

Management of Overactive Bladder

UBC Urology Grand Rounds

5 Oct 2005

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Sponsor: Paladin

OBJECTIVES

- Review pathophysiology of overactive bladder (OAB)
- Review options for management of OAB

OUTLINE

- Introduction (definitions, epidemiology)
- Bladder anatomy and physiology
- Pathophysiology of OAB
- Evaluation and Dx of the patient with OAB
- Non-pharmacologic interventions
- Drugs for OAB (old and new)

INTRODUCTION

ICS, 2002

- Definition of OAB (ICS): urgency $\pm$ urge incontinence, usually with frequency and nocturia, of no identifiable cause
- Detrusor overactivity (ICS): urodynamics observation of involuntary contractions, replaces hyperreflexia and instability
- IC and PBS: both involve pain in contrast to OAB

Prevalence of OAB (Canada)

■ Corcos, Can J Urol 11: 2278, 2004

- Validated computer assisted telephone interview
- 3249 adults ≥ 35 yrs old sampled
- 603 had OAB (18.1%), women $>$ men
- Dry OAB $\gg \gg$ wet OAB $>$ mixed OAB
- Prevalence $\uparrow$ with age

Economic Impact of OAB

■ Hu, Urology 61: 1123, 2003

- Telephone survey of 5204 community dwelling adults ≥ 18 yrs (validated instrument)
- F/u survey of costs incurred in those with OAB (by mail)
- OAB dry: ≥ 4 episodes of urgency in last 4 weeks, and either frequency ≥ 8 /day or use of one or more coping behaviours
- OAB wet: dry + ≥ 3 non-stress incontinence episodes in last 4 weeks

Economic Impact of OAB

- Cost associated with institutionalized patients with OAB limited to those with UI or mixed incontinence only
- Total costs: 12 billion
- Institution dwellers: 3 billion
- Community dwellers: 9 billion
- Cost per community dweller: \$267/yr
- Comparable to costs of osteoporosis and breast cancer

Natural History of OAB

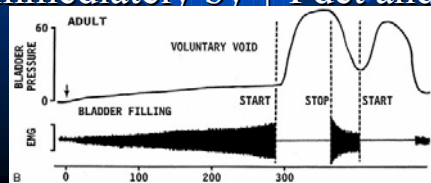
Garnett & Abrams, JU 169: 843, 2003

- No well constructed longitudinal long term, study of patients with OAB
- Keep this in mind when evaluating results of interventions...

ANATOMY AND PHYSIOLOGY

■ Blavais & Wein, Contemporary Urology , 2001

- Bladder: interlacing bundles of disorganized smooth muscle, coalesces into inner long, mid circ, outer long layers at base
- Micturition reflex is initiated by sudden complete relaxation of striated sphincter
- Followed immediately by $\uparrow P_{det}$ and $\downarrow P_{ure}$
→ flow



Neurophysiology of Micturition

- Storage and emptying governed by interactions b/w
 - sacral micturition centre (SMC)
 - Thoracolumbar sympathetic system
 - Pontine micturition centre (PMC)
 - Higher brain centres
- Micturition reflex coordinated by connections b/w PMC and SMC

Neurophysiology: SMC

- Autonomic component (pelvic nerve, S2-4) and somatic component (pudental nerve)
- Preganglionic fibres of efferent parasymp travel thru pelvic nerve to pelvic plexus on either side of rectum
- Postganglionic fibres innervate bladder
- Efferent activity is $\uparrow$ by stretch signalling from afferents in pelvic, hypogastric and pudental

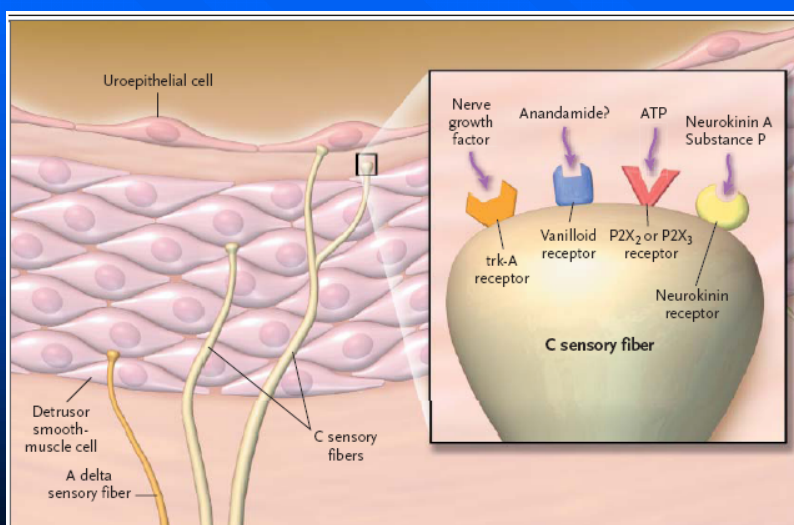
Neurophysiology: thoracolumbar sympathetics

- Sympathetic preganglionic efferents (T10-L2) travel to sup hypogastric plexus
- Postganglionics travel in hypogastric nerve primarily to BN, proximal urethra, trigone
- Also synapse in pelvic plexus at junction of parasymp pre and post ganglionic nerves
- functions in storage:
 - inh pre to post-ganglionic parasymp transmission ($\alpha 2$)
 - Promote relaxation of detrussor ($\beta 2$, $\pm \beta 3$)
 - Internal sphincter contraction ($\alpha 1$)

Neurophysiology: LUT afferents

- Mechanoreceptor bladder afferents (myelinated A-delta) for sensation of distension travel in hypogastric nerve to dorsal column of lumbosacral cord
- Nociceptive afferents (unmyelinated C fibres) travel along pelvic and hypogastric nerves to lateral spinothalamic tracts
- Afferents from striated sphincter and urethra transmit proprioceptive and pain along pudental nerve

Neurophysiology: LUT afferents



Neurophysiology: striated urethral musculature

- Motor axons from Onuf's nucleus (ventral horn of S2-4) → pudental nerve → striated urethral sphincter

Neurophysiology: PMC

- Coordinates micturition reflex
- Medial region controls detrusor contraction via reticulospinal tracts
- Lateral region controls sphincter contraction via corticospinal pathways

