Primary NE
      - never been dry for an extended period of more than 6 months.
   b. Secondary NE
      - previously consistently dry for at least 6 months.

2) Diurnal voiding symptoms (DVS)
   Some children with NE have additional DVS. These include urinary frequency, urinary urgency, urge incontinence, hesitancy and interrupted stream.

3) Monosymptomatic NE
   Enuretics with perfectly normal voiding pattern during waking hours.

INCIDENCE

- Unknown in Singapore. Under-reported
- 6 – 15 % incidence in Western countries
- Prevalence decreases with age, to about 0.5 – 1.0 % in adulthood
- 15 % of enuretics achieve nocturnal bladder control per annum

PATHOPHYSIOLOGY OF NOCTURNAL ENURESIS

NE can be a result of the following:
1. Too much urine production at night
   - Studies have shown that there is a lack of nocturnal surge in the plasma levels of vasopressin or anti-diuretic hormone (ADH) in enuretics compared to non-enuretic children, thus causing relative nocturnal polyuria.

2. Small nocturnal bladder capacity
   - Detrusor overactivity during sleep has been observed in a significant number of enuretics resulting in a reduction in the reservoir capacity of the bladder.

3. Inability of the child to wake up to signals from a full bladder
   - Enuretic children have decreased arousal to a full bladder before micturation occurs.

CLASSIFICATION OF NOCTURNAL ENURESIS

NE can be divided into several subgroups according to history, symptom pattern and response to treatment of desmopressin. Further subgroups may emerge in the future when more information is available about the genetic component of NE.
Table 1. Differentiation between subtypes of NE

<table>
<thead>
<tr>
<th>Time of onset</th>
<th>1) Present from birth (primary NE)</th>
<th>2) Developed after a period of at least 6 months of dryness (secondary NE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatology</td>
<td>1) Night-time symptoms only</td>
<td>2) Combined day-time and night-time symptoms (diurnal NE)</td>
</tr>
<tr>
<td>Presence of nocturnal polyuria</td>
<td>1) Present</td>
<td>2) Absent</td>
</tr>
<tr>
<td>Response to Desmopressin</td>
<td>1) Responder</td>
<td>2) Non-responder</td>
</tr>
</tbody>
</table>

Note: In children with secondary enuresis, urinary tract infection and psychological problems must be excluded.

WHY AND WHEN SHOULD WE TREAT NOCTURNAL ENURESIS?

Nocturnal enuresis should be treated for the following reasons:
- adversely affects the psychosocial development of the child, as it may lower the child’s self image
- constitutes a source of embarrassment and deters the child from healthy outdoor activities like overnight camping and holiday travels
- causes resentment and anxiety in parents and other family members

In Singapore, parents seek treatment because of restricted outdoor activities, parental fatigue, disrupted household sleep and fear of underlying disease.

A child may require treatment if:
1) he/she is above 5 years of age
2) the condition affects his/her normal social and emotional development
3) the condition affects his/her schoolwork

CLINICAL APPROACH TO NOCTURNAL ENURESIS (ALGORITHM 1)

1) Confirm nocturnal enuresis
2) Identify the different subtypes
3) Detailed history and physical examination to assess the child’s drinking, urinary habits (to identify additional diurnal voiding dysfunction), motivation for treatment and previous treatment options. Exclude precipitating psychosocial dysfunction especially in a child with secondary NE.

4) Exclude secondary cause such as urinary tract infection, organic diseases like diabetes mellitus, diabetes insipidus, neurogenic bladder (table 2).

