

Refractory enuresis

Future / futuristic aspects

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Desmopressin resistant nocturnal polyuria

- 1) kidney
- 2) Compliance
- 3) Drug characteristics

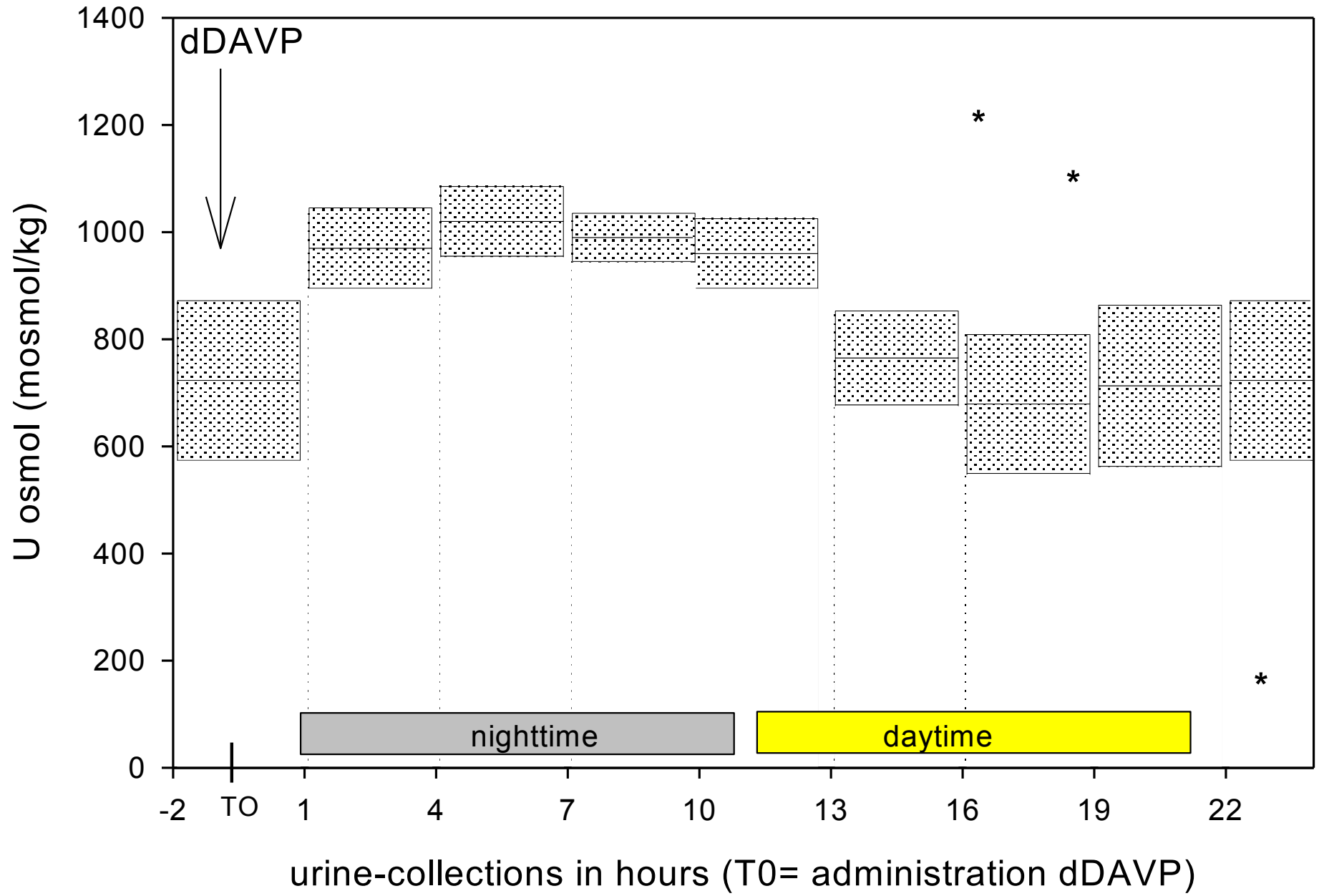
1. Desmopressin resistant nocturnal polyuria

