Refractory enuresis
Future / futuristic aspects

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Desmopressin resistant nocturnal polyuria

1) kidney
2) Compliance
3) Drug characteristics
1. Desmopressin resistant nocturnal polyuria

**Step 1: night time diary**

- 14 days diuresis volume overnight with registration
- weight diaper + morning volume
- On wet + on dry nights
2. Desmopressin resistant nocturnal polyuria

- **Step 1 : night time diary**
  - 14 days diuresis volume overnight with registration
    - weight diaper + morning volume
    - On wet + on dry nights

- **Step 2 : 24 hours urinary concentration prophyle**
  - To differentiate between
    - Deficient concentrating capacity + anti-diuretic effect
    - Deficient anti-diuretic effect despite maximal conc. capacity
  - Only reliable in children who are 7/7 days wet
  - And where correlation between nocturnal diuresis volume of test night with diary registration
Results

U osmol (mosmol/kg)

nighttime                                daytime

TO

dDAVP

Results J.Dehoorne J Urol 2006
2. Desmopressin resistant nocturnal polyuria

**Step 1: night time diary**
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- And where correlation between nocturnal diuresis volume of test night with diary registration
- Increase “sensitivity” by oral fluid intake in the evening >dDAVP
Is fluid-intake dependent
- Up to 50% do not reach U osmol > 850 mosmol/l
- Loss of dDAVP-activity after < 7h
- 30% higher U osmol results in 30% higher diuresis-rate.. And bedwetting

Ann De Guchtenaere J Urology

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2. Desmopressin resistant nocturnal polyuria

- Deficient anti-diuretic effect
  - Nocturnal polyuria = 130% of EBV
  - Relative nocturnal polyuria > Maximal voided volume (within normal range)
2. A. Desmopressin resistant nocturnal polyuria
Deficient concentrating capacity + anti-diuretic effect

- **Deficient concentrating capacity**
  - Normal Urinary osmolality > 850 mosmol/kg during desmopressin
  - Diabetes insipidus is not reaching that level
    - Complete
    - Partial
    - Just < 5 percentile
2. A. Desmopressin resistant nocturnal polyuria
Deficient concentrating capacity + anti-diuretic effect

I. Compliance

1. Increase of compliance: drug intake
   - Regularly contact (nurse, urotherapist, phone, internet)
   - Registration of drugs / prescription
   - Be aware of familial situation
     - Divorce
     - Sports/training

2. Timing of intake: the minimum time to reach maximum concentrating capacity is one hour

3. Voiding before bedtime

4. Avoid fluid intake after / an hour before desmopressin

5. KEY-word = registration in diary

DRIP (C VanHerzeele, J Urology)
2. A. Desmopressin resistant nocturnal polyuria
Deficient concentrating capacity + anti-diuretic effect

II. Pharmacokinetic and dynamic characteristics
Average and maximal urinary osmolality range = +/-2SD

Vande Walle JG et al. BJU Int 2006;97(3):603–9
Duration of action +/- 2SD

Deficient concentrating capacity

J. Dehoorne J Urol 2006

TO LATE

dDAVP

![Graph showing urine-collections in hours (T0= administration dDAVP)]

U osmol (mosmol/kg)

-2 0 1 4 7 10 13 16 19 22

nighttime  daytime

Results

J. Dehoorne J Urol 2006

Deficient concentrating capacity
Deficient concentrating capacity

Results

J. Dehoorne J Urol 2006

TO LATE

ADMINISTER DESMOPRESSIN EARLIER

U osmol (mosmol/kg)

dDAVP

urine-collections in hours (T0= administration dDAVP)

nighttime

daytime

*
Deficient concentrating capacity

J. Dehoorne J. Urol. 2006

U osmol (mosmol/kg)

nighttime                                daytime

-2 TO                            0 TO SHORT

urine-collections in hours (T0= administration dDAVP)
Deficient concentrating capacity

**Results**

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J. Dehoorne J Urol 2006

TO LOW

TO  LOW

Deficient concentrating capacity

U osmol (mosmol/kg)

0

200

400

600

800

1000

1200

1400

dDAVP

nighttime
daytime

Urine-collections in hours (T0= administration dDAVP)
Deficient concentrating capacity

U osmol (mosmol/kg)

nighttime

daytime

urine-collections in hours (T0= administration dDAVP)

TO LOW day + night

dDAVP

*
Results

U osmol (mosmol/kg)

nighttime                                daytime

TO

dDAVP

TO LONG
II. Pharmacokinetic and dynamic characteristics

1. administer desmopressin earlier
2. Increase dose
   1. To maximalise effect
   2. To prolong duration of action
3. Exclude diabetes insipidus (partial)
4. Consider prolonged duration of action
   1. If following oral fluid load in the morning
5. Switch to best biodisponible form : Melt
   1. Superior PK-data
   2. Superior PD-data
   3. Less interference my nutrition
   4. Preferred by young children.

2. A. Desmopressin resistant nocturnal polyuria
   Deficient concentrating capacity + anti-diuretic effect
1. **Reduce fluid intake not only after desmopressine intake, but hour before**

2. **Reduce osmotic load/excretion overnight**
   1. Diet
      1. Especially in the evening
      2. diuretics morning

3. **Influence circadian rhythm**
   1. Prostaglandin inhibitors
   2. Short acting antihypertensives evening
+ Furosemide

A. Deg

**Fig. 1.** Values of diuresis rate (ml per minute) of 4 observation periods plotted as mean ± SD against reference frame of controls for daytime (D1 to D4) and nighttime (N1 to N4) urine collections.
sleep

- Sleep advice
- Melatonine
- “dopamine-analogues”
3. comorbidities

- ADHD, ADD, Autism,…
  - Clear comorbidity
  - Common pathogenetic pathways
  - Amelioration coincides ADHD and enuresis
  - Causality ??? Treatment ??

- Psychological comorbidities
  - Tackle them first

- Constipation
  - Treat this first

- Sleepabnormalities ?
  - sleepadvice
  - Restless legs syndrome ?? Dopamine
  - Melatonine??
4) Therapy resistant (N)-MNE?

- Urotherapy
- Anticholinergics
- Imipramine
- Pelvic floor relaxation therapy
- Biofeedback – uroflow
- Daytime / night time alarm
- Bladder manager
- Neurostimulation
  - Tens
  - Pens
  - Pace-maker (vb Fowler)
4) Therapy resistent (N)-MNE?

- Voiding camps
- Training camps
- Voiding school
5. Voiding school / camps

- A rationalised therapeutic tool
- based on a rationalised diagnostic screening
- by a multidisciplinary team
- in a “school-structure”
- for a therapy resistant population.
  - nocturnal enuresis
  - diurnal incontinence
  - small bladders
  - dysfunctional voiders
Conclusion

- Keep it simple when it is simple
  - In primary care
  - But dare to speak about therapy resistance
- Need for multidisciplinary tertiary enuresis teams
  - For therapy-resistant cases (NMNE and MNE)
- Need for further research