Neurophysiology: Higher centres

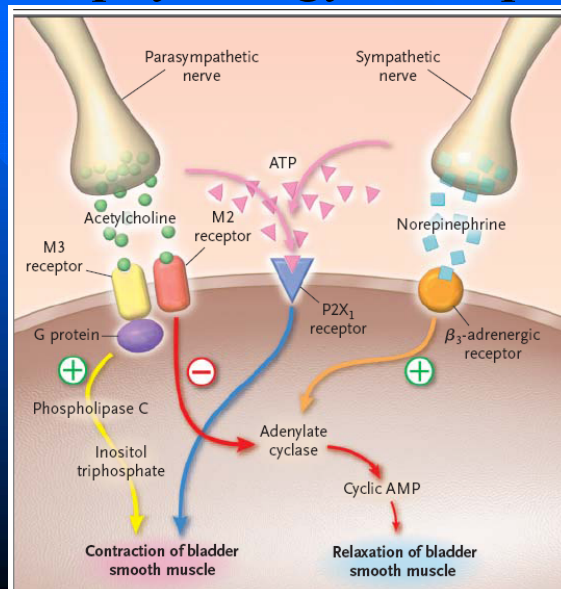
- PMC receives input from cortex, cerebellum, BG, thalamus, and hypothalamus
- Most input from these centres is inhibitory
- frontal cortex and anterior cingulate gyrus most important in control of micturition
- micturition controlled predominately by right side of brain

Neurophysiology: Receptors

Ouslander NEJM 350: 786, 2004

- Detrusor contracted by activation of cholinergic muscarinic receptors (M1 – M5)
- M1 – 3 found in bladder
- M2 predominates (80%) but M3 felt to be primary one mediating contraction
- M2 coactivation may enhance response to M3
- M3 present in other tissues including salivary glands
- “Holy Grail” is bladder-selective antimuscarinic

Neurophysiology: Receptors

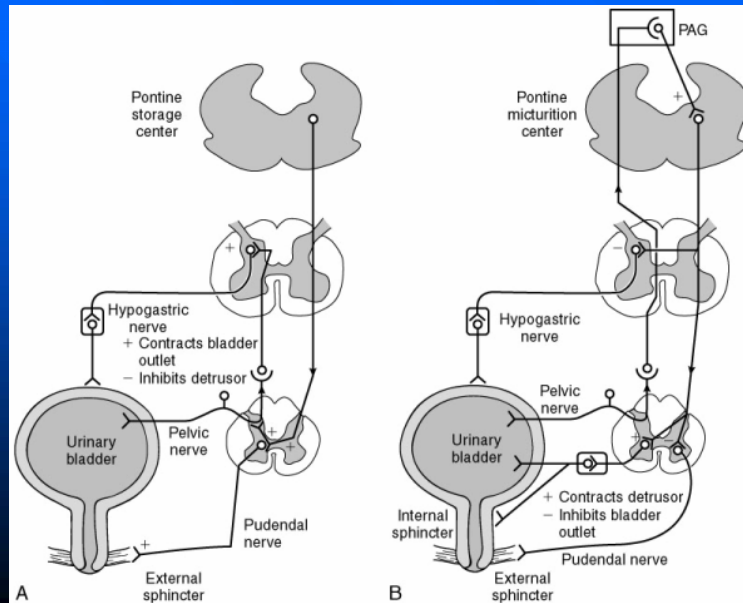


Storage and Emptying

Table 23-4. REFLEXES TO THE LOWER URINARY TRACT

Afferent Pathway	Efferent Pathways	Central Pathway
Urine Storage Low level vesical afferent activity (pelvic nerve)	1. External sphincter contraction (somatic nerves) 2. Internal sphincter contraction (sympathetic nerves) 3. Detrusor inhibition (sympathetic nerves) 4. Ganglionic inhibition (sympathetic nerves) 5. Sacral parasympathetic outflow inactive	Spinal reflexes
Micturition High level vesical afferent activity (pelvic nerve)	1. Inhibition of external sphincter activity 2. Inhibition of sympathetic outflow 3. Activation of parasympathetic outflow to the bladder 4. Activation of parasympathetic outflow to the urethra	Spinobulbospinal

Storage and Emptying

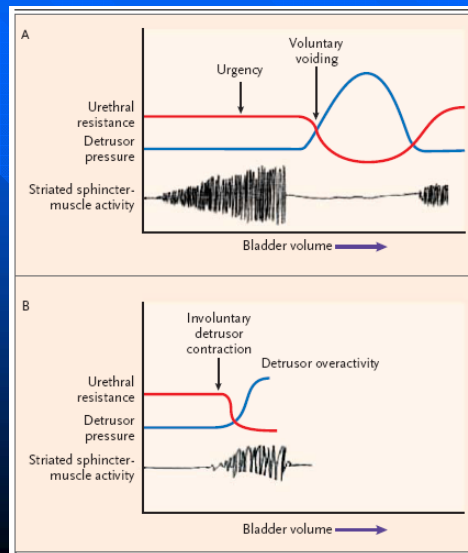


PATHOPHYSIOLOGY OF OAB

■ Blavaïs, Contemporary Urology 2001

- Symptoms of OAB are usually associated with involuntary contractions of detrusor
- Detrusor overactivity has 2 interdependent causes:
 - Neurologic
 - Myogenic
- Neural abnormalities → myogenic abnormalities and vice versa

Pathophysiology: Involuntary detrusor contraction



Ouslander
NEJM 2004

Pathophysiology: Neurologic abnormalities

- Neurologic abnormalities have multiple effects on micturition:
 1. Interfere with circuitry
 2. Induce changes in innervation (plasticity)
→ new neural pathways and control mechs
 3. Induce changes in properties of smooth muscle cells

Pathophysiology: Myogenic abnormalities

1. Extensive electrical coupling noted in smooth muscle preps from OAB patients
2. Supersensitivity to muscarinic stimulation and enhanced depolarization to K^+

Pathophysiology: Role of urothelium

De Groat, Urology 2004

- Urothelial cells have sensory role
- During filling, urothelium stretches → release of ATP
- $P2X_3$ receptors (ligand-gated cation channel) for ATP abundant on bladder afferents
- $P2X_3$ Activation → afferent discharge at lower threshold
- Stretch activated ATP release is ↑ in chronic bladder disorders compared to control

Pathophysiology: Role of urothelium

- Capsaicin evokes painful responses by stimulating ion channel protein vanilloid receptor-1 (TRPV1) on urothelial cells & C fibre afferents
- Endogenous TRPV1 ligand: anandamide
- Activation → NO release, excitement then desensitization of C fibre afferent
- NO release in bladder strips ↓ after removal of urothelium, denervation, or desensitization
- Bottom line: substances released from urothelium can alter excitability of afferents

