

6^{os} ENCONTROS DE ANDROLOGIA

SAÚDE MASCULINA



Nem só a HBP conta... Bexiga Hiperativa no Homem Idoso

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Resumo

• Introdução

- *Lower Urinary Tract (LUT) and symptoms (LUTS)*
- *Overactive Bladder (OAB)*
- OAB no Idoso

• Extensão e natureza do problema

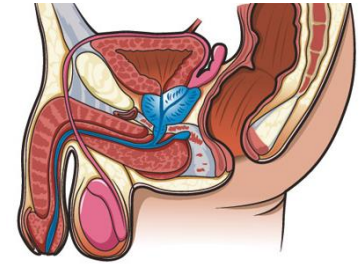
- Alterações do LUT com a idade
- Noctúria
- Estudo EPIC

• Tratamento

- Comportamentos e estilos de vida
- Tratamento farmacológico
- Segurança no Idoso
 - Efeitos laterais
 - Risco de quedas

Introdução – LUTS

- *Lower urinary tract* – LUT
 - **Entidade funcional única**
 - Sintomas associados com etiologia multifatorial



LUT *symptoms* (LUTS) como foco principal

Em vez da antiga ênfase dada à HBP



- ✓ **Queixa comum** do homem adulto
- ✓ Impacto na **QoL**

Introdução – LUTS

EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO)

S. Gravas (Chair), T. Bach, M. Drake, M. Gacci, C. Gratzke,
T.R.W. Herrmann, S. Madersbacher, C. Mamoulakis,
K.A.O. Tikkinen

Guidelines Associates: M. Karavitakis, S. Malde, V. Sakkalis,
R. Umbach

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EAU European
Association
of Urology

HBP inserida na
abordagem dos
LUTS

Introdução – LUTS

- Como **definir LUTS?**

Abrams P. New words for old: lower urinary tract symptoms for "prostatism". *BMJ*. 1994 Apr 9;308(6934):929-30

Holtgrewe HL. Current trends in management of men with lower urinary tract symptoms and benign prostatic hyperplasia. *Urology*. 1998 Apr;51(4A Suppl):1-7

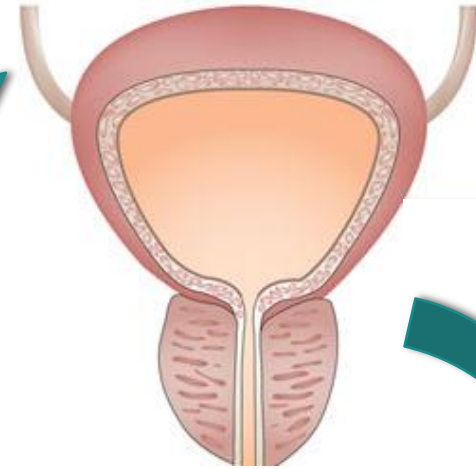


Urology. 2003 Jan;61(1):37-49.

Introdução – LUTS

Armazenamento

- Frequência urinária
- Noctúria
- Urgência miccional
- Incontinência urinária (IU)



Esvaziamento/Pós-miccionais

- Jato urinário fraco
- Hesitação
- Intermitência
- *Straining*
- Gotejamento terminal
- Sensação de esvaziamento incompleto
- Gotejamento pós-miccional

Introdução – LUTS



Gratzke et al. EAU Guidelines on the Assessment of Non-neurogenic Male Lower Urinary Tract Symptoms including Benign Prostatic Obstruction. Eur Urol. 2015 Jun;67(6):1099-1109

Introdução – LUTS

BOX 70-2 Expanded Functional Classification of Lower Urinary Tract Dysfunction

I. Failure to store

A. Because of the bladder

1. Overactivity

a. Involuntary contractions (detrusor overactivity)

- (1) Neurologic disease, injury, or degeneration
- (2) Bladder outlet obstruction
- (3) Increased afferent input or sensitivity
- (4) Inflammation
- (5) Increased neurotransmitter release
- (6) Increased sensitivity to transmitter
- (7) Decreased inhibitory pelvic floor activity
- (8) Idiopathic

b. Decreased compliance

- (1) Neurologic disease or injury
- (2) Fibrosis
- (3) Bladder muscle hypertrophy
- (4) Idiopathic

c. Combination

2. Hypersensitivity

- a. Inflammatory/infectious
- b. Neurologic
- c. Increased neurotransmitter release or sensitivity
- d. Psychological
- e. Idiopathic

3. Underactivity (with retention and overflow incontinence)

4. Combination

B. Because of the outlet

1. Genuine stress urinary incontinence

- a. Lack of suburethral support
- b. Pelvic floor laxity, hypermobility

2. Intrinsic sphincter deficiency

- a. Neurologic disease or injury
- b. Fibrosis

3. Combination (genuine stress urinary incontinence and intrinsic sphincter deficiency)

C. Combination (bladder and outlet factors)

D. Fistula

II. Failure to empty

A. Because of the bladder (underactivity)

1. Neurogenic
2. Myogenic
3. Psychogenic
4. Idiopathic

B. Because of the outlet

1. Anatomic

- a. Prostatic obstruction
- b. Bladder neck contracture
- c. Urethral stricture
- d. Urethral compression, fibrosis

2. Functional

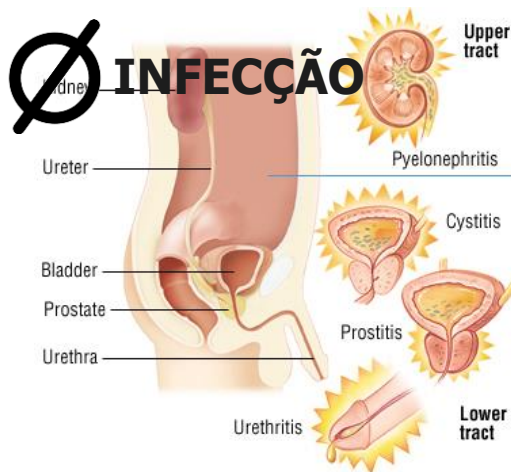
- a. Striated sphincter dyssynergia (neurogenic)
- b. Smooth sphincter dyssynergia or dysfunction (bladder neck dysfunction)
- c. Dysfunctional voiding (non-neurogenic)