- ➔ **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

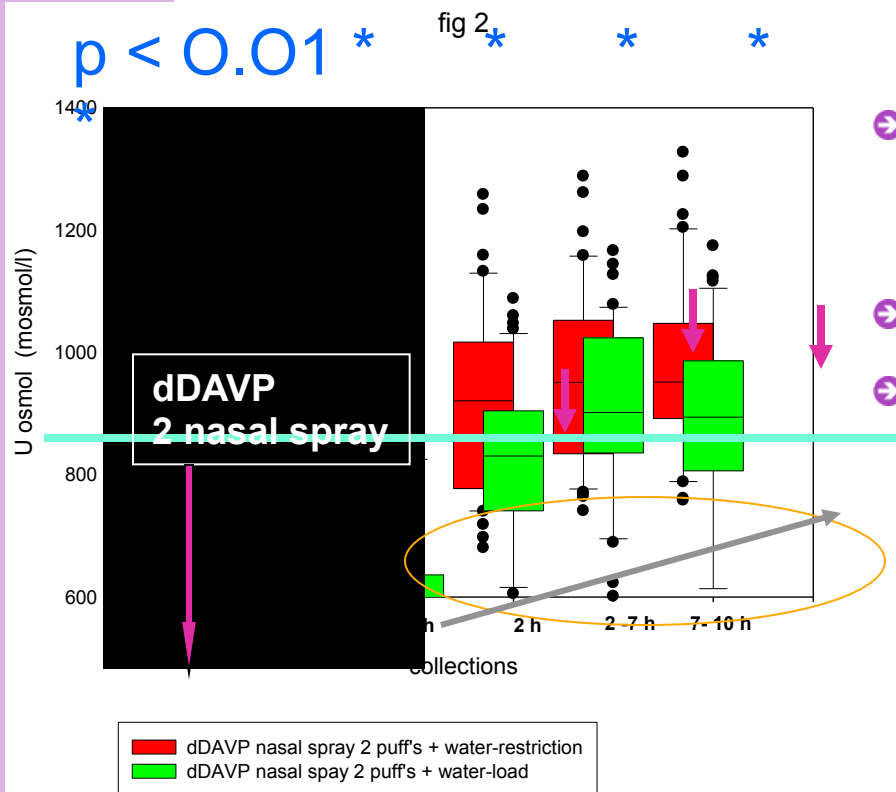
- ➔ **Step 1 : night time diary**
 - ➔ 14 days diuresis volume overnight with registration
 - ➔ weight diaper + morning volume
 - ➔ On wet + on dry nights
- ➔ **Step 2 : 24 hours urinary concentration prophyle**
 - ➔ To differentiate between
 - ➔ Deficient concentrating capacity + anti-diuretic effect
 - ➔ 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



2. Desmopressin resistant nocturnal polyuria

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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)

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

DRIP (C VanHerzeele, J Urology)

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**

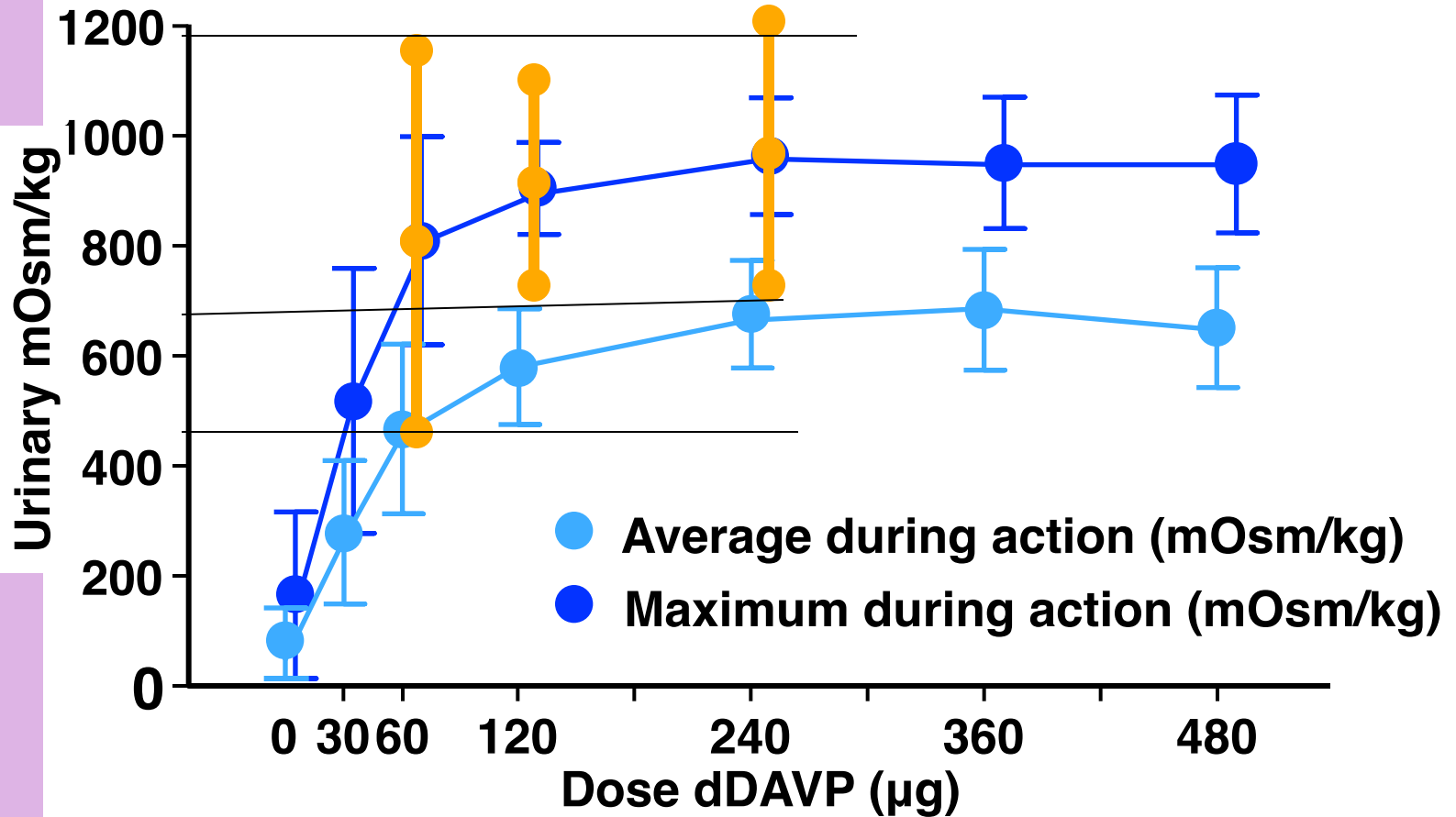
4. **Avoid fluid intake after / an hour before desmopressin**