ETIOLOGY OF OAB

- Ouslander NEJM 350, 2004; Dallosso BJU 92, 2003
- LUT conditions:
 - UTI, Obstruction, bladder abnormalities (stones, tumours, IC)
- Neurologic conditions:
 - Stroke, Alzheimer's, SCI, DM neuropathy
- Functional/Behavioural:
 - Excess carbonated drinks, caffeine, alcohol, obesity

DIAGNOSIS

■ Abrams and Wein, OAB Consensus Conference, 2000

- History
- IPSS, OAB-q, voiding diary
- PE (GU, pelvic, rectal, lower extremity neuro)
- U/A
- ± uroflow, PVR, cytology, cystoscopy, UDS

MANAGEMENT OVERVIEW

- Behaviour modifications
- Classic anticholinergics (ditropan, detrol)
- New antimuscarinics (solifenacin, darifenacin, trospium)
- Botox
- Acupuncture
- Neuromodulation

Behaviour Modification

- Education
- Appropriate fluid intake, timing of intake
- Avoidance of irritants
- Managing constipation
- Physiotherapy
- Bladder training

Pelvic Physiotherapy

- Wang, Urology 63: 61, 2004
- 103 OAB women randomized to 12 wks:
 1. Pelvic floor muscle training (PFMT)
 2. Biofeedback assisted PFMT (BAPFMT)
 3. Intravaginal electrical stimulation (ES, 20 mins of ~ 50 mA, 10 Hz, twice/wk)
- Outcomes: voiding diary, pad test, QoL questionnaire, UDS

Pelvic Physiotherapy

TABLE II. Comparison of changes in domains of King's Health Questionnaire after treatment

QOL Domain	PFMT (n = 34)	BAPFMT (n = 34)	ES (n = 35)	P Value*			
				Overall	B vs. ES	P vs. ES	B vs. P
General health perception	14.66 ± 24.57	12.10 ± 20.28	16.96 ± 24.58	0.376			
Incontinence impact	6.03 ± 120.82	37.42 ± 37.11	47.03 ± 35.45	0.067			
Role limitation	25.86 ± 26.57	30.64 ± 30.15	34.52 ± 31.73	0.669			
Physical limitation	25.29 ± 26.58	33.33 ± 33.88	28.57 ± 28.99	0.693			
Social limitation	17.05 ± 21.20	22.76 ± 29.20	20.84 ± 27.45	0.799			
Personal relationships	2.30 ± 13.89	10.75 ± 26.37	3.57 ± 22.39	0.167			
Emotions	19.31 ± 29.68	22.22 ± 27.82	46.83 ± 37.33	0.005	0.003	0.007	0.751
Sleep/energy	18.83 ± 26.18	26.88 ± 24.60	38.10 ± 39.51	0.249			
Severity measures	14.71 ± 20.27	20.65 ± 31.19	31.23 ± 23.83	0.004	0.029	0.001	0.587
Total score	50.27 ± 171.42	185.86 ± 176.57	180.08 ± 176.03	0.003	0.952	0.004	0.003

Key: QOL = quality of life; other abbreviations as in Table I.

Data presented as the mean ± SD.

Values determined by subtracting post-treatment scores from pretreatment scores.

* Denotes overall comparison among three groups using the Kruskal-Wallis test or pairwise comparison using the Mann-Whitney U test.

Most confidence intervals for changes measures include 0, lack of efficacy vs responsiveness of measure used.

Bladder Training

■ Wallace, Cochrane DSR, 2003

- Timed voiding with increasing intervals
- 10 trials, 1366 participants, predominantly female
- Inconclusive data
- Tendency to favour bladder training
- More, better research needed

Behavioural Therapy

- Lifestyle interventions
- Bladder retraining
- Pelvic floor muscle therapy (PFMT)
 - Basic
 - Simple biofeedback - with devices
 - Advanced biofeedback - electrical stimulation

Combination Therapy is Most Effective for Overactive Bladder

Percent reductions in incontinence episodes after 8 weeks

Drug therapy alone (N = 18) 59.1%	Switched to behavioral (N = 18) 77.1%	P-value .109
Behavioral therapy alone (N = 8) 57.5%	Drug therapy added (N = 8) 88.5%	0.034
Drug therapy alone (N = 27) 72.7%	Behavioral therapy added (N = 27) 84.3%	0.001

Burgio KL et al. *J Am Geriatr Soc.* 2000;48:370-374.

Combination Therapy Conclusions

- Combination therapy is more effective than either therapy alone
- 29% of patients randomized to oxybutynin alone chose to discontinue drug therapy and crossed over to behavioural therapy alone because of:
 - unwanted side effects
 - unwillingness to continue long-term drug therapy
- Drugs such as tolterodine with fewer side effects may encourage patients to choose combination therapy

Burgio et al. *J Am Geriatr Soc.* 2000;48:370-374.

Combination Therapy Conclusions

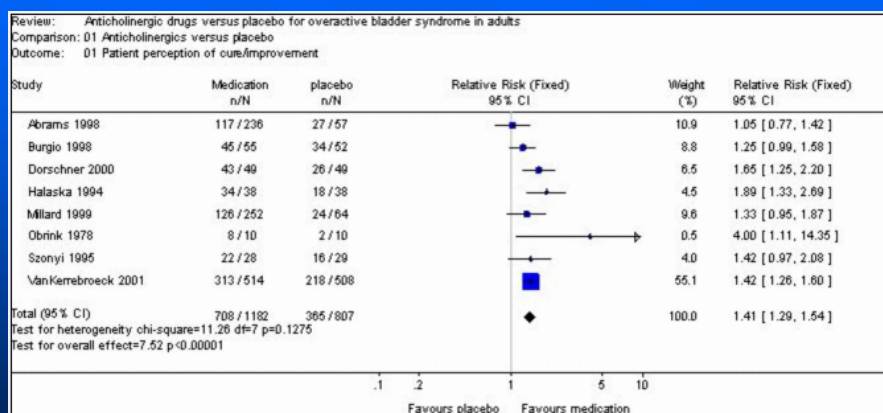
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Burgio et al. *J Am Geriatr Soc.* 2000;48:370-374.