C. Combination

Introdução – *Overactive Bladder* (OAB)

- **OAB** → Síndrome da Bexiga Hiperativa

Urgência miccional, com ou sem incontinência, normalmente associada a **frequência** e **noctúria**



Introdução – OAB no Idoso

Overactive bladder syndrome in older people

Adrian S. Wagg, Linda Cardozo¹, Christopher Chapple², Dirk De Ridder³, Con Kelleher⁴, Michael Kirby⁵, Ian Milsom⁶ and Mark Vierhout⁷, on behalf of the Overactive Bladder Faculty

Department of Geriatric Medicine, University College London Hospitals, ¹Department of Gynaecology, King's College Hospital, London, ²Department of Urology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, ³Department of Urology, University Hospitals KU Leuven, Leuven, Belgium, ⁴Department of Obstetrics and Gynaecology, Guys and St Thomas' NHS Foundation Trust, London, ⁵HertNet - The Hertfordshire Primary Care Research Network, and CRIPACC, Faculty of Health & Human Sciences, University of Hertfordshire, UK, ⁶Department of Gynaecology, Sahlgrenska University Hospital, Goteborg, Sweden, and ⁷Department of General Gynaecology, Radboud University Hospital, Nijmegen, the Netherlands

Accepted for publication 19 September 2006

Introdução – OAB no Idoso

- Idosos – grupo **heterogéneo**:

- *Fit*
- Comorbilidades múltiplas



- ***Frail elderly*** 

- > 65 anos
- Actividade física, mobilidade, força motora, cognição, nutrição...
- Dependência nas AVDs