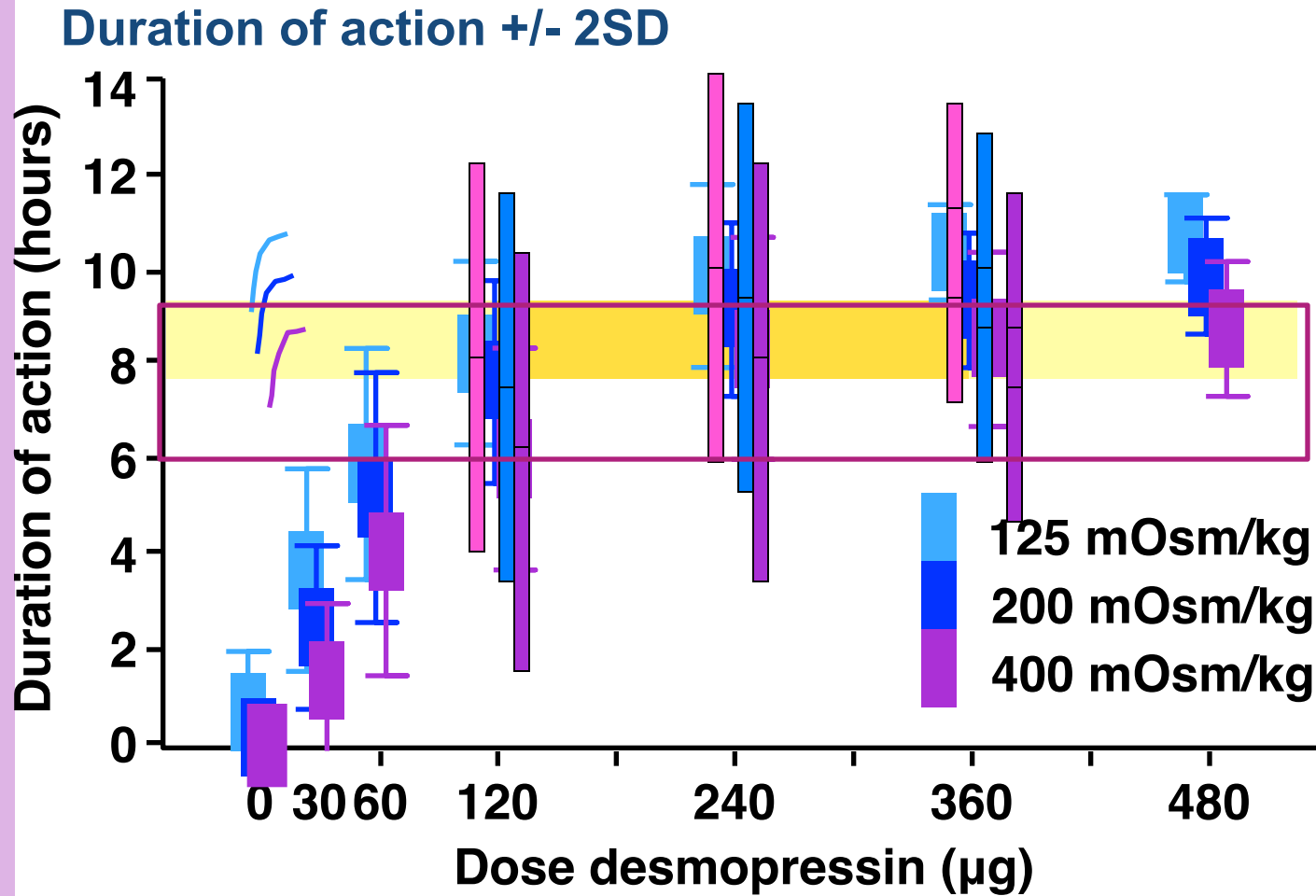
5. **KEY-word = registraton in diary**

2. A. Desmopressin resistant nocturnal polyuria **Deficient concentrating capacity + anti-diuretic effect**

