Pharmacotherapy for urinary incontinence in children

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According to the current ICCS terminology guidelines:
- DUI: daytime urinary incontinence
- NE: nocturnal enuresis
- Expected bladder capacity (EBC): \([\text{age (yrs)} + 1] \times 30 \text{ ml}\)
- Normal voided volume: 65 – 150% of expected bladder capacity
- Nocturnal polyuria: > 130% X EBC
Daytime wetting
Background for DUI

• Prevalence DUI in children 17%  
  – 20% wet 2 or more times per week  
  
• DUI caused by many different underlying conditions  

• DUI in children associated with urge incontinence in adults  

• DUI impacts quality of life (worse than for NE)
Common causes of DUI

- Overactive bladder*
- Voiding postponement
- Dysfunctional voiding
- Bladder outlet obstruction/bladder neck dysfunction*
- Constipation*
- Vaginal reflux
- Pollakiuria
- Giggle incontinence*
- UTIs, diabetes mellitus, diabetes insipidus
Limited evidence about pharmacotherapy for DUI
Anticholinergics

- Inhibitory effects on detrusor muscle
  - Increase bladder capacity
  - Increase bladder compliance
  - Reduce uninhibited detrusor contractions
- Useful for treating overactive bladder
- May be used in conjunction with other treatments in NE
- Need to monitor for incomplete bladder emptying, constipation
- (More effective with urotherapy and fluids)
Anticholinergics

- Oxybutynin hydrochloride (PBS listed)
  - Potent, side effects in 10%
  - 5mg tablets: bd or tds
  - 36mg transdermal patches: 1/2 to 1 twice weekly
- Tolterodine (off label, limited evidence)
  - Moderately potent, less side effects
  - 1 & 2mg tablets: bd
- Solifenacin (approved for adults)
  - Potent, less side effects
  - 5 & 10mg tablets: once daily
Alpha blockers

- Alpha adrenergic antagonist which relaxes smooth muscle in bladder neck area
- Useful for primary bladder neck dysfunction (incomplete bladder emptying with recurrent UTI)
- Should be prescribed by specialist after urodynamic study
- Prazosin (off label, limited evidence)
  - 1 & 2 mg tablets: (0.5mg daily, increase as necessary)
- Terazosin (off label, limited evidence)
  - Tablets 1-2mg: (0.5mg daily, increase as necessary)

(Donohoe 2005)
Laxatives

• Osmotic Laxatives
  – Macrogols (polyethylene glycol 3350) - for disimpaction and maintenance (daily)
  – Lactulose (bd)
• Faecal softeners
  – Liquid paraffin/mineral oil
• GIT Stimulants
  – Sodium picosulphate (daily)
  – Biscodyl (daily)
  – Senna (daily)
  – Docusate sodium (tds)

(Taste important for children!)

Yazbeck 1987, Norton 2010
CNS Stimulants

- Giggle incontinence ? a form of cataplexy
- Stimulants prevent spontaneous activation of the pontine micturition center in response to laughter
- Useful for true giggle incontinence
- Methylphenidate  
  - Tablets (LA or IA) 0.2-0.5mg/kg daily  
  - Side effects common
Other treatments

• Botox injections
• Treatment for UTI, diabetes mellitus and diabetes insipidus beyond the scope of this talk
Nocturnal Enuresis
Background for NE

• NE is common in childhood
  – 20% 5 yrs → 10% 10 yrs → 3% 15 yrs → 0.5-2% adults

• Contributing factors
  – Poor sleep arousal
  – Nocturnal polyuria
  – Small bladder capacity

• Pharmacotherapy targets these factors
Pharmacotherapy for NE

- Level I evidence (Cochrane systematic reviews)
  - Desmopressin
    - Glazener 2002
  - Tricyclics
    - Glazener 2003
  - Other medications
    - Deshpande 2012
Desmopressin

- Synthetic analogue of pituitary hormone, arginine vasopressin
- Anti-diuretic effect – increased water permeability of renal collecting tubule
- Reduces number of wet nights in 70% children
- No sustained effect when treatment stopped (Glazener 2002)
- Great for sleep-overs (short term)
- Good for 2nd line, treatment failure or combination with other treatments (eg alarm, anticholinergics)
- (Helpful for breaks eg alarm fatigue, menstruation)
Desmopressin

• Formulations:
  – Tablets (200mcg) – max 400mcg
  – Melts (120mcg, 240mcg) – max 240mcg
  – Nasal spray (10mcg/puff) – not recommended

• Importance of fluid restriction

• Timing of medication – best 1 hour before bed

• Never use for daytime wetting (except DI)!
Tricyclics

• Mechanism of action uncertain (?anticholinergic effect)
• One of the earliest medications successfully used for NE
• Modest reduction in wet nights (20% cure), high relapse
• Useful for treatment failure
• Main concerns
  – potentially serious (but uncommon) side effects: cardiac arrhythmias, hypotension, hepatotoxicity, central nervous system depression,
  – interaction with other medications
  – intoxication by accidental overdose
• If prescribing, need ECG monitoring, gradual increase or decrease in dose

(Glazener 2003)
• Anticholergics are often useful in treating NE, particularly in combination with other therapies (eg alarm, desmopressin)
• Other drugs tried found to be not particularly useful
• (We are currently investigating the role of medication to treat sleep problems in NE)

(Despande 2012)
Summary

• Pharmacotherapy has a role in treating urinary incontinence in children. However, drugs alone are often ineffective
• There is good evidence base for pharmacotherapy in NE, but the evidence for DUI is limited
• More research is needed to determine the optimum role for pharmacotherapy in combination with other therapies for treating urinary incontinence in children
References

• Deshpande AV, Caldwell PHY, Sureshkumar P. Drugs for nocturnal enuresis in children (other than desmopressin and tricyclics). Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD002238. DOI: 10.1002/14651858.CD002238.pub2