Anticholinergics in OAB and NMNE

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I have no conflicts of interests
Detrusor overactivity
involuntary detrusor contractions during filling


– 10% in normal children
– >50% in children with VUR

Symptoms:
Urgency
Frequency
Urge-incontinence
Holding maneuvers
OAB?

Uroflow

A.

B.
Monosymptomatic nocturnal enuresis:
bedwetting without any other LUT symptoms

NMNE : Bedwetting + LUTS

Urgency
Frequency
(Urge-) incontinence
Holding maneuvers
Infrequent voiding postponing
Recurrent lower urinary tract infections
Abnormal voiding (Dysfunctional /obstructive)
Associated constipation
Urotherapy

Antimuscarinics
A-blockers:
  – Doxazosin, tamsulosin, terazosin

Tricyclic antidepressant: imipramine

B3-adrenoreceptor agonist
  – Betmiga

Botulinum toxin

Neuromodulation

Reuptake inhibitor of serotonin and norepinephrine
  – Duloxetine
  – Reboxitine
Blocking the binding of acetylcholine at the muscarinic receptors (M₃) => bladder relaxation
EBM in NMNE?
Lower succes-rates than in adults

Oxybutinin
High SAE in children with ADHD
T1/2.... : Doses !
Only oxybutinin is FDA approved for treatment in children

- Disadvantage: multiple side effects (4x more than in adults)
  - Dry mouth (17-97%)
  - Constipation (4-50%)
  - Blurred vision (3-24%)
  - Behavior and concentration problems
  - Headache
  - Fascial flushes
  - Heat stroke
  - Tachycardia

\[ \Rightarrow \] 10% stops treatment
Oxybutinin:

– To bypass the first pass metabolism in the liver:
  • Oxybutinin ER
  • Transdermal patch
  • Intravesical oxybutinin

– Recommended daily dose: 0,3 mg/kg body weight
Medication used in adults and not registered for children:

- Selective M3 bladder specific antimuscarinics
  - Tolterodine
  - Solifenacine
  - Fesoterodine

`\{ \text{Less side effects} \}`
• **Tolterodine** *(Detrusitol):*
  – Well tolerated in children
  – **Doses:** 1mg twice daily *(Hjalmas)*
    * = efficacy as 2mg
    * < adverse events with 1mg
  – **Effective in:**
    * Non-neurogenic overactive detrusor
    * Neurogenic overactive detrusor
**ANTIMUSCARINICS ?**

- **Solifenacine: (vesicare)**
  - Daily doses: 5mg
  - Hoebeke et al. illustrated the safety and efficacy of solifenacin 5 mg daily in children suffering therapy resistant overactive bladder. The overall efficacy was 85%
  - Nadau et al. high subjective and objective success rates in neurogenic detrusor overactivity and refractory detrusor overactivity

- **Fesoterodine: (Toviaz)**
  - Malhotra et al. Oral administration in children > 25 kg with overactive detrusor or neurogenic detrusor overactivity produced steady-state plasma 5-hydroxyl-methyltolterodine exposures similar to those in adults. The doses: 4 and 8mg were well tolerated.
Propiverine

- In some countries approved for use in children
- Recommended daily doses: 0.8 mg/kg body weight

- Marschall-Kehrel et al: overactive bladder in children aged 5-10 year
  - Good tolerability
  - Superior to placebo

- Madersbacher et al: neurogenic detrusor overactivity
  - Better tolerated then oxybutinin
  - As effective as oxybutinin
• Selective stimulation of β-receptors:
  – Mirabegron:
    • β3-adrenergic receptor agonist
    • Not approved in children
    • Minimal adverse events:
      – tachycardia
• LUTS

• In the past
  – **Vesicocentric vision**: the bladder as the centre of all evils when it comes to voiding problems

• At present
  – **Neurocentric vision**: the central nervous system as the primary site for most LUTS in children
CONCLUSION

Only Oxybutinin FDA approved
Large choice of ‘off label’

Very limited evidence in children

Be aware of dosages
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