II. Pharmacokinetic and dynamic characteristics

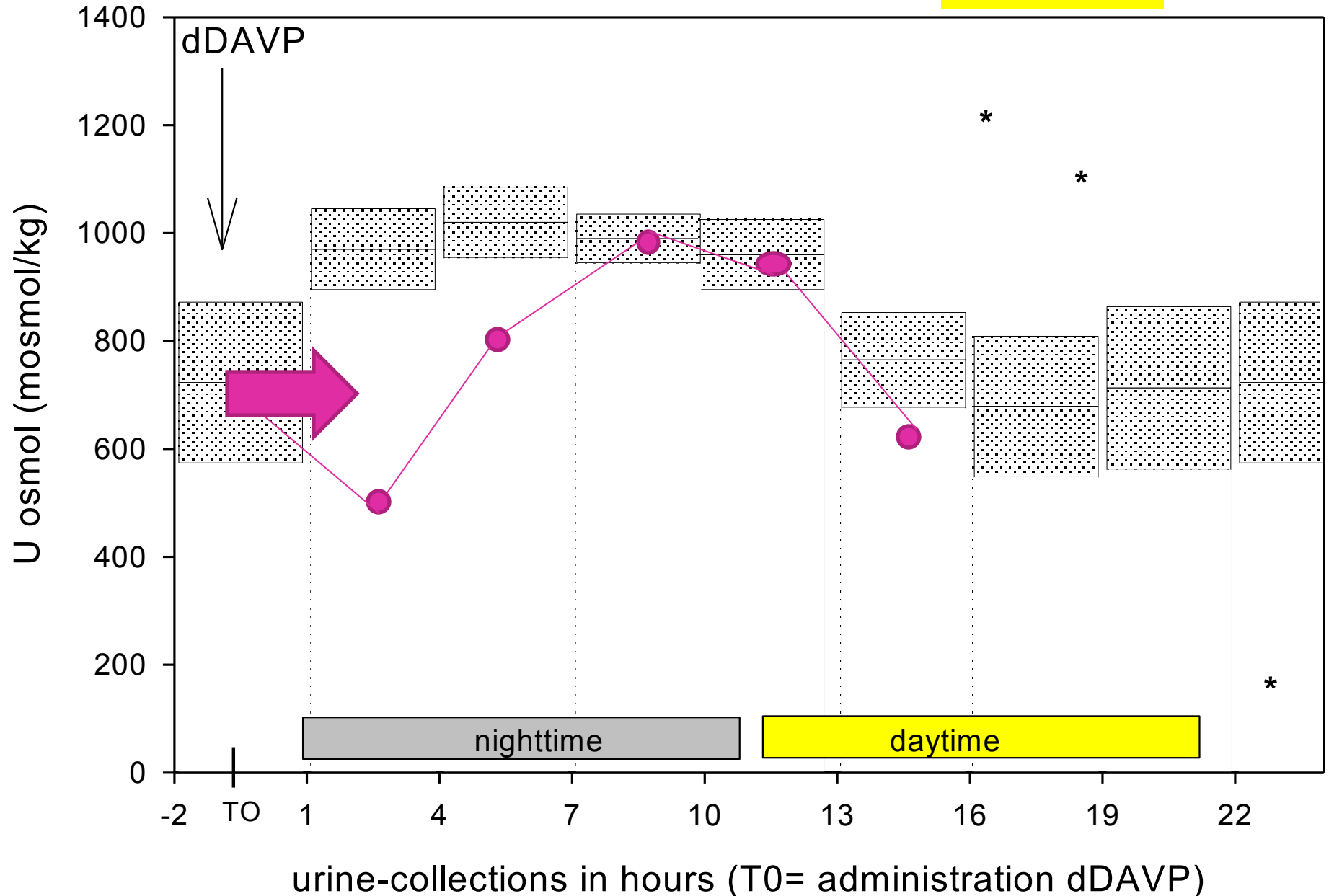
Average and maximal urinary osmolality range = +/-2SD