Introdução – OAB no Idoso

CHAPTER 18

Committee 13

Incontinence in the Frail Elderly

Chairman

D. FONDA (AUSTRALIA),

Co-Chair

C. E. DuBEAU (USA)

Members

D. HARARI (UK),

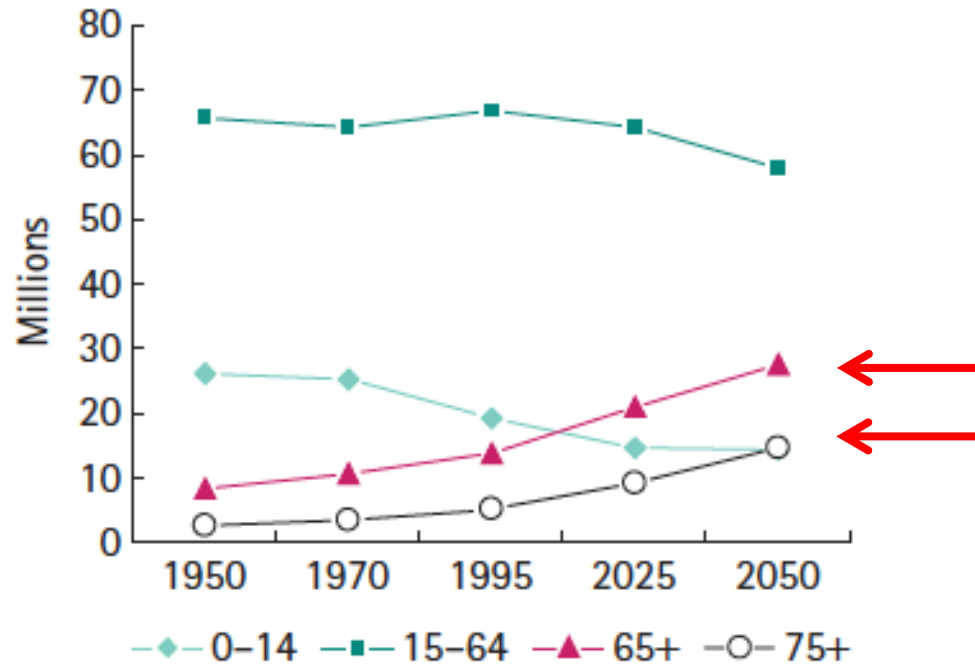
J. G. OUSLANDER (USA),

M. PALMER (USA),

B. ROE (UK)

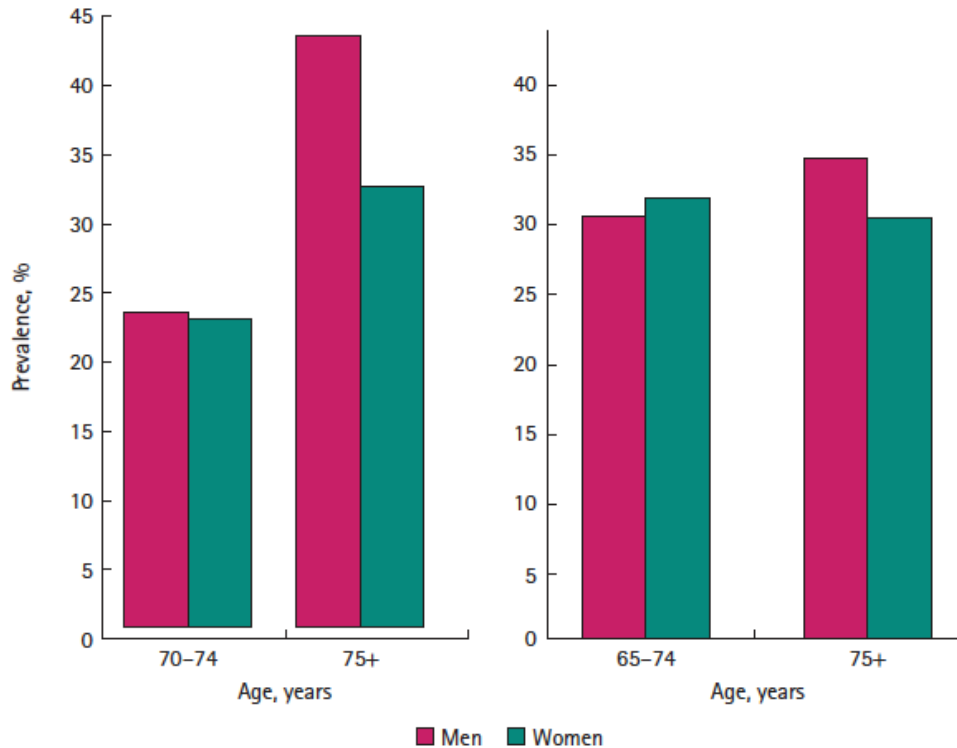
Extensão e natureza do problema

- População **mais envelhecida**



Extensão e natureza do problema

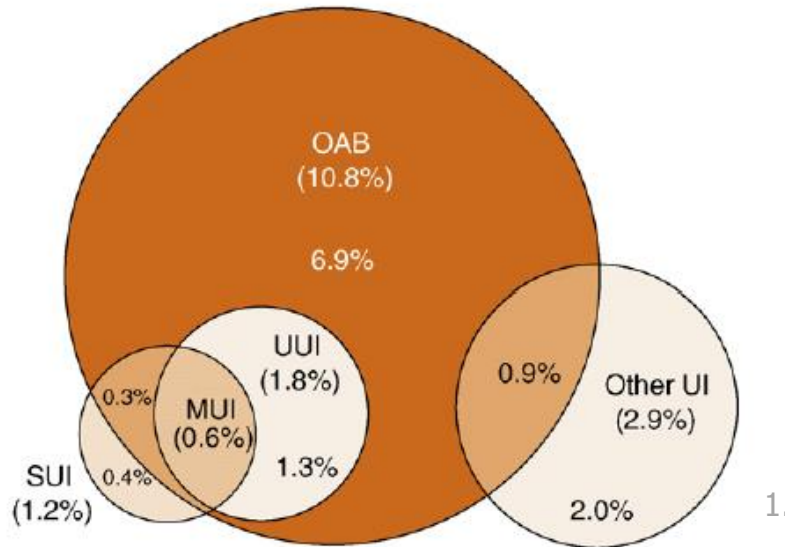
- **OAB mais prevalente com a idade**



Extensão e natureza do problema

• OAB na população geral masculina

(A) Men
Prevalence (%*) in the general population



40-44 anos
3%



>75 anos
42%

1. Irwin et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. *Eur Urol.* 2006 Dec;50(6):1306-14; discussion 1314-5.
2. Milsom et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int.* 2001 Jun;87(9):760-6.

Extensão e natureza do problema

- Patologia ou envelhecimento normal?

REVIEWS

Incontinence in the elderly, 'normal' ageing, or unaddressed pathology?

William Gibson and Adrian Wagg

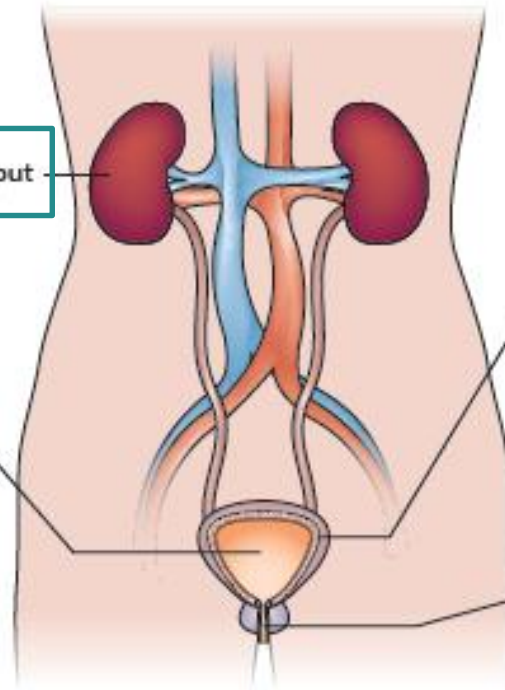
Abstract | The prevalence of urinary incontinence and other lower urinary tract symptoms (LUTS) increases in association with increasing age. This effect is more noticeable in men after the seventh decade of life and, in women, postmenopausally. However, the changes in the lower urinary tract, peripheral nervous system and central nervous system that underpin this observation are both multifactorial and inadequately understood; much debate exists regarding whether these observed changes are pathological or are a part of the 'normal' ageing process; with both health professionals and older people often holding the view that incontinence is an expected part of normal ageing. Here we aim to summarize the current level of knowledge regarding the physiological and hormonal changes that take place during the ageing process and discuss whether the occurrence of urinary incontinence or other LUTS in later life better reflect part of the 'normal' ageing process or the presence of unaddressed pathology.

Alterações do LUT com a idade

Ritmo circadiano de produção de ADH



↓ Daytime urine output



↑ Post-void residual
↓ Capacity?

+++
↑ Collagen content
↑ Spontaneous contractions
↓ Contractile function
↓ Filling sensation

