

Update: Medikamentöse Therapie der überaktiven Blase

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Definition: Überaktive Blase

Imperativer Drang mit oder ohne Inkontinenz, häufig kombiniert mit gehäufter Miktions tagsüber und/oder nachts, ohne dass ein Harnwegsinfekt oder eine andere offensichtliche Pathologie (z. B. ein Blasen-tumor) besteht.

Diagnose

OAB

ICS, 2002

Definition: Imperativer Drang

Symptom

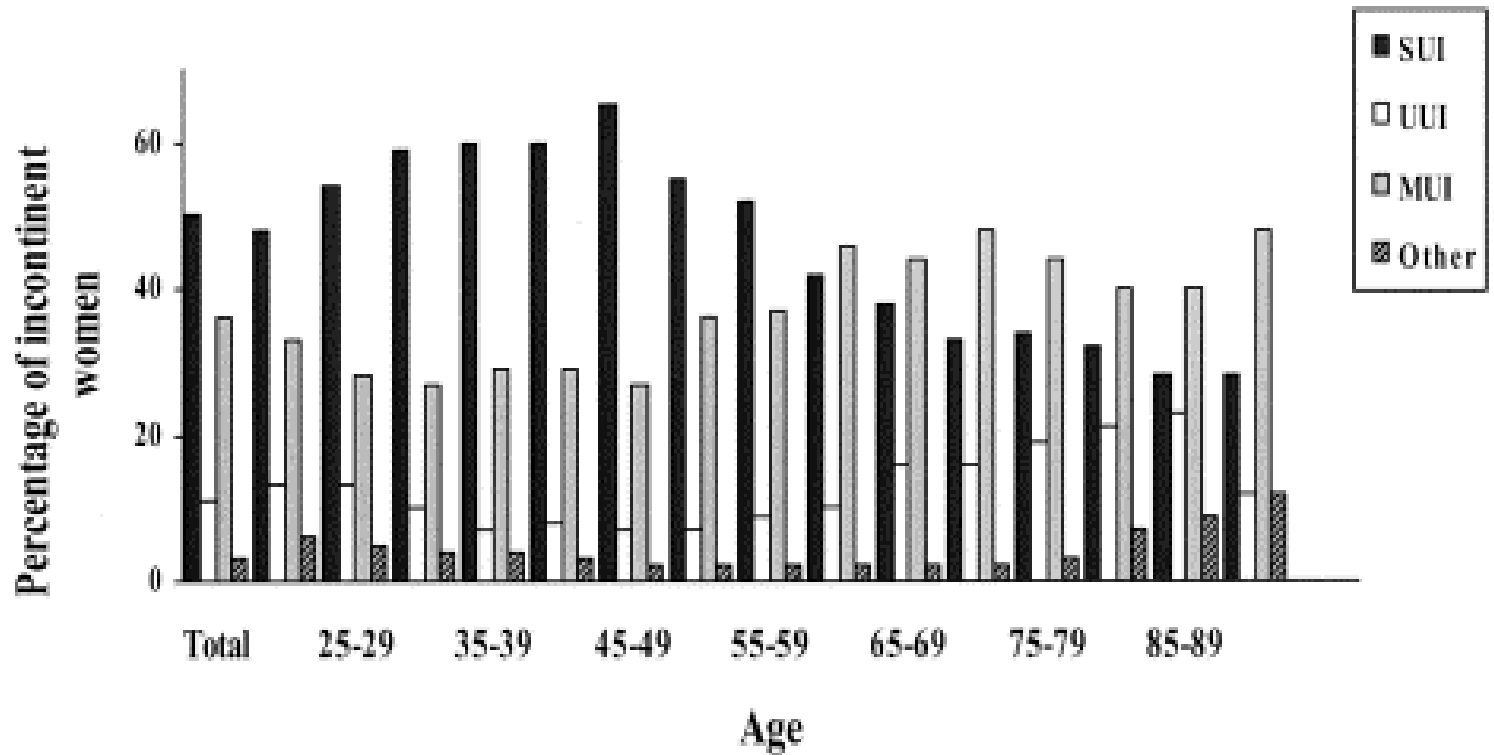
Urgency

Das plötzlich auftretende, nicht unterdrückbare Verlangen die Harnblase zu entleeren.