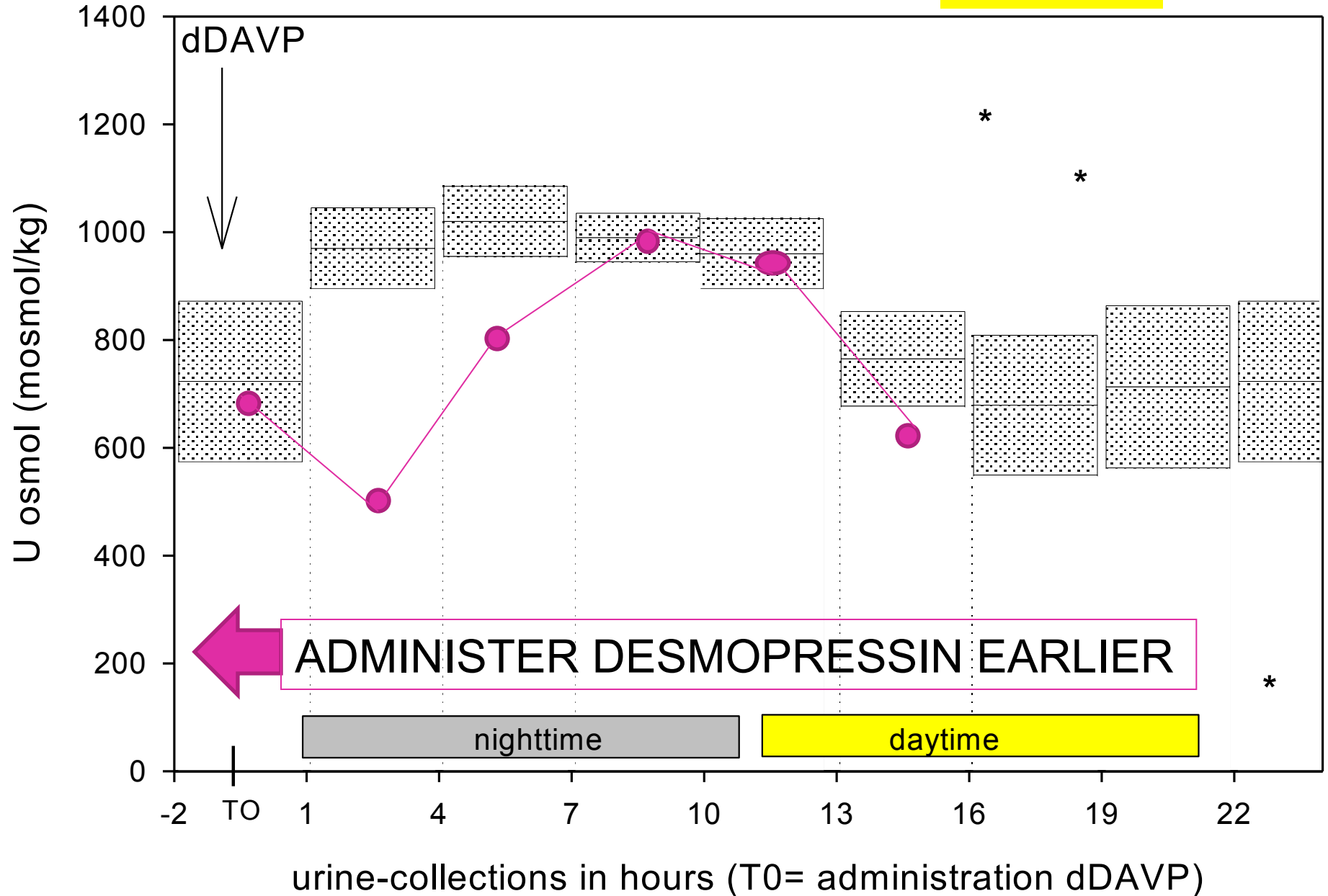
Deficient concentrating capacity

TO LATE



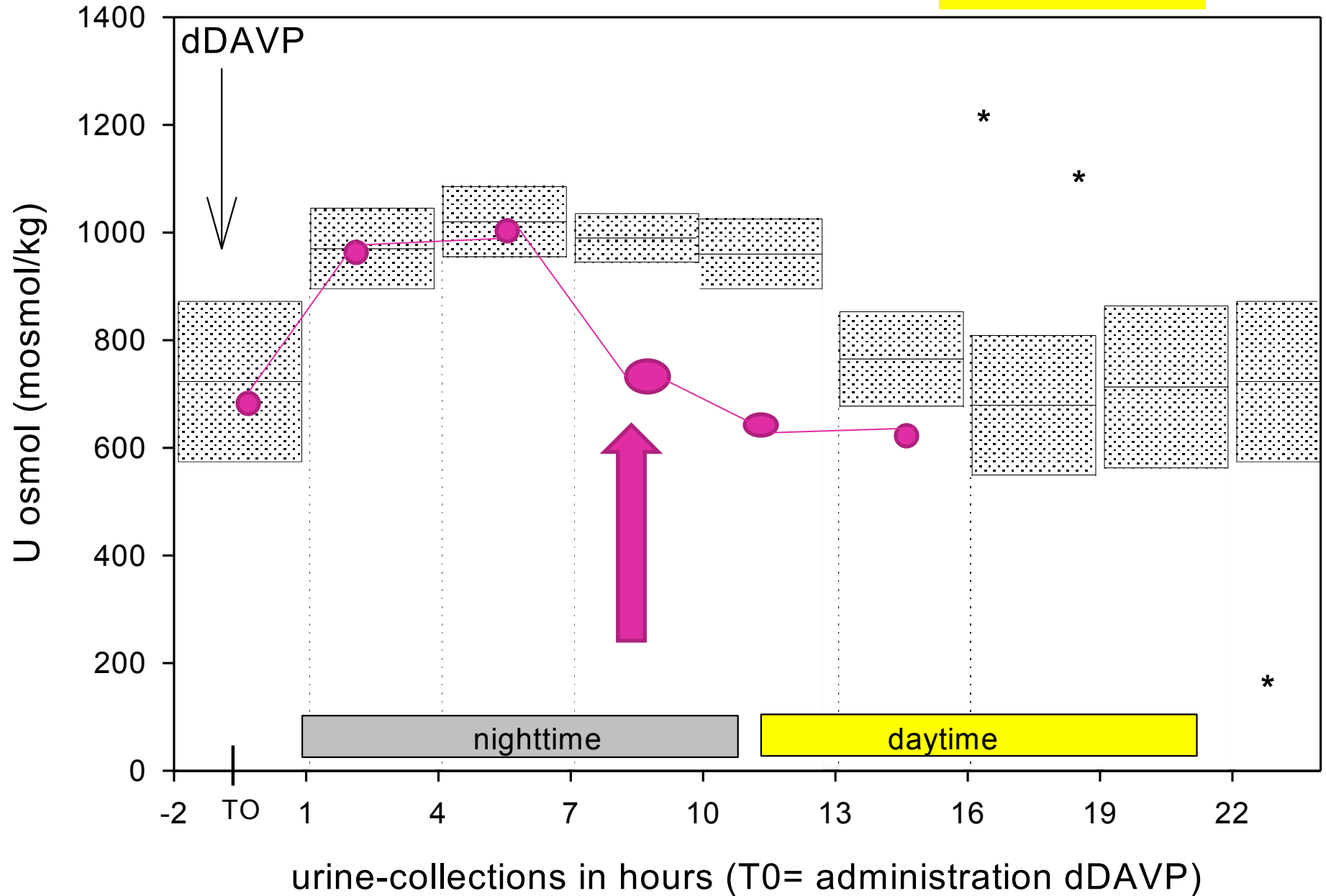
Deficient concentrating capacity

TO LATE



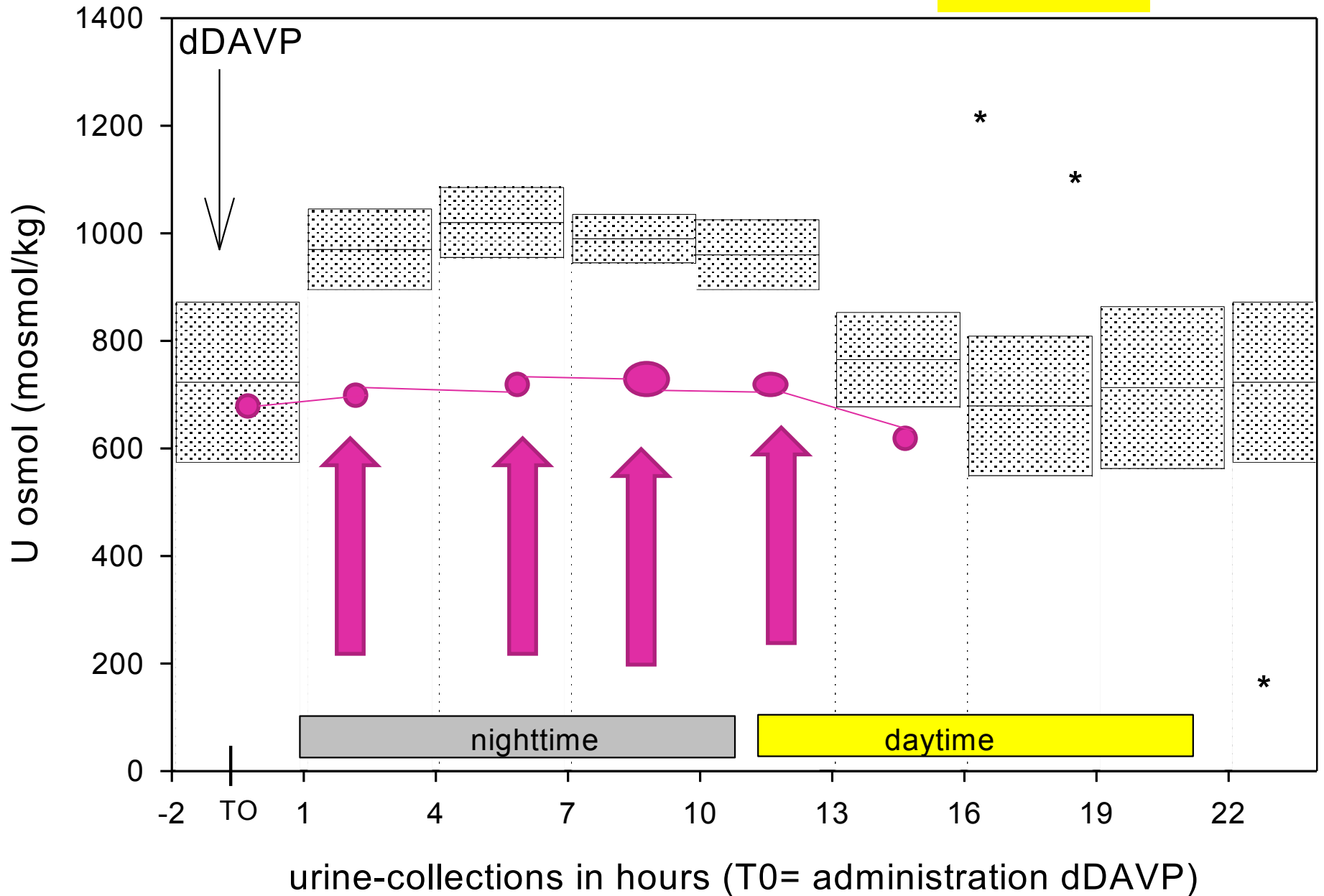
Deficient concentrating capacity

TO SHORT