↑ Prostate size (men)
↓ MUCP

Alterações do LUT com a idade

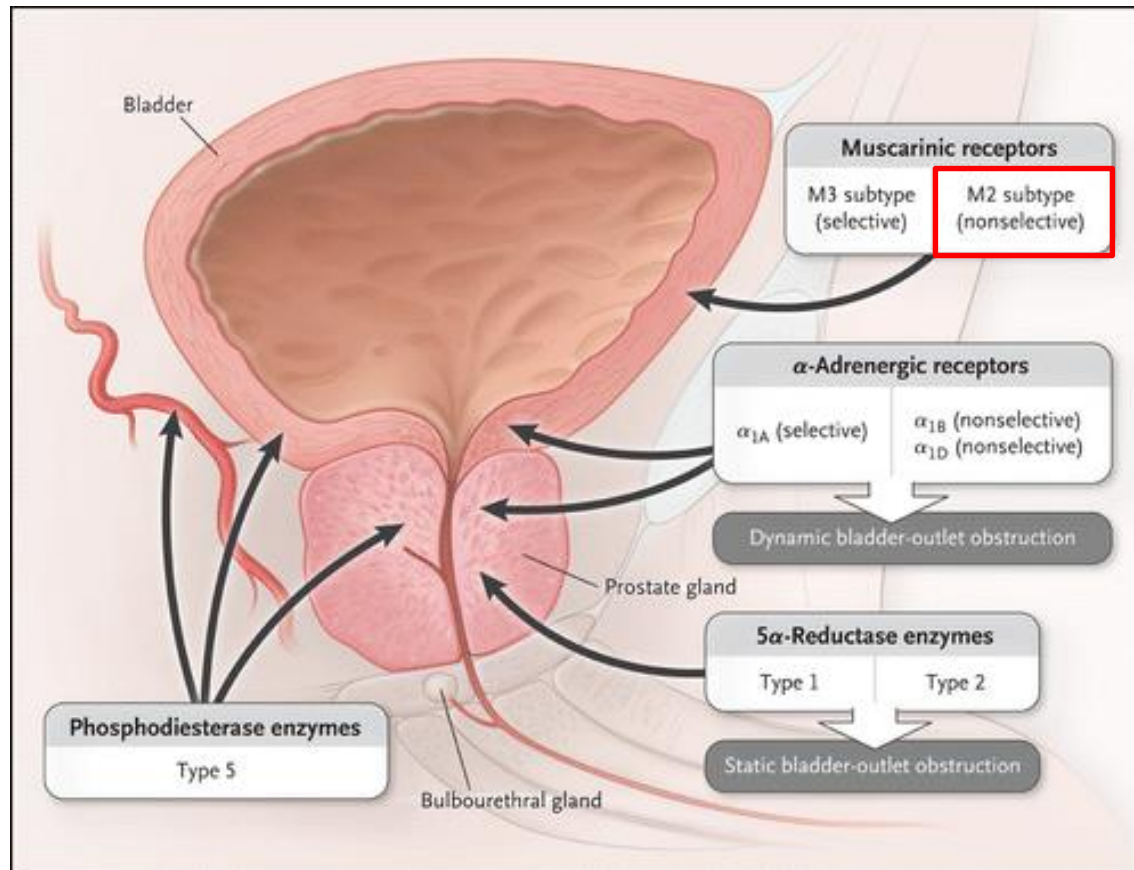
• Bexiga

- Alterações na **resposta aos NT**
 - Desinervação colinérgica
 - ↓ seletiva de receptores M_3 ($M_2 \rightarrow$ sensação de **urgência miccional**)
- ↑ **contrações** vesicais involuntárias
- ↑ **colagénio**/músculo no detrusor
- ↓ **contractilidade** vesical
 - Isquémia
 - Obstrução
- **Espessamento** da parede vesical

LUTS armazenamento

Alterações do LUT com a idade

• Bexiga



Alterações do LUT com a idade

• Próstata

- Fraca associação entre o tamanho da próstata e LUTS
- **HBP induz expressão de receptores** no detrusor e urotélío
 - 5-HT_{3A} e 5-HT₇
 - **M₂** e M₃

LUTS armazenamento

• Urotélío

- **↑ libertação** não neuronal de **ACh**

LUTS armazenamento

Alterações do LUT com a idade

- Cérebro

- *White matter hyperintensities* (WMH)

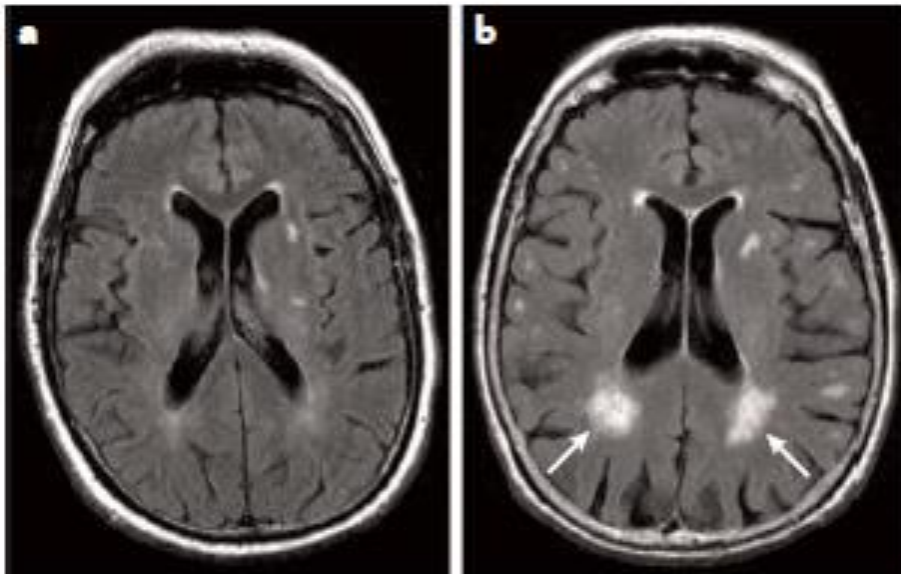


Figure 2 | White matter hyperintensities. Axial MRI images of the brains of two 80-year-old patients. a | Brain MRI image of an 80-year-old without extensive white matter hyperintensity. b | Brain MRI image of an 80-year-old with extensive white matter hyperintensity predominantly located in the periventricular region (indicated by white arrows). The presence of such hyperintensities is correlated with urinary incontinence and several other geriatric syndromes, such as falls and cognitive impairment. Reproduced from 'The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: systematic review and meta-analysis' by Stéphanie Debette, *BMJ* 2010; 341:c3666, with permission from BMJ Publishing Group Ltd.

Alterações do LUT com a idade

- **WMH**

Anormalidades estruturais da massa encefálica que aparecem com a idade e estão relacionadas com a **doença de pequenos vasos**.

WMH na **região frontal inferior direita** e no **giro cingulado**



IU

WMH na **radiação talâmica anterior direita**



OAB

Alterações do LUT com a idade

- Doentes **idosos** vs. jovens:
 - Têm **síndromas de incontinência mais severos**
 - Têm maior probabilidade de **pedir medicação** para problemas relacionados com o LUT
 - Necessitam de **maiores doses**
 - **Aderem mais à terapêutica** (apesar de reportarem **mais efeitos laterais**)

Noctúria

- **Sintoma + comum** no homem com **OAB**
 - ↓ capacidade vesical
 - Poliúria nocturna

Table 1: Categories of nocturia

CATEGORY	Disproportionate urine production (at all times, or during sleep)	Low volume of each void (at all times, or overnight)
<i>Behavioural</i>	Inappropriate fluid intake	"Bladder awareness" due to secondary sleep disturbance
<i>Systemic</i>	Water, salt and metabolite output	
<i>Sleep disorder</i>	Variable water and salt output	"Bladder awareness" due to primary sleep disturbance
<i>LUTD</i>		Impaired storage function and increased filling sensation