5) Investigations

- urinalysis (dipstick) and culture to rule out urinary tract infection and glucosuria
- urine specific gravity or urine osmolarity when there is significant polyuria

Note: Imaging studies of the urinary tract are generally not indicated, unless the following are present:
   i) Diurnal voiding symptoms
   ii) Evidence of urinary tract infection
   iii) Neurological signs

Table 2. Differentiating causes of bedwetting

<table>
<thead>
<tr>
<th>History and physical examination</th>
<th>Primary enuresis</th>
<th>Secondary enuresis</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day time incontinence with stress</td>
<td></td>
<td>+</td>
<td>ectopic ureter</td>
</tr>
<tr>
<td>Dysuria, frequency, cloudy urine and fever</td>
<td></td>
<td>+</td>
<td>urinary tract infection (UTI)</td>
</tr>
<tr>
<td>Abnormal neurological examination</td>
<td>+</td>
<td>+</td>
<td>neurogenic bladder</td>
</tr>
<tr>
<td>Polyuria</td>
<td></td>
<td>+</td>
<td>diabetes mellitus (DM) diabetes insipidus (DI)</td>
</tr>
<tr>
<td>Encopresis with normal neurological examination</td>
<td></td>
<td>+</td>
<td>psychosocial disturbances</td>
</tr>
<tr>
<td>Child never dry since young, no daytime wetting</td>
<td>+</td>
<td></td>
<td>functional</td>
</tr>
<tr>
<td>Voiding frequently but in small volumes</td>
<td>+</td>
<td></td>
<td>small bladder capacity, detrusor hyperactivity</td>
</tr>
<tr>
<td>Child dry for 6 months, then begin wetting</td>
<td></td>
<td>+</td>
<td>psychosocial disturbance, UTI, DM, DI</td>
</tr>
</tbody>
</table>
Algorithm 1:  Clinical approach and assessment of Nocturnal Enuresis

HISTORY

- Establish the diagnosis of NE
- Primary or secondary
- Presence of diurnal voiding symptoms
- Is there incontinence?
- Urinary symptoms suggestive of UTI

- Drinking habits
- Bowel habits (constipation, encopresis)
- Motivation for treatment
- Family history
- Any psychological stress?

PHYSICAL EXAMINATION

- Signs of renal impairment
- Assessment of kidney and bladder size
- Abnormality of external genitalia
- Spinal abnormalities and associated lower limb neurological deficits
- Abnormality of external genitalia
- Spinal abnormalities and associated lower limb neurological deficits

NOCTURNAL ENURESIS

FREQUENCY URGENCY

POLYURIA SYNDROMES

INCONTINENCE

OFFER TREATMENT

SPECIALIST REFERRAL

TREATMENT OF NOCTURNAL ENURESIS (ALGORITHM 2)

1) Patient education
   - reassurance that it is not a sinister disorder
   - education of the child and the family about NE and the pathogenetic factors
   - advice in lay language and with the help of diagrams as to why enuresis occurs
   - inform about the actions, cost and side effects of the different therapeutic options
   - help them decide which option best suits their lifestyle

2) General measures
   - restrict fluid intake 3 to 4 hours prior to bedtime (after dinner)
   - empty the bladder just before retiring to bed
- encourage the child to make a bedtime resolution to stay dry and to keep a chart of wet and dry nights
- reward for dry nights (positive reinforcement)

Note: **Punitive reaction to the child’s bedwetting should be discouraged.**

3) Bladder training
- useful in those with diurnal voiding symptoms
- encourage child to void at fixed times (about 2-3 hourly) during the day, to develop awareness of bladder fullness

4) Moisture alarm
- alarm triggered by moisture
- dryness due to lightening of sleep stage or to decrease in detrusor activity
- ‘overconditioning’: if child remains completely dry for 3 weeks, “stress” the bladder by drinking water before bedtime, and continue the alarm. If child is able to stay dry, resolution rate can reach up to 80%
- reasons for non-acceptance of alarm: inability to wake, disturbance of family, inconvenient.