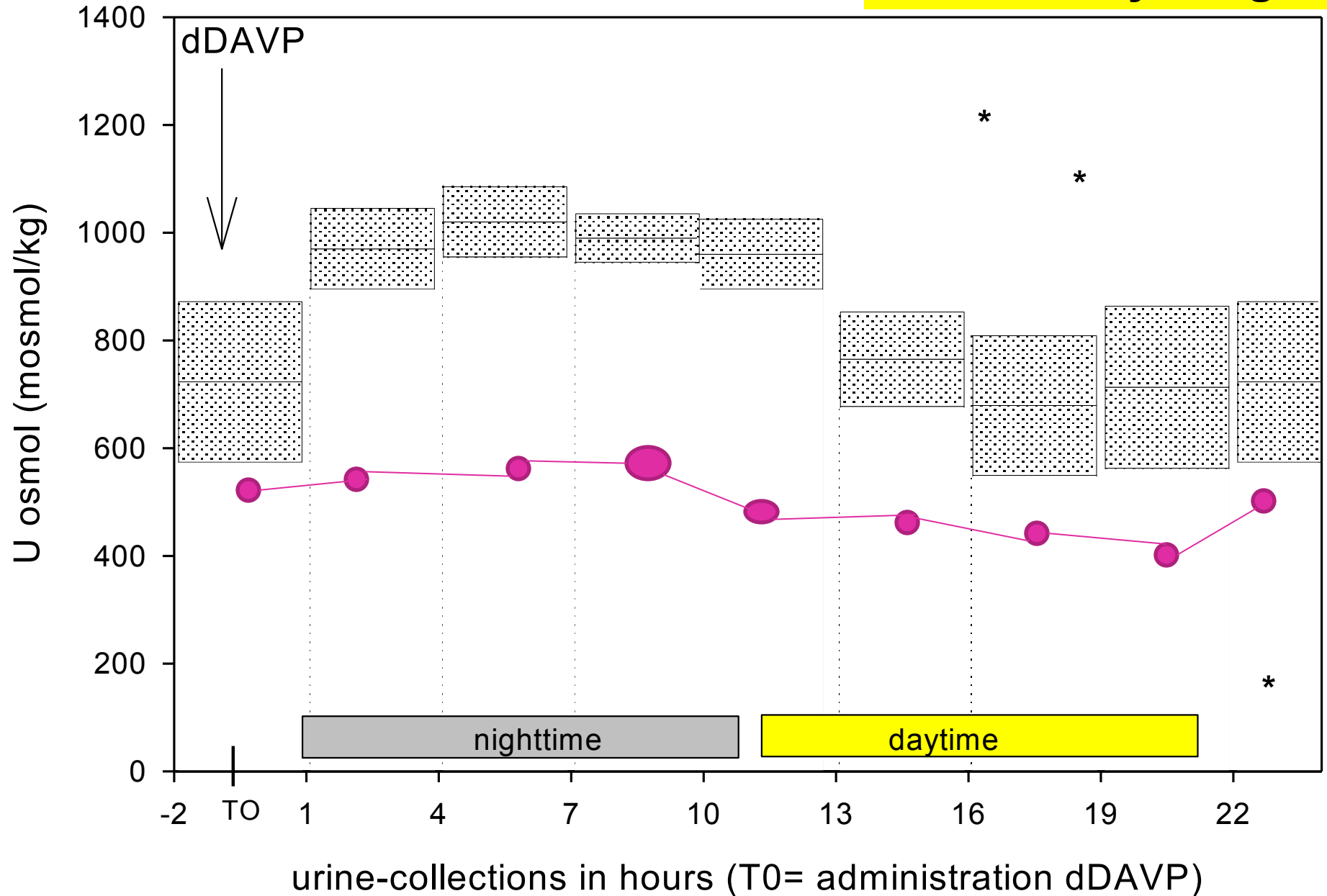


Deficient concentrating capacity

TO LOW

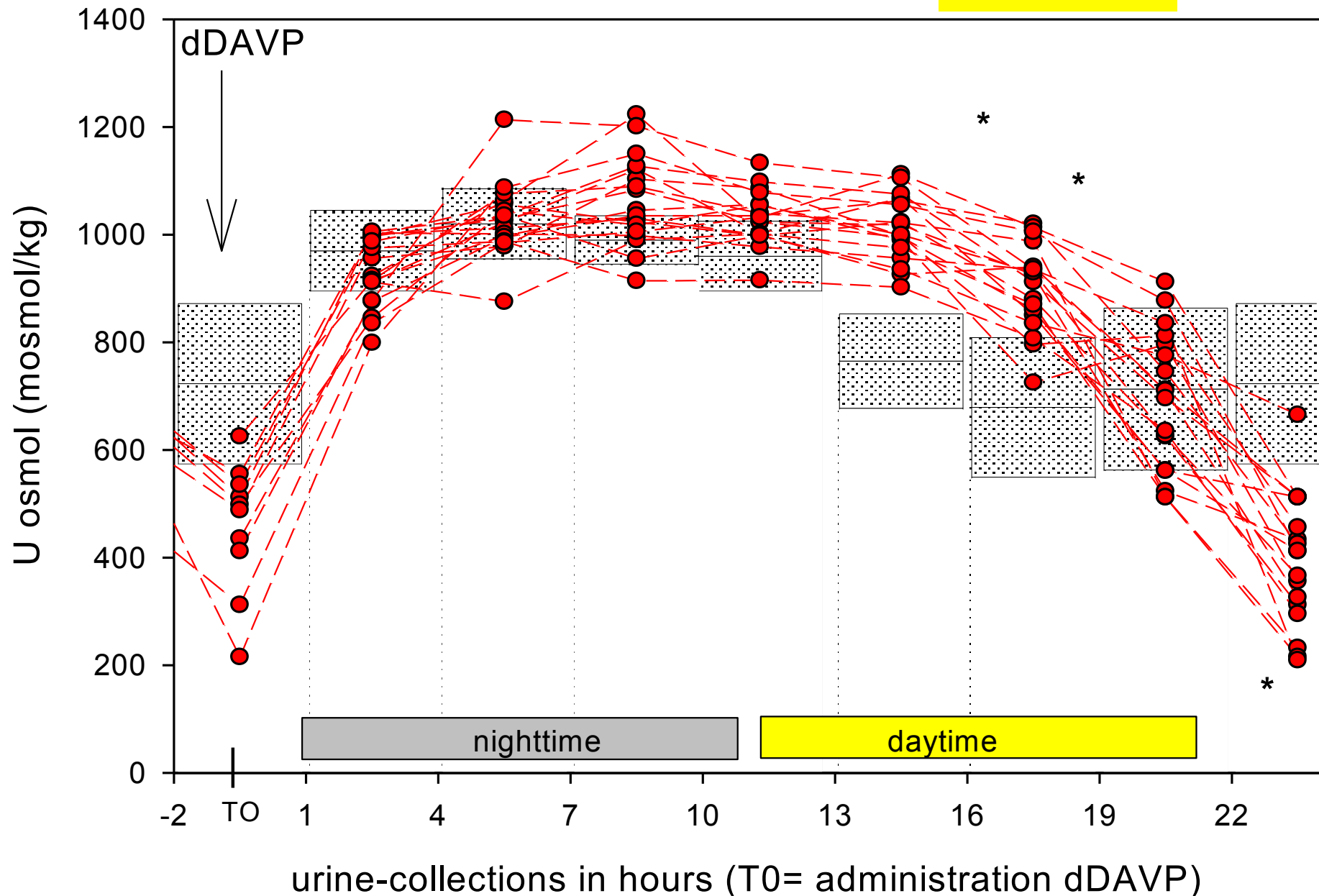


TO LOW day + night



Results

TO LONG



2. A. Desmopressin resistant nocturnal polyuria **Deficient concentrating capacity + anti-diuretic effect**