Estudo EPIC

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology



Platinum Priority – Voiding Dysfunction

Editorial by Christopher R. Chapple on pp. 21–23 of this issue

Prevalence, Severity, and Symptom Bother of Lower Urinary Tract Symptoms among Men in the EPIC Study: Impact of Overactive Bladder

Debra E. Irwin^{a,}, Ian Milsom^b, Zoe Kopp^c, Paul Abrams^d, Walter Artibani^e, Sender Herschorn^f*

Irwin et al. Prevalence, severity, and symptom bother of lower urinary tract symptoms among men in the EPIC study: impact of overactive bladder. Eur Urol. 2009 Jul;56(1):14-20

Estudo EPIC

Avaliação da prevalência dos LUTS usando as definições da ICS

- **LUTS – 62,5%** (7210 homens)
- Prevalência individual **↑ com a idade**
- LUTS de **armazenamento +++** (51,3%)
- **Noctúria – sintoma + comum** (48,6%)
- Sobreposição de sintomas (armazenamento, esvaziamento e pós-miccionais) entre a população geral e homens com OAB
- **> Percepção subjectiva** de frequência e noctúria nos homens com OAB

Tratamento 1ª linha

- **Mudar estilos de vida + medidas comportamentais**

- **Objectivo:** ↓ frequência urinária e ↑ volume vesical
- Depende do status cognitivo do doente

- **Dieta e Flúidos**

- Ingestão hídrica adequada
- Evicção de irritantes vesicais
- Dieta anti-obstipação
- Perda de peso

Tratamento 1ª linha

- **Mudar estilos de vida + medidas comportamentais**

- **Objectivo:** ↓ frequência urinária e ↑ volume vesical
- Depende do status cognitivo do doente

- **Medidas comportamentais**

- **Treino vesical**
- Urinar por **incitação** (*prompted voiding*)
 - Monitorização regular
 - Incitação a urinar num esquema regular
 - Elogio e feedback positivo
- Urinar pelo **relógio** (*timed voiding*)

Tratamento 2ª linha – farmacológico

• Anti-muscarínicos (AM)

- Disfunção sensorial associada à OAB
- **sucesso equivalente; ≠ tolerabilidade**

<i>Drug</i>	<i>t_{max} (h)</i>	<i>t_{1/2} (h)</i>	<i>Recommended daily dose (mg)</i>
Darifenacin ER	7	12	1 x 7.5-15
Fesoterodine	5	7	1 x 4-8
Oxybutynin IR	1	2-5	2-3 x 5
Oxybutynin ER	4-6	13	1 x 5-30
Propiverine IR	2	14-22	2 x 15
Propiverine ER	10	20	1 x 30
Solifenacin	3-8	45-68	1 x 5-10
Tolterodine IR	1-2	2	2 x 2
Tolterodine ER	4	7-10	1 x 4
Trospium IR	5	18	2 x 20
Trospium ER	5	36	1 x 60

Table S.18: Trials with antimuscarinic drugs only in elderly men with LUTS, predominantly with OAB symptoms

Trials	Duration (weeks)	Treatment	n	Voiding frequency (%)	Nocturia (%)	Urgency incontinence (%)	IPSS (%)	LE
Kaplan et al. (2005) [74]	25	Tolterodine 1 x 4 mg/d (after β -blocker failure)	43	-35.7 ^a	-29.3 ^a	-	-35.3 ^a	2b
Roehrborn et al. (2006) [75]	12	Placebo	86	-4	-	-40	-	1b
		Tolterodine 1 x 4 mg/d	77	-12	-	-71 ^b	-	
Kaplan et al. (2006) [76]	12	Placebo	374	-7.9	-17.6	-	-	1b
		Tolterodine 1 x 4 mg/d	371	-10.8 ^b	-18.8	-	-	
Kaplan et al. (2006) [77]	12	Placebo	215	-13.5	-23.9	-13	-44.9	1b
		Tolterodine 1 x 4 mg/d	210	-16.5	-20.1	-85 ^b	-54	
Dmochowski et al. (2007) [78]	12	Placebo	374	-5.6	-17.6	-	-	1b
		Tolterodine 1 x 4 mg/d	371	-8.7 ^b	-18.8	-	-	
Höfner et al. (2007) [79]	12	Tolterodine 1 x 4 mg/d	741	-20 ^a	-42.9 ^a	-100 ^a	-37.9 ^a	2b
Herschorn et al. (2010) [80]	12	Placebo	124	-10.2	-	-59.3	-	1b
		Fesoterodine 1 x 4 mg/d	111	-13.2 ^b	-	-84.5 ^b	-	
		Fesoterodine 1 x 8 mg/d	109	-15.6 ^b	-	-100 ^{b,c}	-	
Chapple et al. (2014) [81]	12	Placebo	386	-12.5	-	-53.6	-	1b
		Fesoterodine 1 x 4 mg/d	790	-19.8	-	-74.3	-	
		Fesoterodine 1 x 8 mg/d	779	-23.6	-	-79.5	-	

IPSS = International Prostate Symptom Score.

^a = significant compared with baseline ($p < 0.01$; indexed wherever evaluated); ^b = significant compared with placebo ($p < 0.05$); ^c = significant compared with fesoterodine 4 mg ($p < 0.05$).

Tratamento farmacológico

- **Agonistas $\beta 3$**

- **Mirabegron**, 50 mg id
- Boa tolerabilidade
- Efeito adverso + comum: **HTA (9,9%)**
- Sem efeitos no SNC

- **Alternativa aos AM?**

Tratamiento farmacológico



Current Medical Research and Opinion



ISSN: 0300-7995 (Print) 1473-4877 (Online) Journal homepage: <http://www.tandfonline.com/loi/icmo20>

Oral pharmacotherapy for overactive bladder in older patients: mirabegron as a potential alternative to antimuscarinics

Adrian Wagg, Victor W. Nitti, Con Kelleher, David Castro-Diaz, Emad Siddiqui & Todd Berner

Wagg et al. Oral pharmacotherapy for overactive bladder in older patients: mirabegron as a potential alternative to antimuscarinics. *Curr Med Res Opin.* 2016;32(4):621-38.