Anticholinergics

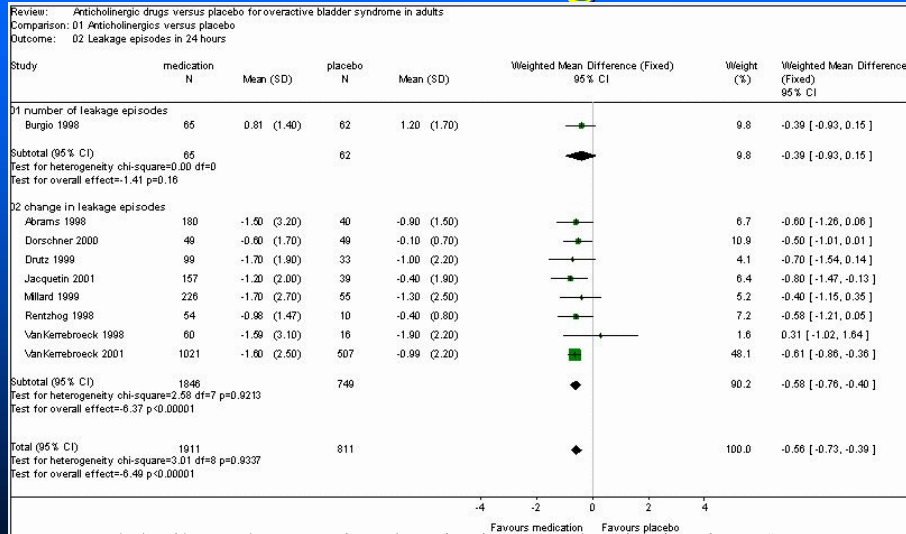
- Hay-Smith, Cochrane DSR, 2002
- 51 trials
- 6713 adults
- 7 medications: oxybutynin, tolterodine, trospium, darifenacin, emepronium, propiverine, propantheline

Anticholinergics



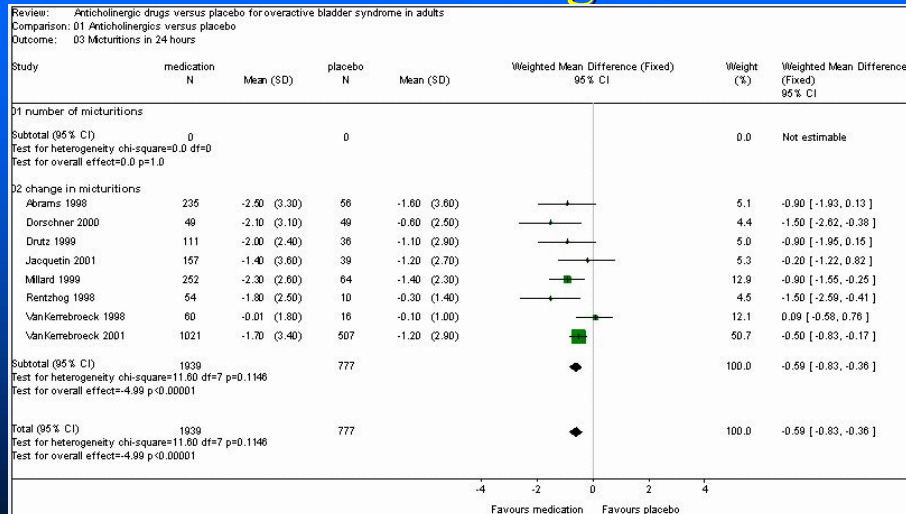
Anticholinergics vs placebo: patient perception of cure/improvement, favours anticholinergics

Anticholinergics



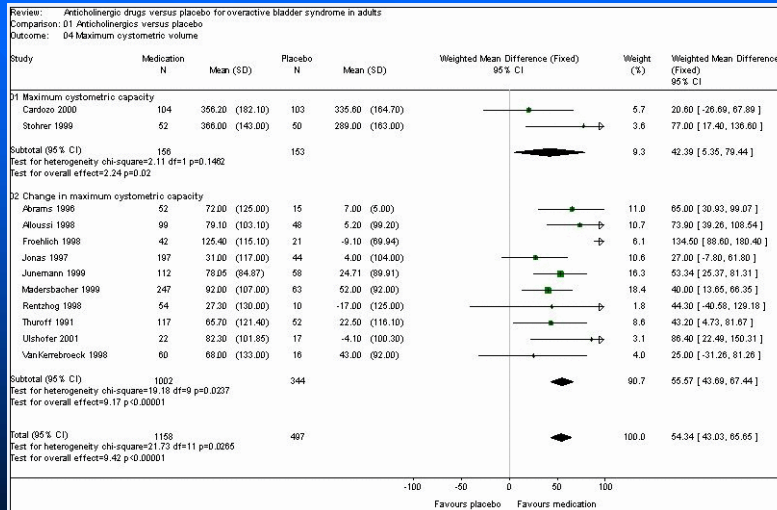
Anticholinergics vs placebo: leakage episodes/24 hrs, favours anticholinergics

Anticholinergics



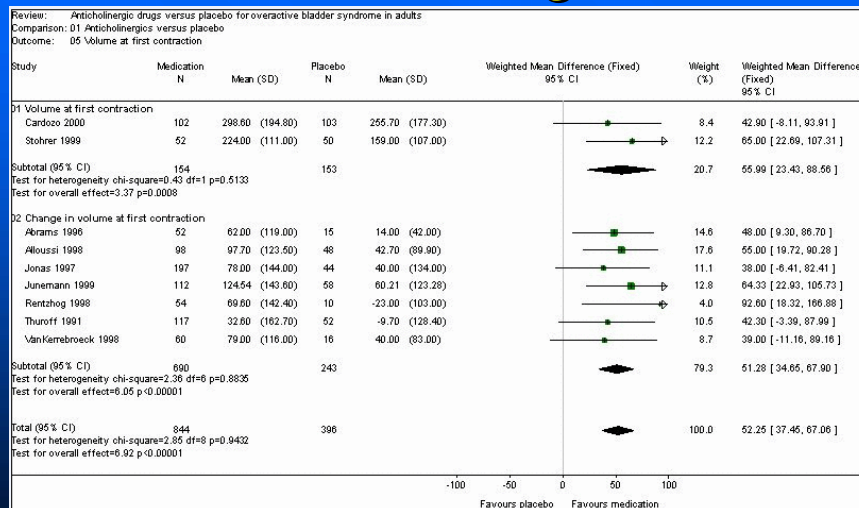
Anticholinergics vs placebo: micturitions/24 hrs, favours anticholinergics

