

Review: Drugs do not improve symptoms in urinary urge incontinence and may have side effects

Haeusler G, Leitich H, van Trotsenburg M, Kaider A, Tempfer CB. Drug therapy of urinary urge incontinence: a systematic review. *Obstet Gynecol.* 2002;100:1003-16.

QUESTION

Is drug therapy effective for urinary urge incontinence (UI)?

DATA SOURCES

Studies published up to October 2000 were identified by searching MEDLINE (from 1966), EMBASE/Excerpta Medica (from 1989), and the Cochrane Controlled Trials Register.

STUDY SELECTION

Original English-language studies were selected if they were randomized placebo-controlled trials of drug therapies other than hormone therapy in patients with UI confirmed by urodynamic assessment and outcomes included ≥ 1 of subjective improvement, results of a urodynamic evaluation, or adverse effects.

DATA EXTRACTION

3 independent investigators extracted data on number of patients, inclusion and exclusion criteria, type of drug, and outcomes. Quality of individual trials was assessed on the basis of the randomization process, patient exclusions after randomization, and patient compliance.

MAIN RESULTS

47 trials met the selection criteria, but 11 trials of terodiline were excluded from analysis because it was withdrawn from the market. Sample sizes in the remaining 36 trials ranged from 20 to 316. Meta-analysis was not done because of heterogeneity among trials. Only drugs that were assessed in > 1 trial are reported here. Results for the anticholinergic drugs oxybutinin, emepronium, and tolterodine are summarized in the Table.

12 trials assessed *alternative drug regimens*. Flavoxate had no effect on symptoms in 1 of 1 trial ($n = 38$) or adverse effects in 2 of 2 trials ($n = 91$). Flurbiprofen improved symptoms in 1 of 1 trial ($n = 58$), but increased

adverse effects in 1 of 1 trial ($n = 61$) and had no effect on dry mouth in 2 of 2 trials ($n = 121$) or adverse effects that stopped treatment in 2 of 2 trials ($n = 126$).

CONCLUSION

Limited evidence suggests that drugs commonly used for incontinence—oxybutinin, emepronium, tolterodine, and flavoxate—are either ineffective or have a low rate of effectiveness that is counterbalanced by an increase in specific adverse effects.

Source of funding: No external funding.

For correspondence: Dr. C.B. Tempfer, University of Vienna School of Medicine, Vienna, Austria. E-mail clemens.tempfer@akh-wien.ac.at. ■

Effectiveness of anticholinergic drugs for urinary urge incontinence

Outcomes	Oxybutinin (number of patients)	Emepronium (number of patients)	Tolterodine (number of patients)
Symptoms	Improved in 2 ($n = 137$) of 5 trials ($n = 456$)	Improved in 1 ($n = 36$) of 5 trials ($n = 192$)	No difference in 2 of 2 trials ($n = 449$)
Bladder stability	No difference in 2 of 2 trials ($n = 145$)	No difference in 1 of 1 trial ($n = 40$)	Not assessed
Adverse effects	Increased in 3 ($n = 507$) of 4 trials ($n = 546$)	Increased in 1 ($n = 36$) of 4 trials ($n = 156$)	No difference in 4 of 4 trials ($n = 587$)
Dry mouth	Increased in 5 ($n = 662$) of 7 trials ($n = 845$)	No difference in 4 of 4 trials ($n = 156$)	Increased in 2 ($n = 491$) of 5 trials ($n = 903$)
Adverse effects that stopped treatment	Increased in 1 ($n = 70$) of 5 trials ($n = 523$)	No difference in 5 of 5 trials ($n = 196$)	No difference in 4 of 4 trials ($n = 823$)

COMMENTARY

Despite decades of using anticholinergic drugs for UI, few well-designed, controlled trials support the efficacy of these drugs. Haeusler and colleagues identified double-blind trials that were published up to October 2000. Only 8 of 36 studies enrolled > 100 patients, and outcomes were mostly based on subjective reports by patients rather than urodynamic results. Trials of nonpharmacologic therapies (1) that incorporated independent drug-placebo comparison arms that might have been included were not. 3 studies quoted by the U.S. Public Health Service Clinical Practice Guideline (2) as establishing the effectiveness of oxybutinin are not mentioned.

Only a small proportion of the trials with outcome data reported significant benefits. This may reflect small sample sizes, heterogeneous patient populations, and a relatively high placebo response rate (approximately 40% for reduction in incontinence episodes) (1). Better results have been obtained with biofeedback and behavioral therapy in geriatric outpatients (1). These techniques are not currently available in routine clinical practice but perhaps should be part of our clinical training. None of the trials included elderly patients with dementia, a group

with a high frequency of UI in whom delirium associated with anticholinergic agents is a major adverse effect.

An effective, safe, pharmacologic solution for incontinence continues to elude us, but clinicians can at least rely on easily implemented guidelines for diagnostic stratification (2, 3) and assist patients with treatment decisions, which may include a trial of medication.

Fitzhugh C. Pannill 3d, MD
Southbury Medical Associates
Southbury, Connecticut, USA

References

- Burgio KL, Locher JL, Goode PS, et al. Behavioral vs drug treatment for urge urinary incontinence in older women: a randomized controlled trial. *JAMA.* 1998;280:1995-2000.
- Fantl JA, Newman DK, Colling J. Urinary incontinence in adults: acute and chronic management. Clinical Practice Guideline, No. 2. AHCPR Publication No. 95-0682. Rockville, MD: Agency for Health Care Policy and Research, 1996. <http://www.ahcpr.gov/research/may96/dept5.htm>
- Resnick NM. Urinary incontinence. In: Cassel CK, Leipzig RM, Cohen HJ, Larson EB, Meier DE, eds. *Geriatric Medicine: An Evidence Based Approach.* 4th ed. New York: Springer;2003:931-55.