Tratamento farmacológico

Received: 12 January 2017 | Accepted: 16 April 2017

DOI: 10.1002/nuu.23309

REVIEW ARTICLE

WILEY   

Systematic literature review of clinical trials evaluating pharmacotherapy for overactive bladder in elderly patients: An assessment of trial quality

Kristin D. Kistler PhD¹  | Yingxin Xu PharmD, PhD¹ |
Kelly H. Zou PhD, PStat®² | Fady Ntanios PhD² |
Douglass S. Chapman MS² | Xuemei Luo PhD²

Revisão de ensaios clínicos de qualidade que avaliam o uso **de anti-muscarínicos e agonistas β_3** em **doentes idosos com OAB.**

Kistler et al. Systematic literature review of clinical trials evaluating pharmacotherapy for overactive bladder in elderly patients: An assessment of trial quality. *NeuroUrol Urodyn.* 2017 Aug 1. [Epub ahead of print]

Tratamento farmacológico

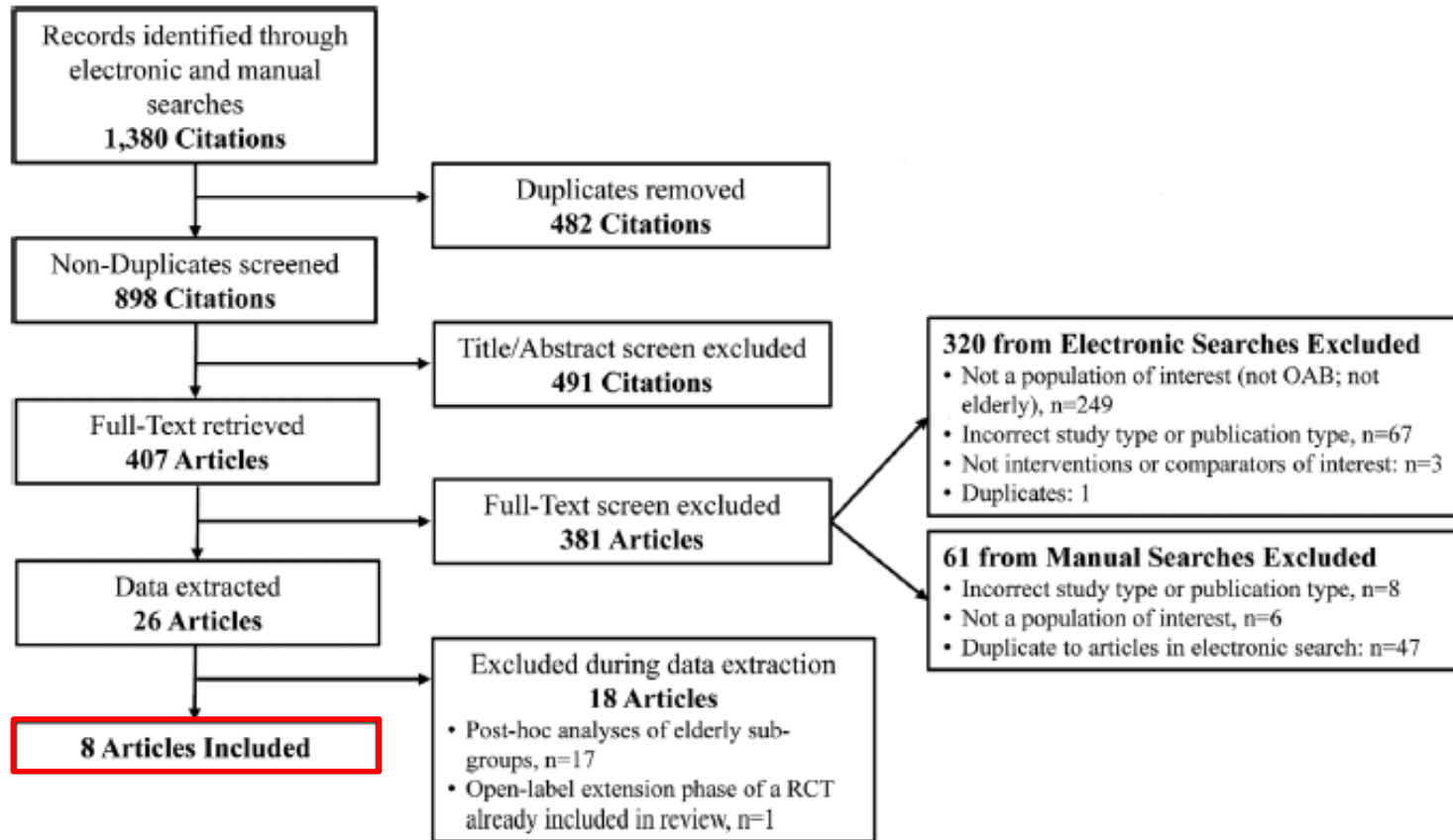


FIGURE 1 Study attrition flow diagram

Apenas 3 com qualidade forte (Strong – Escala EPHPPQA)

Tratamento farmacológico

- **Idoso *Fit***

- Tratar como alguém de “meia idade”
- Terapêuticas de 3ª linha (BTXA, neuromodulação)

- **Idoso *Frail***

- **Desafio terapêutico**
- Recomenda-se apenas **mudança de estilos de vida + medidas comportamentais**
- Alguns AM são seguros...
- Mirabegrom como uma ótima opção nestes doentes

Segurança no idoso e AM

REVIEW ARTICLE

IJCP THE INTERNATIONAL JOURNAL OF
CLINICAL PRACTICE

Review of cognitive impairment with antimuscarinic agents in elderly patients with overactive bladder

A. Wagg,¹ C. Verdejo,² U. Molander³

- ✓ Diferenças nos **perfis de ligação** dos fármacos aos **receptores**
- ✓ Capacidade de **atravessar a barreira hemato-encefálica (BHE)**

• Doentes com > risco

- Défice cognitivo sub-clínico
- Vulnerabilidade inerente às comorbilidades
- **Polimedicação**

Wagg et al. Review of cognitive impairment with antimuscarinic agents in elderly patients with overactive bladder. Int J Clin Pract. 2010 Aug;64(9):1279-86.