Anticholinergics



Anticholinergics vs placebo: max cystometric capacity, favours anticholinergics

Anticholinergics



Anticholinergics vs placebo: volume at first contraction, favours anticholinergics

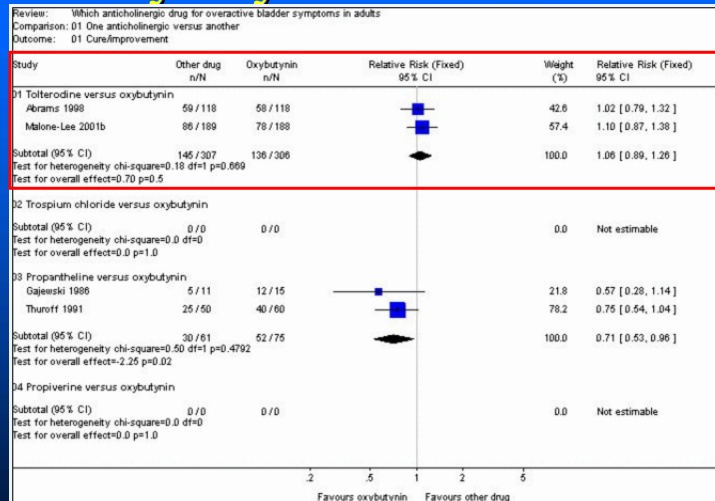
Halfway



Oxybutynin vs Tolterodine

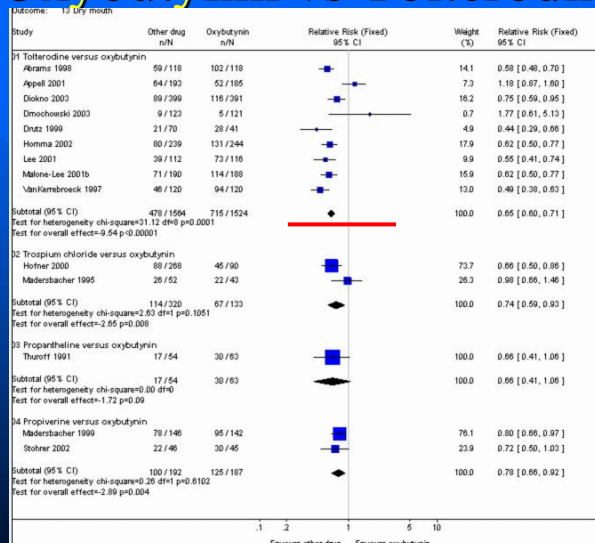
- Hay-Smith, Cochrane DSR, 2005
- 49 trials
- 11 332 patients
- Primary drugs: oxybutynin, tolterodine

Oxybutynin vs Tolterodine



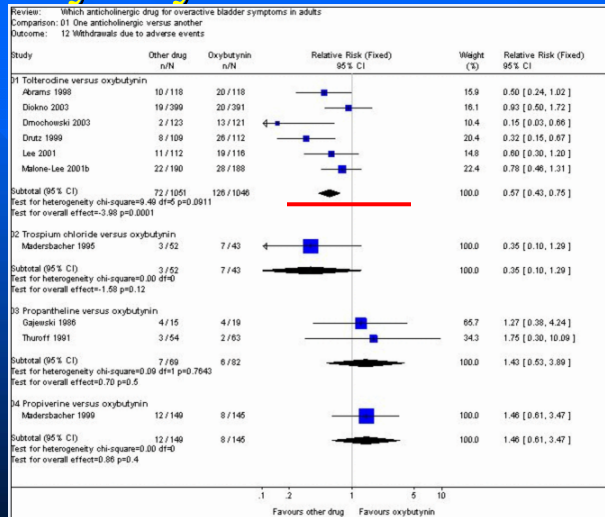
Oxybutynin vs tolterodine: cure or improvement, favours detrol

Oxybutynin vs Tolterodine



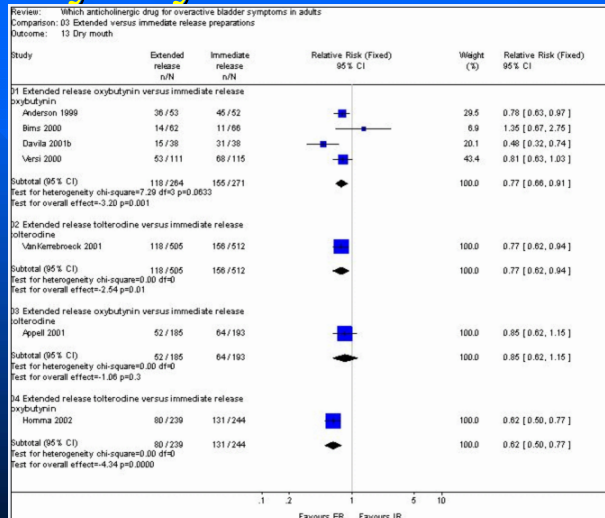
Oxybutynin vs Tolterodine: dry mouth, favours tolterodine

Oxybutynin vs Tolterodine



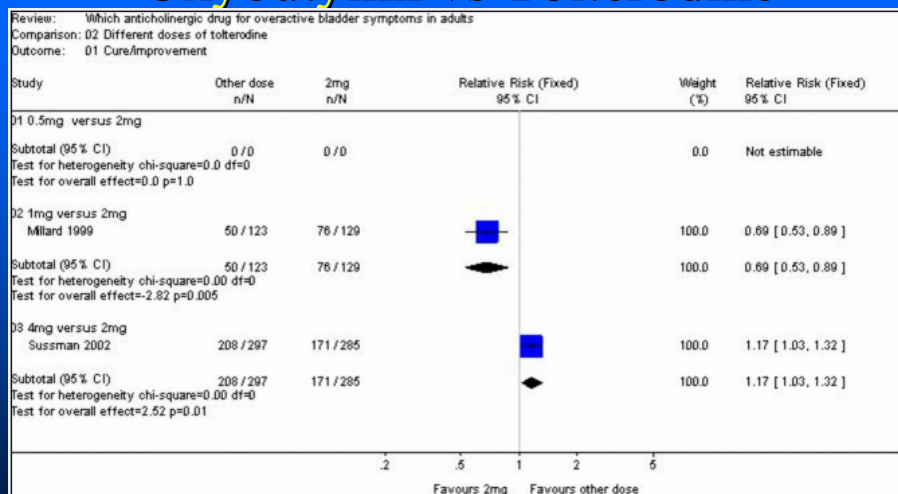
Oxybutynin vs Tolterodine: withdrawals due to adverse effects, favours tolterodine