ICS, 2002

Prävalenz

10%



Risikofaktoren Dranginkontinenz

| Autoren | Einfluss | Inkontinenz | OR | 95% CI |
|--------------|----------------------------------|-------------|-----|---------|
| Moeller 2000 | 1. Geburt | Urge | 1,9 | 0,8-4,2 |
| | 2. Geburt | | 3,0 | 1,5-5,9 |
| | Diuretika | | 2,7 | 1,5-4,7 |
| | BMI >25 | | 2,2 | 1,3-3,6 |
| Arya 2000 | Kaffee (inkl Cola, Tee) >400mg/d | Urge | 2,7 | 1,2-5,8 |
| | Rauchen | | 1,9 | 1,0-3,8 |
| | Abgewöhnt | | 0,6 | 0,3-1,1 |
| Brown 1999 | Diabetes mellitus | Urge | 1,5 | 1,1-2,0 |

Stürze und Inkontinenz (3 Jahre Follow-up)

Typ adj. OR (95% CI) für Sturz

Drang 1.26 (1.14 to 1.40)

Stress 1.06 (0.95 to 1.19)*

relative hazard (CI) für Fraktur

Drang 1.34 (1.06 to 1.69)

Stress 0.98 (0.75 to 1.28)*

*nicht signifikant.

Medikamente & Inkontinenz

| Mechanismus | | Substanz | |
|---|----------------------------------|-------------------------|---------------------------------|
| Intravesikale Druckstei- gerung | vermehrte Harnproduk- tion | Diuretika | Furosemid Hydrochlorothiazid |
| | Detrusor- instabilität | Bethanechol Cisaprid | |
| unvollstän- dige Blasen- entleerung | | Anticholinergika | Hyoscyamin Oxybutinin |
| | | Antiparkinson Mittel | Benztropin Trihexyphenidyl |

Medikamente & Inkontinenz

| Mechanismus | Agent |
|-------------------|------------------------------------|
| Indirekte Effekte | Husten ACE Hemmer Enalapril |
| Obstipation | Eisen Narkotika |
| Sedierung | Alkohol Sedativa Anxiolytika |

Medikamentöse Therapie

- Anticholinergika
 - Oxybutinin
 - Tolterodin
 - Trospiumchlorid
 - Solifenacin
- Östrogene
- Alphablocker
- Antispastika
- Hyaluronsäure (intravesikal)
- Botulinum Toxin Injektionen

Kognition

Cholinesterasehemmer

Demenz und Inkontinenz

- Medikamente die bei Alzheimer und Demenz zum Einsatz kommen (Donezepil, Galantamin, Rivastigmin) sind Cholinesterasehemmer und wirken den Anticholinergika entgegen

Harninkontinenz kann die Nebenwirkung des Demenzmittels, Demenz die Nebenwirkung des Anticholinergikums sein

Anticholinergic drugs versus placebo for overactive bladder syndrome in adults

Naby D, Cody J

Cochrane Incontinence Group, 2009

- Authors' conclusions:
The use of anticholinergic drugs by people with overactive bladder syndrome results in **statistically significant improvements in symptoms**. Recent trials suggest that this is associated with **modest improvement in quality of life**. Dry mouth is a common side effect of therapy but did not seem to have an effect on the numbers of withdrawals. **It is not clear whether any benefits are sustained during long-term treatment or after treatment stops.**

Oxybutinin

- Tertiäres Amin
- Immediate-Release-Form
- Extended-Release-Form (gleichmäßiger Wirkspiegel, höhere Bioverfügbarkeit)
- Starke ZNS-Affinität

**Detrusan[®], Ditropan[®], Oxybutinin Hexal[®], Erwo[®]
oder Ratiopharm[®],**

Kentera[®]

Transdermal oxybutynin: sticking to the facts

Cartwright R, Cardozo L

Eur Urol, 2007

- Transdermal oxybutynin offers equivalent efficacy to variable dose oral oxybutynin IR and tolterodine LA 4 mg/d
- The balance of efficacy and tolerability suggests that **transdermal oxybutynin should be considered as a potential first-line therapy in OAB**

Tolterodin

- Tertiäres Amin ohne Muskarinrezeptor-Selektivität
- Günstiges Nebenwirkungsprofil
- Geringe ZNS-Affinität

Detrusitol®

Trospiumchlorid

- Quartäres Amin
- Passiert Blut-Hirn-Schranke nicht
- Geringste Auswirkung auf die Kognition

Spasmolyt[®], Spasmourgenin[®], Inkontan[®]

Urivesc[®]

Trospium chloride once-daily extended release is effective and well tolerated for the treatment of overactive bladder syndrome: an integrated analysis of two randomised, phase III trials.

