Review: Drugs for urgency urinary incontinence improve continence in women

Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. ***Benefits and harms of pharmacologic treatment for urinary incontinence in women: a systematic review.*** *Ann Intern Med. 2012;156:861-74.*

Clinical impact ratings: GM ★★★★★☆☆ G ★★★★★★☆

Question

What are the benefits and harms of drug therapy for urgency urinary incontinence (UI) in community-dwelling women?

Review scope

Included studies compared drugs available in the USA for urgency UI (darifenacin, fesoterodine, oxybutynin, trospium, solifenacin, and tolterodine) with each other or placebo and enrolled ≥ 75% women. Outcomes included continence and treatment discontinuation due to adverse effects (AEs).

Review methods

MEDLINE, Cochrane Library, SCIRUS, Google Scholar, US Food and Drug Administration reviews, and clinical trial registries were searched for English-language, randomized, controlled trials (RCTs) and individual patient data (IPD) analyses. 94 studies met selection criteria; 8 were IPD analyses. Risk for bias was low: 73% studies adequately described randomization, 23% had clear allocation concealment, 39% performed intention-to-treat analyses, and 99% were double-blind.

Main results

Fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium each improved continence compared with placebo (Table). Fesoterodine and oxybutynin had higher rates of discontinuation, whereas solifenacin and trospium had borderline increases (Table).

Conclusions

Drugs for urgency urinary incontinence improve continence in women. Fesoterodine and oxybutynin are more frequently discontinued due to adverse effects than other drugs.

Active drugs vs placebo for urgency urinary incontinence in women*

Outcomes	Active drug	Number of trials (*n*)	Event rates		RBI (95% CI)	NNT (CI)
			Drug	Placebo		
Continence	Fesoterodine	2 (2465)	61%	49%	30% (10 to 50)	8 (5 to 17)
	Oxybutynin	4 (992)	27%	16%	70% (30 to 110)	10 (7 to 17)
	Solifenacin	5 (6304)	39%	28%	50% (40 to 60)	10 (7 to 17)
	Tolterodine	4 (3404)	53%	44%	20% (10 to 40)	12 (8 to 25)
	Trospium	4 (2677)	28%	17%	70% (50 to 100)	10 (8 to 13)
					RRI (CI)	NNH (CI)
Discontinuation†	Darifenacin	7 (3138)	4.6%	3.3%	19% (–29 to 94)	NS
	Fesoterodine	4 (4433)	6%	3%	94% (19 to 200)	34 (17 to 100)
	Oxybutynin	5 (1483)	10%	5%	90% (9 to 233)	17 (8 to 100)
	Solifenacin	7 (9080)	5%	4%	28% (0 to 65)	NS
	Tolterodine	10 (4466)	4%	3%	10% (–20 to 67)	NS
	Trospium	6 (3936)	5.8%	3.9%	47% (0 to 110)	NS

**NS = not significant; other abbreviations defined in Glossary. RBI, NNT, and CI for continence calculated from relative risks and risk differences in article using a random-effects model. RRI and CI for discontinuation calculated from control event rates and Bayesian odds ratios in article using a random-effects model; NNH calculated from the reported risk difference.*

†Treatment discontinuation due to adverse effects.

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Commentary

Shamliyan and colleagues report results of a well-done and thorough systematic review of antimuscarinic drugs for urgency UI and reached conclusions similar to those of previous systematic reviews (1). One assumes that behavior modification was part of therapy for all participants with urgency UI. Shamliyan and colleagues found that currently available agents for urgency UI were all better than placebo for efficacy outcomes. Studies varied in their assessments of quality of life (QOL), and so the effect of drugs on this outcome was not conclusive. In subjective symptom syndromes, such as urgency UI, improved QOL is the most clinically relevant subjective benefit. Although QOL generally correlates with diary data, it often reflects benefits that are not completely conveyed by objective outcomes. These benefits can be substantive for community-dwelling patients, allowing them to be active in social, work, and other societal contexts (abilities often substantially affected by urgency UI).

So what are the risks associated with this class of agents? Shamliyan and colleagues report roughly similar discontinuance rates in the trials. Urgency UI has variable effects and may become less bothersome with time for some patients. Some may find that improvement is not persuasive enough to continue long-term medication or that side effects are too bothersome. Finally, human nature probably affects adherence to antimuscarinic drugs; daily dosing may not be consistent with patient lifestyles.

This medication class is generally safe, and such AEs as dry mouth and constipation are bothersome but rarely dangerous. However, AEs may be more common in certain subgroups, such as the frail elderly. Some antimuscarinic agents cross the blood–brain barrier and may affect cognition in at-risk individuals (e.g., frail elderly, those with preexisting cognitive dysfunction, and those taking certain concomitant medications). Appropriate provider assessment of these risks is critical.

Patient and provider engagement in the management of this condition is important and should include education, reasonable expectation setting, and reappraisal of patient response to therapy for optimization of symptom control.

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Reference

1. **Madhuvrata P, Cody JD, Ellis G, Herbison GP, Hay-Smith EJ.** Which anticholinergic drug for overactive bladder symptoms in adults. Cochrane Database Syst Rev. 2012;(1):CD005429. .