Segurança no idoso e AM

Polimedicação

• Carga anti-colinérgica

- Pelo menos **50%** medicados com fármaco com efeitos AC
- Doentes ≥ 65 anos:
 - 60% faz 1 fármaco
 - **1/3 faz ≥ 5 fármacos**

Table 3. Commonly Used Medicines That Have Anticholinergic Effects^a

Antihistamines	Corticosteroids
Diphenhydramine	Corticosterone
Hydroxyzine	Dexamethasone
Cardiovascular	Hydrocortisone
Captopril	Prednisolone
Chlorthalidone	Gastrointestinal
Digoxin	Atropine
Diltiazem	Cimetidine
Dipyridamole	Ranitidine
Furosemide	Immunosuppression
Hydrochlorothiazide	Azathioprine
Hydralazine	Cyclosporin
Isosorbide mononitrate	Infection
Methyldopa	Ampicillin
Nifedipine	Cefalothin
Triamterene	Cefamandole
Warfarin	Cefoxitin
Central nervous system	Clindamycin
Alprazolam	Cycloserine
Amitriptyline	Gentamicin
Chlordiazepoxide	Piperacillin
Codeine	Tobramycin
Desipramine	Vancomycin
Diazepam	Muscle relaxants
Doxepin	Pancuronium
Flurazepam	Respiratory system
Imipramine	Theophylline
Oxazepam	
Oxycodone	
Phenelzine	
Phenobarbital	

^aData from Tune et al.¹⁵

Segurança no idoso e AM

- Características farmacocinéticas
 - Peso < **400 KDa**
 - **Lipossolubilidade**
 - **Carga neutra** (baixo grau de ionização)

Table 1 Pharmacokinetic characteristics of commonly used antimuscarinics for treatment of OAB. Data from ref. (38–41)

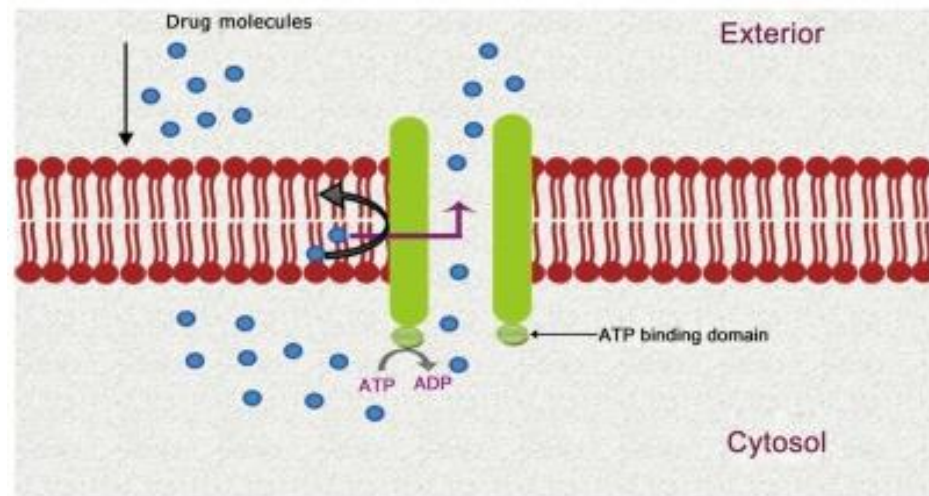
Antimuscarinic	Chemical structure (type of amine)	Molecular weight of the base compound (kDa) (the MW of the conjugated salt is given in parenthesis)	Lipophilicity
Oxybutynin	Tertiary	357.5 (chloride: 393.9)	High
Darifenacin	Tertiary	426.6 (hydrobromide: 507.5)	Moderate
Solifenacin	Tertiary	362.5 (succinate: 480.6)	Low-moderate
Tolterodine*	Tertiary	325.5 (tartrate: 475.6)	Low-moderate
Fesoterodine*	Tertiary	411.6 (fumarate: 527.7)	Low-moderate
5-Hydroxymethyl tolterodine*	Tertiary	341.49 (not applicable)	Low-moderate
Trospium	Quaternary	392.1 (chloride: 428.0)	Very low (hydrophilic)

*Fesoterodine and tolterodine are both rapidly hydrolysed to an active metabolite, 5-hydroxymethyl tolterodine (5-HMT). OAB, overactive bladder.

Segurança no idoso e AM

- Transporte ativo através da BHE (efluxo)
 - **Glicoproteína P (P-gp)**

- Darifencina
- Fesoterodina
- Cloreto de Tróspio
- (Mirabegron)



Segurança no idoso e AM

- Afinidade (pKi)
 - M1 – cérebro
 - M3 – detrusor e urotélio

Table 2 Mean binding affinities (pKi) of antimuscarinic drugs for M₁ and M₃ receptors. Data have been compiled from various sources (42–45) and might not be directly comparable between the different antimuscarinics – the most important information is the relative affinity for these receptors shown by each individual antimuscarinic

Antimuscarinic	pKi for M ₁ receptors	pKi for M ₃ receptors
Oxybutynin (42)	9.9	12.3
Desethyloxybutynin* (42)	6.0	5.5
Darifenacin (43)	8.2	9.1
Solifenacin (44)	7.6	8.0
Tolterodine (45)	8.5	7.9
Fesoterodine (45)	6.2	< 6
5-HMT† (45)	8.7	8.2
Tropium (43)	9.1	9.3
Propiverine (43)	6.6	6.4

*The major metabolite of oxybutynin.

†The major metabolite of fesoterodine and tolterodine; 5-HMT is also known as ASPM7605 in the literature. 5-HMT, 5-hydroxymethyl tolterodine.

Segurança no idoso

- Quais os fármacos **seguros**?



Expert Opinion on Drug Safety



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Safety issues associated with using medication to treat overactive bladder

George Araklitis & Linda Cardozo

Araklitis et al. Safety issues associated with using medication to treat overactive bladder. Expert Opin Drug Saf. 2017 Nov;16(11):1273-1280.

Segurança no idoso

- Quais os fármacos **seguros**?