Oxybutynin vs Tolterodine



Oxybutynin and Tolterodine: ER vs IR formulations and dry mouth, favours ER

Oxybutynin vs Tolterodine

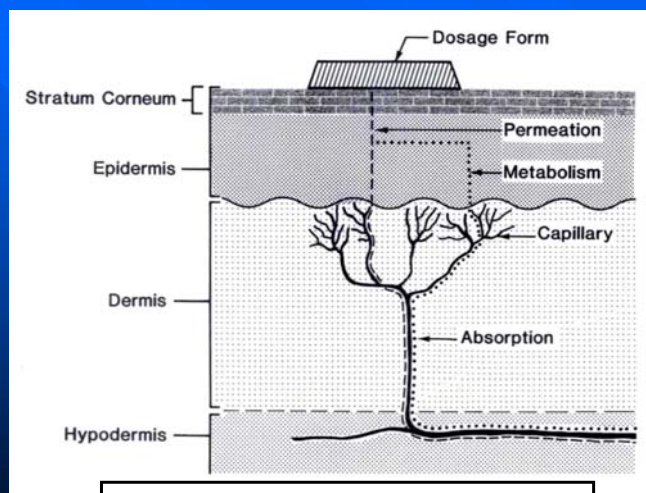


Tolterodine dosing: favours 4 mg/day

Transdermal Oxybutynin

- Oral oxybutynin undergoes extensive first pass metabolism to active metabolite, N-desethyloxybutynin
- [N- desethyloxybutynin] = 4-10[oxybutynin]
- N-desethyloxybutynin responsible for s/e
- Transdermal dosing yields lower [N-desethyloxybutynin]

Transdermal oxybutynin



Schematic of Skin Absorption

Transdermal oxybutynin

- RCT of 530 adults with urge or mixed UI
- 12 weeks followed by 12 week open-label dose titration (1.3, 2.6, 3.9 mg)
- 3.9 mg daily significantly reduced weekly incontinence episodes, daily urinary frequency, increased average volume voided, and improved QoL
- Adverse Events
 - pruritis 10-16% versus placebo 6%
 - Dry mouth: 7% versus 8%

Dmochowski et al. J Urol 2002; 168:580-586

Transdermal oxybutynin versus tolterodine ER

- 12 week RCT of transdermal oxybutynin, tolterodine ER, and placebo
- 361 adults who previously responded to anticholinergics
- Significant decrease in UUI episodes, increase in voided volume, improvement in symptoms and QoL
 - tolterodine and oxybutynin versus placebo ($P < 0.05$)
 - No significant difference between treatment groups
- Pruritis: oxy (14%) versus placebo (4%) ($P < 0.05$)
- Dry mouth: oxy (4.1%), tol (7.3%), placebo (1.7%)

Dmochowski et al. Urology 2003; 62:237-242

Solifenacin (Vesicare)

- Selective M_3 -receptor antagonist
- Bladder selective compared to salivary gland
 - In vitro and in vivo animal models - more than tolterodine or oxybutynin
- Dose dependent effect on salivary gland secretion - but similar to placebo

Ikeda et al. NS Arch Pharm 2002; 366:97-103
Smulders et al. ICS Heidelberg 2002, Abstr. 4

Solifenacin (Vesicare)

- Multicentre 12 week RCT
- 1281 patients with OAB and UII – 1033 evaluated
- Solifenacin 2 mg, 5 mg, once daily versus tolterodine 2 mg bid or placebo
- Sig. reduction in urge episodes/24h
 - Placebo (-32.7%); Solifenacin 5 mg (-51.9), 10 mg (54.7%); not sig. reduction with tolterodine (-37.9%)
- Sig. reduction in incontinent episodes with Solifenacin but not with Tolterodine (-1.4 versus -1.1)
- Sig. improvement in frequency and voided volume with all 3 drugs

Chapple et al. BJU Int 2004; 93:303-

Solifenacin: Side effects

Characteristic	Placebo	Solifenacin, mg (once daily)		Tolterodine 2 mg (twice daily)	Total
		5	10		
N	267	279	268	263	1077
Discontinuing					
Adverse event	10 (3.7)	9 (3.2)	7 (2.6)	5 (1.9)	31 (2.9)
Consent withdrawal	10 (3.7)	11 (3.9)	7 (2.6)	8 (3.0)	36 (3.3)
Lost to follow-up	2 (0.7)	1 (0.4)	2 (0.7)	6 (2.3)	11 (1.0)
Protocol violation	5 (1.9)	4 (1.4)	0	3 (1.1)	12 (1.1)
Insufficient response	2 (0.7)	2 (0.7)	1 (0.4)	3 (1.1)	8 (0.7)
Patient died	0	0	1 (0.4)	1 (0.4)	2 (0.2)
Other	2 (0.7)	1 (0.4)	1 (0.4)	0	4 (0.4)
Total	32 (12.0)	28 (10.0)	10 (3.7)	26 (9.9)	106 (9.9)
Major side-effects					
Dry mouth	13 (4.9)	39 (14.0)	57 (21.3)	49 (18.6)	
Constipation	5 (1.9)	20 (7.2)	21 (7.8)	7 (2.6)	
Blurred vision	7 (2.6)	10 (3.6)	15 (5.6)	4 (1.5)	

Chapple et al. BJU Int 2004; 93:303-

Darifenacin (Enablex)

- Highly selective M₃-receptor antagonist
- Displays some selectivity for bladder in the dog model
- Originally developed for treatment of irritable bowel syndrome
 - inhibits bowel motility (dog model)
 - inhibits resting and food-stimulated colonic motility
- 1996 abstract:
 - 2.5 mg: no efficacy and no effect on salivation
 - 10 mg: efficacy but significant effects on salivation

Scarpignato C, Pelosini I. *Can J Gastroenterol*. 1999;13(suppl A):50-65.
Broadley KJ, Kelly DR. *Molecules*. 2001;6:142-193.