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.

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

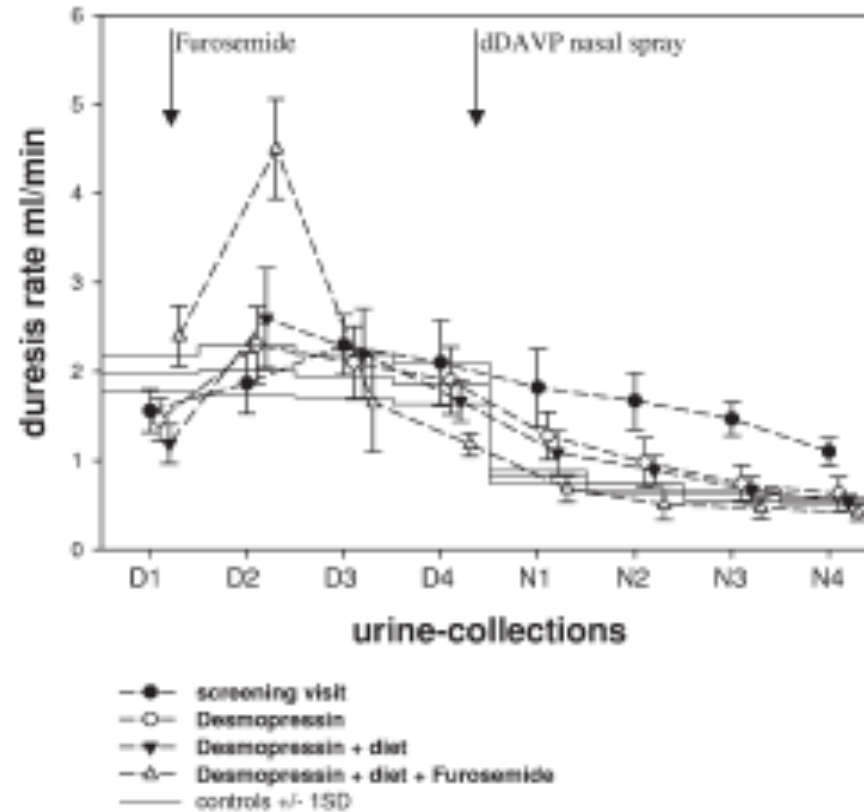


FIG. 1. Values of diuresis rate (ml per minute) of 4 observation periods plotted as mean \pm SD against reference frame of controls for daytime (D1 to D4) and nighttime (N1 to N4) urine collections.

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 resistant (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



„Höhenrekord der Luftschiffer-Abteilung!“

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**