

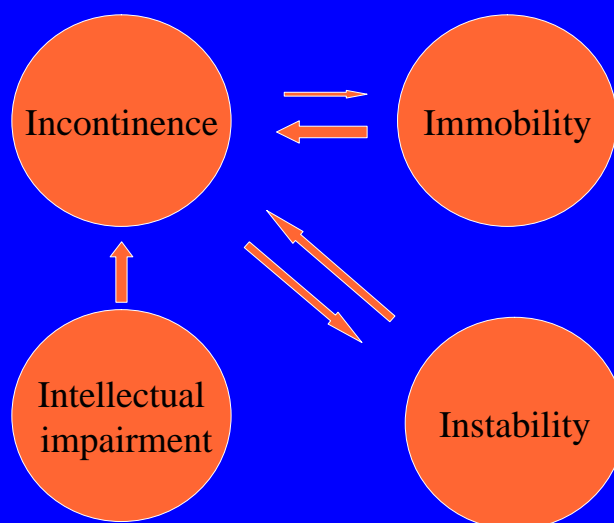
Pharmacological treatment of incontinence

Students' state of the art lecture
EAMA VIIth, June 24, 2008

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Geriatric Giants



Types of Incontinence

Fecal Incontinence

- Overflow incontinence
- Reservoir incontinence
- Rectosphincteric incontinence

Urinary Incontinence (UI)

- Urge-UI
- Stress-UI
- Mixed-UI
- Chronic urinary retention with UI
- Extra-urethral UI
- Uncategorized UI

Management of fecal incontinence

- Treatment of underlying diseases (e.g. clostr.-diff.-infection, inflammatory bowel disease, anorectal cancer)
- Control of diarrhoe
- Removal of fecal impaction
- Treatment of constipation
- Perineal strenghtening exercizes
- Surgery for defects of the external sphincter muscle
- Anal hygiene

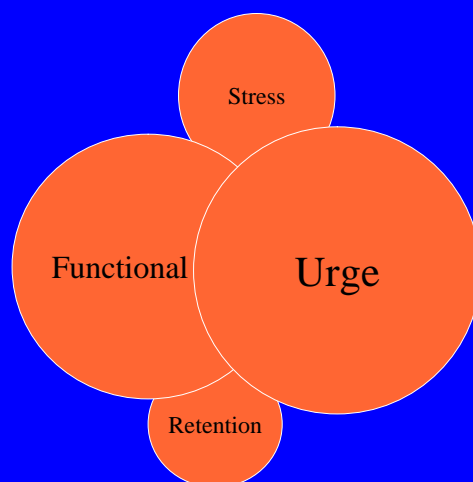
Drug treatment for fecal incontinence

- Loperamide oxide for control of diarrhoe
- Lactulose and/or Macrogol for stool regulation
- Topical phenylephedrine gel to enhance anal sphincter tone

In clinical trials limited evidence that antidiarrhoeal drugs and drugs which enhance anal sphincter tone may reduce fecal incontinence in patients with liquid stools.

Cheetham M, Brazzelli M, Norton C, Glazener CMA. Drug treatment for faecal incontinence in adults. *Cochrane Database of Systematic Reviews* 2002, Issue 3.

Geriatric Urinary Incontinence



Drugs associated with Urinary Incontinence

- Acetylcholinesterase inhibitors
- Alpha-adrenergic agonists
- Alpha-adrenergic antagonists
- Anticholinergics
- Antipsychotics/neuroleptics
- Bromocriptine
- Calcium-channel blockers
- Clonazepam
- Diuretics
- Ethanol
- Lithium
- Metoclopramide
- Misoprostol
- Phenytoin
- Sedatives/hypnotics
- Skeletal muscle relaxants
- Sympatholytics

Urinary Incontinence Treatment options

	Stress UI	Urge UI	Retention
Education	+	+	+
Environmental modifications	+	+	+
Garments/ pads	+	+	
Catheters	?	?	+
Bladder training/ Toileting interventions	+	+	
Pelvic floor muscle exercises	+	+	?
Vaginal pessaries	+		
Drug therapy	+	+	?
Urethral bulking injections	+		
Surgery (Burch, sling)	+	?	
Botox injections		+	
Sacral neurostimulation		+	

M. Pfisterer, Management of urinary incontinence, EAMA June 2007

Drugs used for treatment of stress incontinence I

Duloxetine

- Selective serotonin and norepinephrine reuptake inhibitor
- Increases urethral sphincter contraction during the storage phase of urination cycle
- Dosage 40 mg bid
- Side-effects: Nausea, dizziness, somnolence, fatigue

Effects in RCTs compared to placebo:

- Decrease in incontinence episode frequency: 50% vs 27%
- Improvement in incontinence quality of life questionnaire: 11,0 vs 6,8
- Discontinuation rate for adverse effects: 24% vs 4%

Dmochowski et al; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of North American women with stress urinary incontinence. *J. Urol.*, 170(4 Pt 1):1259, 2003