Darifenacin (Enablex)

- Multicentre 12 week RCT
 - 561 patients with OAB and UII
 - 3.75 mg, 7.5 mg, 15 mg once daily versus placebo
 - Rapid onset of effect within 2 weeks
 - Sig. reduction in incontinence episodes
 - » 7.5 mg (-67.7%); 15 mg (-72.8%); placebo (-55.9%)
 - Sig. improvement in frequency, frequency of urgency, not in nocturia
 - Mild-to-moderate dry mouth (20-30% versus 8.5%) and constipation (15% versus 6.7%)
 - No CNS or cardiac side effects

Haab et al. *Eur Urol* 2004; 45:420-42

Trospium (Sanctura)

- Atropine derivative with low lipophilicity
- Does not cross BBB; Less CNS effects than oxybutynin
- Cardozo et al. BJU Int 2000; 85:659
 - 208 patients; placebo RCT; significant increase in capacity, volume at unstable contraction ($P=0.005$); patient's perception of efficacy ($P=0.005$)
 - Side effects similar to placebo
- U.S. randomized trials completed – Results expected to confirm European trials
- 10,000 patients in 20 clinical trials already reported

Trospium

(Hofner et al. World J Urol 2001; 19:336-343)

- Review of 20 clinical trials with >10,000 patients
- 4 RCTs, 3 comparative studies, and most post-marketing surveillance studies
- All age groups, neurogenic, enuresis

Trospium

(Hofner et al. World J Urol 2001; 19:336-343)

Table 2 Frequency of side effects summing up to 10,759 patients from post-marketing surveillance studies (From [20–22, 39, 41])

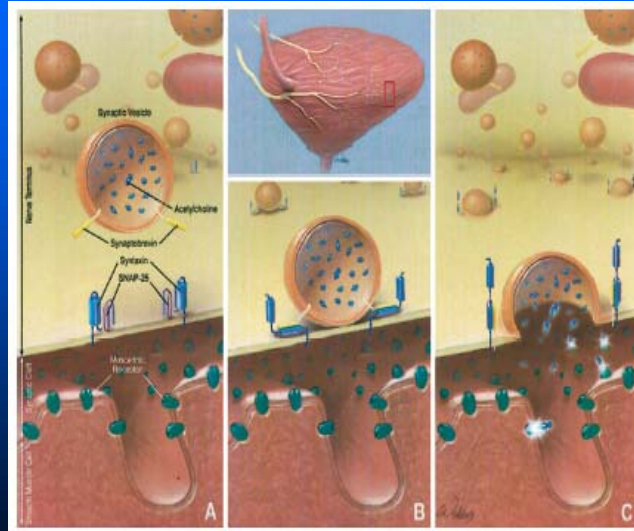
Adverse event	%
Dryness of mouth	4.1
Constipation	0.3
Visual disorders	0.6
Abnormalities of heart rate	0.7
Nausea/other gastrointestinal side effects	0.4
Residual urine	0.06
Other complaints	0.4
Total percentage of patients with adverse events	5.1

Botox

Smith, JU 171: 2128, 2004

- Botulinum poisoning first described as result of sausage poisoning in Germany 1700
- *C. botulinum* identified in 1897
- Active neurotoxins are bi-peptides disulphide linked
- Toxins binds to unidentified nerve terminal receptor
- Toxin is internalized where it interferes with NT release

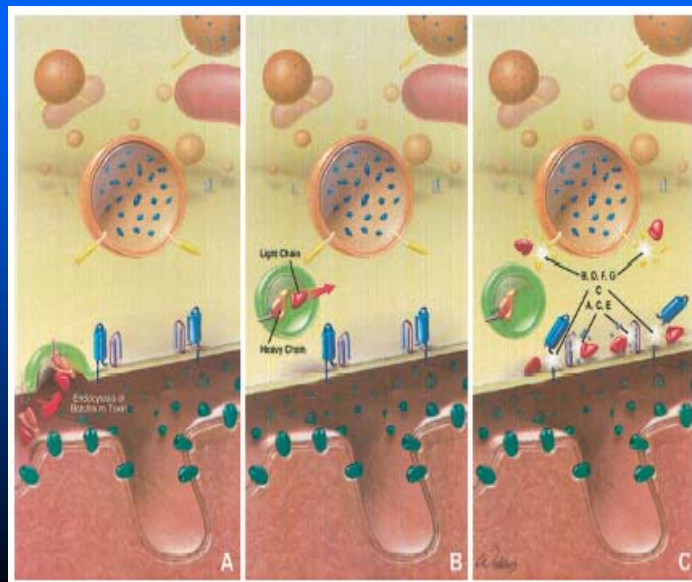
Botox



Release of ACh
and activation of
receptor

Smith CP. J Urol 2004;171:2128-213

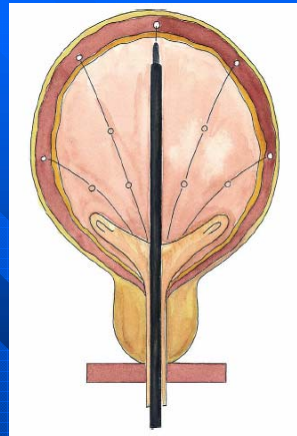
Botox



Release
prevented by
BTX-A

Botulinum toxin A

- 4 small studies with idiopathic OAB, many more studies of neurogenic bladders
- Injected in multiple sites in bladder endoscopically
- Dilution/dosing not determined
- 59 patients
- 20/30 improved continence for up to 8 months¹
- 12 improved at one month²
- 4/7 improved³
- 8/10 improved⁴



1. Loch et al. Eur Urol Suppl 2003;2:172
2. Radziszewski Eur Urol Suppl 2002;1:134
3. Zermann et al. Neurourol Urodyn 2001;20:412
4. Chancellor M et al. J Urol 2003;169:351

Estrogen Therapy

- Evidence-based review
- 87 References
 - included non–placebo-controlled studies
- Efficacy
 - SUI: probably not
 - UUI: probably not
 - Urgency: maybe

Hextall A. *Maturitas*. 2000;36:83-92.

Estrogen Therapy for OAB: A Meta-analysis

- Review of published literature from 1969 to 1999
- Included 10 randomized studies
 - estrogen (n = 239)
 - placebo (n = 215)
- Estrogen administered systemically or locally for various times (3 weeks to 6 months)

Cardozo et al. Presented at the 2nd International Consultation on Incontinence, July, 2001.