FORTA – Fit FOR The Aged

A – Absolutely

B – Benficial

C – Careful

D – Don't

Table 1. Selected drugs for the long-term treatment of lower urinary tract symptoms in older people

Drug class (drugs in alphabetical order)	Agent	FORTA class ^a	Number of raters ^b	Consensus coefficient, Round 1 (cut-off 0.800)	Expert ratings on a numerical scale: A = 1, B = 2, C = 3, D = 4		
					Round 1 (R1)	Round 2 (R2)	Mean (Mode)
5 α -reductase inhibitors	Dutasteride	B	5	1.000	2.0; 2		
	Finasteride	B	5	0.900	2.2; 2		
α_1 -blockers	Alfuzosin	D	5	0.900	3.8; 4		
	Doxazosin	D	5	0.900	3.8; 4		
	Silodosin	C	5	1.000	3.0; 3		
	Tamsulosin	C	5	1.000	3.0; 3		
	Tenzosin	D	5	0.800	R1: 3.6; 4 R2: 3.8; 4		
Antimuscarinics	Darifenacin	C	5	1.000	3.0; 3		
	Fesoterodine	B	5	0.900	2.2; 2		
	Oxybutynin standard dose/ immediate release	D	5	0.900	3.8; 4		
	Oxybutynin low dose/extended release	C	4	1.000	3.0; 3		
	Propiverine	D	5	0.700	R1: 3.4; 3 R2: 3.8; 4		
	Solifenacin	C	5	1.000	3.0; 3		
	Tolterodine	C	5	1.000	3.0; 3		
	Trospium	C (B)	5	0.800	R1: 2.4; 2 R2: 2.6; 3		
β_3 -agonist	Mirabegron	C	5	1.000	3.0; 3		
PDE5 inhibitor	Tadalafil	C	5	0.900	2.8; 3		

LUTS, lower urinary tract symptoms.

^aOriginal FORTA class in parentheses if different from consensus results.

^bNo changes between Rounds 1 and 2.

Risco de quedas

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REVIEW ARTICLE

International Journal of
 Clinical Practice

Lower urinary tract symptoms, incontinence and falls in elderly people: time for an intervention study

V. Morris, A. Wagg

CLINICAL INVESTIGATION

Urinary Incontinence: Does it Increase Risk for Falls and Fractures?

Jeanette S. Brown, MD,^{†‡} Eric Vittinghoff, PhD,[†] Jean F. Wyman, RN, PhD,[†] Katie L. Stone, PhD,[†] Michael C. Nevitt, PhD,[†] Kristine E. Ensrud, MD, MPH[¶], and Deborah Grady, MD, MPH^{†‡§} For the Study of Osteoporotic Fractures Research Group*

1. Morris et al. Lower urinary tract symptoms, incontinence and falls in elderly people: time for an intervention study. *Int J Clin Pract.* 2007 Feb;61(2):320-3.
2. Brown et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. *J Am Geriatr Soc.* 2000 Jul;48(7):721-5.

Take Home Messages

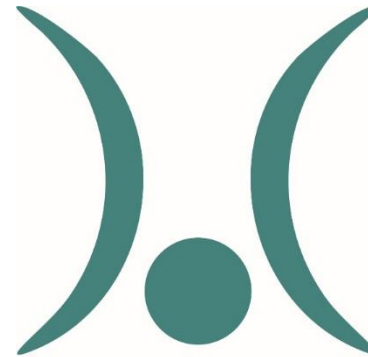
- **OAB** é um problema **comum** na população idosa
 - Alterações fisiológicas do LUT com a idade
 - Prevalência crescente
- A **OAB no idoso** é **mais severa** e a **procura de tratamento é maior**
- O tratamento depende do **status cognitivo** do doente
- **Atenção** extra aos **efeitos laterais** do tratamento farmacológico
 - Carga anti-colinérgica
 - Idoso *Frail*

Obrigada pela vossa atenção



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Alterações do LUT com a idade

Table 3. Age-related changes that can contribute to urinary incontinence in frail elderly people

Age-Related	Change Potential Effects on Continence
1. Bladder ultrastructure on electron microscopy a. Dysjunction pattern b. Muscle and axon degeneration	Bladder overactivity and urge incontinence ← Impaired bladder contractility, increased residual urine, and decreased functional bladder capacity
2. Bladder function a. Decreased capacity b. Increased involuntary detrusor contractions c. Decreased contractility during voiding d. Increased residual urine	Increased likelihood of urinary symptoms and incontinence ←
3. Urethra a. Decreased closure pressure in women	Increased likelihood of stress and urge incontinence
4. Prostate a. Increased incidence of benign prostatic obstruction	Increased likelihood of urinary symptoms and incontinence ←
5. Decreased estrogen (women)	Increased incidence of atrophic vaginitis and related symptoms Increased incidence of recurrent urinary tract infections Decreased urethral pressure
6. Increased nighttime urine production	Increased likelihood of nocturia and nighttime incontinence ←
7. Altered central and peripheral neurotransmitter concentrations and actions	Increased likelihood of lower urinary tract dysfunction ←
8. Altered immune function	Increased likelihood of recurrent urinary tract infections

Segurança no idoso e AM

Table 6. pharmacokinetics in older people

Parameter	Age-associated Changes	Potentially Affected UI Drugs
Absorption	Minimal quantitative change despite ↓ gastric motility, yet little known regarding effect on slow-release agents	Extended release preparations
	↓ Skin thickness	Transdermal preparations
Distribution	Decrease in lean body mass leads to ↓ Vd / ↓ T for hydrophilic drugs and ↑ Vd / ↑ T for lipophilic agents	Lipophilic agents, tricyclic antidepressants
	Decreased protein binding in frail patients with low albumin, leading to higher concentration of free drug	<u>Tolterodine</u> (highly protein bound) [20]
Hepatic metabolism	↓ Phase I reactions (oxidation/ reduction)	Tricyclic antidepressants
	No change in Phase II reactions (glycosylation)	
	↓ Hepatic blood flow and ↓ hepatic mass, leading to reduced clearance for agents with first-pass metabolism	<u>Oxybutynin</u> <u>Tolterodine</u> (higher serum concentrations) [20]
	Stereoselective selectivity in metabolism (hypothetical)	Enantiomers
	Cytochrome P450	<u>Oxybutynin</u> (CYP3A4), [19] <u>Tolterodine</u> (CYP2D6) [20]
Clearance	Decrease in renal clearance	<u>Tolterodine</u> [20] Trospium

Vd = volume of distribution, T = half life