Staskin D, Rosenberg M

Int J Clin Pract., 2009

- 1165 subjects were randomised
- Compared with placebo, subjects treated with trospium XR had significantly greater **reductions from baseline in the mean number of toilet voids/day (-1.9 vs. -2.7; $p < 0.001$)** and **UUI episodes/day (-1.8 vs. -2.4; $p < 0.001$)** at week 12
- The most frequent AEs considered possibly related to study treatment were **dry mouth (trospium XR, 10.7%; placebo, 3.7%)** and **constipation (trospium XR, 8.5%; placebo, 1.5%)**
- Notably, rates of central nervous system (CNS) AEs were lower with trospium XR vs. placebo (dizziness: 0.2% vs. 1.0%; headache: 1.4% vs. 2.4%)

Extended-Release Trospium Chloride Improves Quality of Life in Overactive Bladder

Dmochowski R, Rosenberg M
Value Health, 2009

- 1165 subjects were randomized
- Once-daily trospium 60 mg ER improved the QoL of subjects with OAB, as assessed using the KHQ and the OAB-q, in two large Phase III clinical trials.

Solifenacin

- Tertiäres Amin mit hoher M₃-Rezeptor-Selektivität
- Einmalige Gabe pro Tag
- Geringe ZNS-Affinität

Vesicare®

Treatment outcomes in the STAR study: a subanalysis of solifenacin 5 mg and tolterodine ER 4 mg

Chapple C, Fianu-Jonsson A
Eur Urol, 2007

- CONCLUSIONS:

Within 4 weeks **solifenacin 5mg was statistically significantly better than tolterodine ER 4 mg** in improving incontinence and reducing incontinence pad use.

Exploratory pilot study assessing the risk of cognitive impairment or sedation in the elderly following single doses of solifenacin 10 mg

Wesnes K, Edgar C

Expert Opin Drug Saf, 2009

- CONCLUSION:

In this pilot study, single 10 mg doses of **solifenacin did not show any clear propensity to impair cognitive function** in a healthy elderly population.

Improved quality of life in patients with overactive bladder symptoms treated with solifenacin

Kelleher C, Cardozo L
BJU Int, 2005

Warning Time

- CONCLUSIONS:
Results from the KHQ in study participants in the two double-blind studies showed that **solifenacin significantly improved the QoL** in patients with OAB symptoms after 12 weeks of treatment, with further improvements during long-term administration up to 1 year

Follow-up at 24 months after treatment of overactive bladder with 0.2 % sodium chondroitin sulfate

Gauruder-Burmester A, Popken G

Aktuelle Urol, 2009

- 82 patients with chronic OAB
- Duration of treatment was 12 months
- Repeat follow-up after 24 months
- Instillation treatment with 0.2 % sodium chondroitin sulfate results in a more sustained improvement or cure of the symptoms of overactive bladder

Botulinum toxin injections for adults with overactive bladder syndrome

Duthie J, Herbison G

Cochrane Incontinence Group, 2009

- Authors' conclusions:
Intravesical botulinum toxin **shows promise as a therapy** for overactive bladder symptoms, but as yet too little controlled trial data exist on benefits and safety compared with other interventions, or with placebo. Practitioners should be aware that **at present there is little more than anecdotal evidence**, in the form of case reports to support the efficacy of intravesical botulinum toxin; there is not much in the way of substantial, robust safety data. Furthermore, **the optimal dose of botulinum toxin for efficacy and safety has not yet been demonstrated.**

Zusammenfassung

- Anticholinergika verbessern die Blasenkapazität (**Compliance!**).
- Extended-Release-Formen besser verträglich
- Langzeitwirkung?
- Lokale Östrogentherapie verbessert die Symptomatik (ca. 60%)
- Hyaluronsäure intravesikal
- Botulinum Toxin



Danke