5) Desmopressin (DDAVP)
- synthetic analogue of vasopressin or ADH
- decreases urine volume during sleep
- given intranasally or orally ½ to 1 hour before bedtime
- intranasal administration may be a problem in children with allergic rhinitis
- after initial successful response, can be used on an “as need” basis for sleepovers

**Important precaution: advise against drinking water 1-2 hours before administration of DDAVP to prevent water intoxication.**

6) Other pharmacological treatment
- anticholinergics such as oxybutynin are useful as adjunct treatment only if there is detrusor instability
- imipramine is the most efficacious of the tricyclic antidepressants, however, its current use is limited due to the potential for fatal cardiotoxicity
Algorithm 2: Management of Monosymptomatic NE

TREATMENT OF MONOSYMPTOMATIC NE

COUNSELLING
- restrict fluid intake 3 to 3½ hours prior to bedtime
- empty bladder before retiring to bed
- make bedtime resolution to stay dry
- reward and encourage child for dry night
- NEVER take punitive action for wet nights

DDAVP
- Oral
  - 0.2-0.4 mg
  - for at least 1/12
- Intranasal
  - 20 – 40 ug
  - for at least 3/12

ENURESIS ALARM + BLADDER TRAINING

Partial/good response
- ↓ wet nights by >50–100%
- ↓ wet nights by < 50%
- Increase dose
  - 0.4 – 0.6 mg
- Poor response
- Add enuresis alarm
- Good response
- Poor response

ADD DDAVP
- Reassess
- Good compliance
- Poor compliance
- Wet
- Dry
- Continue treatment
  - 3/12 up to 1 year
  - decrease dose to 0.1-0.2 mg (oral)
  - 10 – 20 mg (IN) before discontinuing
  - reassess at 3 monthly intervals
- Dry
- Specialist referral
- Discharge

CONSIDER DDAVP
- Discharge

Good response after 1/12
- ↓ wet nights by < 50%
- ADD DDAVP
- Reassess
- Good compliance
- Poor compliance
- Wet
- Dry
- Re-try alarm

Good response after 3/12
- ↓ wet nights by >50–100%
- OFF ALARM

Poor response after 1/12
- ↓ wet nights by < 50%
- ADD DDAVP
- Reassess
- Good compliance
- Poor compliance
- Wet
- Dry
- Re-try alarm
Table 3. Summary of pharmacological and non-pharmacological treatments

<table>
<thead>
<tr>
<th>Mode</th>
<th>Action</th>
<th>Dose</th>
<th>Comments</th>
<th>Side-effects</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder training</td>
<td>Conditioning therapy</td>
<td>Nil</td>
<td>Useful in patients with diurnal voiding symptoms</td>
<td>Nil</td>
<td>70–80%</td>
</tr>
<tr>
<td>Enuresis alarm</td>
<td>Conditioning therapy</td>
<td>Nil</td>
<td>Useful in patients with decreased sleep arousal</td>
<td>Nil</td>
<td>50–70%</td>
</tr>
<tr>
<td>DDAVP</td>
<td>Decrease nocturnal production of urine</td>
<td>20-40 µg IN 0.2-0.4 mg oral (maximum dose: 0.6 mg)</td>
<td>Useful in presence of nocturnal polyuria</td>
<td>Water intoxication, nasal stuffiness, nausea, seizures, headache, epistaxis, abdominal pain,</td>
<td>50–80%</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Lightening the level of sleep to a full bladder. Anticholinergic effect reduce frequency and amplitude of unstable detrusor contraction</td>
<td>1.5 – 2 mg/kg</td>
<td>May be useful in patients with decreased sleep arousal</td>
<td>Cardiotoxicity, anorexia, poor concentration, sleep disturbance</td>
<td>40–50%</td>
</tr>
<tr>
<td>Oxybutynin</td>
<td>Abolish uninhibited detrusor contraction</td>
<td>2.5 – 5 mg</td>
<td>Useful in patients with frequency-urgency syndrome</td>
<td>Flushing, tachycardia, dry mouth, nausea</td>
<td>Limited success</td>
</tr>
</tbody>
</table>
CONCLUSION

Nocturnal enuresis is caused by a mismatch between
- nocturnal urine production
- functional bladder capacity during sleep
- arousal from sleep when the bladder is full

This can be a difficult problem for the affected child and the family and, therefore, treatment should be considered seriously. The first choice of treatment should be the one most acceptable to the whole family. The treatment strategy must be easy to follow, and allowances should be made for the wishes, motivation and lifestyle of the individual child and his or her family.