Similar results were reported by Millard et al and van Kerrebroeck et al

(Millard et al; Duloxetine UI Study Group. Duloxetine vs placebo in the treatment of stress urinary incontinence: a four-continent randomized clinical trial. *BJU Int*, 93(3):311, 2004)

(Van Kerrebroeck et al; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of European and Canadian women with stress urinary incontinence. *BJOG*,111(3):249,2004)

Drugs used for treatment of stress incontinence II

Imipramine

2 small open studies showed improvement of SUI (questionnaire, pad-test, maximal urethral closure pressure) under 3x25 mg Imipramine

Glija et al; Conservative treatment of female stress incontinence with imipramine. *J Urol*, 132:909, 1984

Lin et al; Comparison of treatment outcomes for imipramine for female genuine stress incontinence. *Br J Obstet Gynaecol*, 106:1089, 1999

No RCTs on the effects of imipramine were published

Local estrogen

Beneficial for treating vaginal atrophy, atrophic vaginitis and urethritis. No significant effect on stress incontinence

Fantl et al; Estrogen therapy in the management of urinary incontinence in postmenopausal women: a meta-analysis. First report of the Hormones and Urogenital Therapy committee. *Obstet Gynecol*, 83:12, 1994.

Sultana et al; Estrogen and urinary incontinence in women: a meta-analysis. *Maturitas*, 20:129, 1990.

Alpha-adrenergic stimulants

Moderate effect on stress incontinence, not recommended for this indication because of side effects

Abrams et al, 2nd International Consultation on Incontinence, Pharmacological treatment of Urinary Incontinence, Health Publication Ltd 2002, 809-854

Drugs used for treatment of urge incontinence I

Antimuscarinics

- Block muscarinic receptors
- Decrease tonus of the detrusor muscle

	Oxybutinine	Tolterodine	Trospium	Solifenacine	Darifenacine
Dosage	2,5–5mg IR tid 10mg ER qd 3,9 mg/d patch	1-2mg IR bid 2-4mg ER qd	5-20mg bid	5-10mg qd	7,5-15mg qd
M-Receptor	non-selective	non-selective	non-selective	non-selective	M3-selective
Penetration into CNS	yes	yes	(no)	yes	yes

Effectiveness of antimuscarinic drugs for treatment of Urge-UI (Meta-Analysis of RCTs)

32 Trials (n=6800 subjects)

	Antimuscarinic	Placebo	Relative risk (95% CI)
Subjective improvement or cure	708/1182	365/807	1.41 (1.29 to 1.54)
Leakage episodes in 24 h	1911 participants	811 participants	-0.56 (-0.76 to -0.40)
Micturitions in 24 h	1939 participants	777 participants	-0.59 (-0.83 to -0.36)
Withdrawal due to side effects	197/3016	72/1153	1.01 (0.78 to 1.31)

Herbison P et al. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. *BMJ* 2003;326:841-844

Antimuscarinic Side Effects

- Dry mouth
- Constipation
- Urinary retention
- Blurred vision
- Dizziness/confusion/memory deficits

Possible prescribing cascade acetylcholinesterase-inhibitor ?
antimuscarinic drug

- Patients treated with ChIs seem to have an increased risk of subsequently receiving an anticholinergic drug (Gill et al. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. Arch Intern Med. 2005; 165(7): 808-813)
- In higher-functioning NH residents dual use of ChIs and oxybutinine or tolterodine may result in greater rates of functional decline than under use of ChIs alone (Kaycee et al. Dual Use of Bladder Anticholinergics and Cholinesterase Inhibitors; Long-Term Functional and Cognitive Outcomes. Journal of the American Geriatrics Society 56 (5) , 847-853 doi:10.1111/j.1532-5415.2008)

Drugs used for treatment of urge incontinence II

Propiverine

- Antimuscarinic and calcium channel blocker properties. Efficacy similar to oxybutinine. Possibly lower incidence of dry mouth.

Flavoxate

- Efficacy not well documented, few side effects.

Imipramine

- Beneficial effect on nocturia and nocturnal enuresis can be observed
- Side effects (hypotension, bradycardia, dysrhythmias, dizziness, fatigue) limit the use in the frail elderly.

Abrams et al. 2nd International Consultation on Incontinence, Pharmacological treatment of Urinary Incontinence, Health Publication Ltd 2002, 809-854

Drugs used for treatment of overflow incontinence

Alpha-adrenoreceptor antagonists

- Established in treatment of prostatic hyperplasia
- Proposed for treatment of vesical neck obstruction and neurogenic voiding dysfunction (Nitti W, *Rev Urol*. 2005; 7(Suppl 4): S49-S55)
- Selective alpha1a-AR antagonists (Alfuzosin, Tamsulosin) cause less orthostatic hypotension

Baclofen

- Can decrease bladder outflow resistance in disorders associated with motor spasticity

In most cases the therapeutic effect of pharmacotherapy is limited and other procedures to assure the urinary outflow become necessary

Take home messages

- Check medication for drugs associated with incontinence
- Pharmacotherapy is only one among several treatment options
- Pharmacotherapy depends on the type of incontinence

Thank you