Estrogen Therapy for OAB: A Meta-analysis

- Estrogen significantly better than placebo at improving
 - urge incontinence
 - diurnal frequency
 - nocturia
 - bladder capacity
 - volume at first sensation
- Topical estrogen significantly better than placebo for all efficacy variables including urgency
- Systemic estrogen significantly better than placebo for incontinence episodes, but not for other efficacy variables

Cardozo et al. Presented at the 2nd International Consultation on Incontinence, July, 2001.

Estrogen: Conclusions

- Mixed evidence that exogenous estrogen is effective in treating urge incontinence or OAB
- Increasing evidence favoring the use of local (eg, VagiFem or Estring) versus systemic estrogen
- Use of hormone replacement therapy in combination with other therapies for OAB, including antimuscarinics, remains unreported

Accupuncture

Emmons, Obs & Gyne 106: 138, 2005

- 44 women received accupuncture designed to address OAB, 4 treatments
- Needles placed bilaterally on inner legs, outer knee folds, low back, midline low abdo (total 7 needles)
- Needles placed then twisted clockwise until warmth or tightening sensed (deqi)
- Controls had needles placed at locations designed for relaxation

Accupuncture

- Primary endpoint: # of incontinent episodes reduced by 59% vs 40% (not sign)
- Significant improvement in frequency, urgency, functional bladder capacity, incontinence impact questionnaire score
- No significant adverse effects
- Comparable to results seen with anticholinergics

Neuromodulation

- Underlying principle: reflex inhibition of pelvic efferents through stimulation of afferent input in pudental and sacral roots.
- Inhibitory effect of afferent stimulation in humans has been determined

Sacral Neuromodulation

Hassouna JU 163: 1849, 2003

- 51 patient with refractory urgency-frequency
- Excluded: cap < 100, abnormal upper tracts, neurogenic bladder, SUI, pelvic pain synd.
- Trial test stimulation of sacral nerves (perc stim of S3,4)
- Those with successful trial went on to implantation of Interstim device

Sacral Neuromodulation

- SC implanted device includes neurostimulator, lead placed adjacent to targetted sacral nerves and extension connecting the two
- 25 assigned to stimulation
- 26 assigned to std medical therapy
- Cross over at 6 months
- Primary endpoints: number of voids/day, volume/void, degree of urgency before void

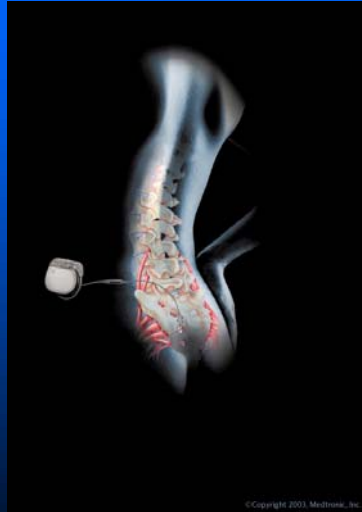
Sacral Neuromodulation

- Significant drop in number of voids daily from 16.9 to 9.3 ($p < 0.0001$), no change in control group
- Significant increase in voided volume from 118 to 226 ($p < 0.0001$)
- Explant in one due to therapy related bowel dysfunction
- When turned off at 6 months, return to baseline
- Sustained clinical benefit 18 – 24 months
- Significant improvement in QoL (SF-36)

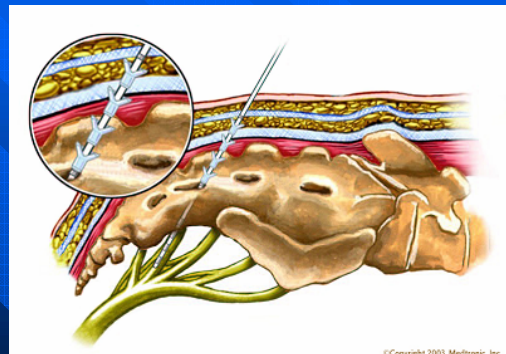
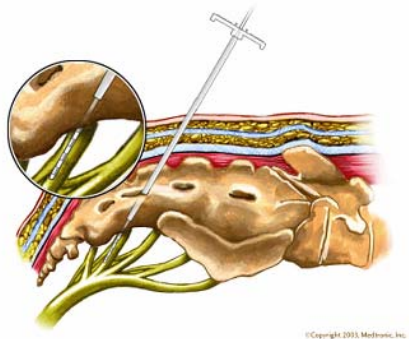
Neuromodulation: InterStim

- Option for those who fail conservative medical therapy
- Must demonstrate relief during test stimulation
- Neurostimulator is implanted subcutaneously in upper buttock or abdomen
- Lead is placed adjacent to appropriate sacral nerve and attached to neurostimulator
- Approved in Canada, available in Halifax, Montreal, Toronto, Edmonton

InterStim, Medtronic



InterStim, Medtronic



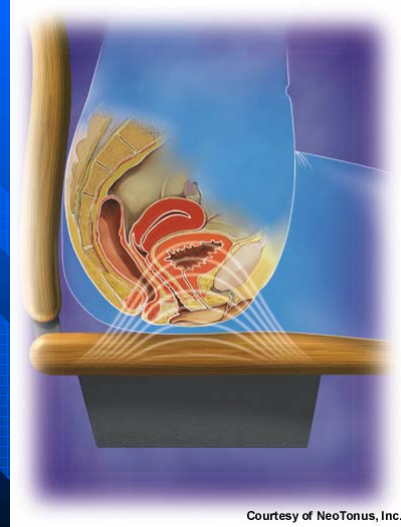
InterStim, Medtronic



Neuromodulation: NeoControl

- Extracorporeal magnetic innervation
- Pulsed magnetic field (5 Hz intermittently for 10 minutes, rest, 50 Hz intermittently for 10 min)
- Patients sit fully clothed on chair for 20 min x 2/week for 6 week course
- How stimulation suppresses detrusor contraction is not known

NeoControl, Neotonus



Neuromodulation: Neocontrol

Quek, Curr Opin Urol 15: 231, 2005

- Well documented increase in cystometric capacity, inhibition of detrusor overactivity, reduction of OAB symptoms *acutely*
- Short term symptomatic improvement in ~ 75%
- Mixed long term data
- > 1 million patients in US yet little literature

SUMMARY

- Anticholinergics effective
- Best evidence for tolterodine 4 mg ER OD vs other anticholinergics
- Even better when combined with behavioural modification
- Sacral neuromodulation option in refractory cases
- Paucity of literature supporting “Stretch and Burn”