

Treating overactive bladder in the elderly

Adrian Wagg, MB, FRCP, FHEA

Division of Geriatric Medicine, Department of Medicine, University of Alberta, Edmonton, AB

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Abstract

The prevalence of the overactive bladder (OAB) symptom complex increases with age. Older people also appear to experience more severe incontinence syndromes, including OAB, than their younger counterparts. Older patients are more likely than younger individuals to ask for medication for bladder problems and to require higher doses of medication. Conventional treatment for OAB with conservative and lifestyle measures in combination with antimuscarinic pharmacotherapy is effective in older people. Although there is a theoretical potential for cognitive impairment with antimuscarinic agents, the newer antimuscarinics are cognitively safe in cognitively intact older people.

The overactive bladder (OAB) symptom complex, much like all lower urinary tract symptoms, is increasingly prevalent in association with increasing age.^{1,2} This brief review outlines the epidemiology of these symptoms in later life and discusses the particular changes that occur in the aging lower urinary tract. In addition, the use of antimuscarinic agents in older patients is reviewed, including a discussion of the potential for the antimuscarinic effects to have a detrimental impact on cognitive function.

Changes in the urinary tract associated with aging

Natural changes in the urinary tract may account for some of the apparent increase in lower urinary tract symptoms with increasing age. The sensation of bladder filling is reduced and bladder capacity falls, leading to an older person having less time to respond to the call to urinate and perhaps explaining why many older people complain of severe urge, rather than urgency, as defined by the International Continence Society.³ However, older people also experience a more severe degree of incontinence, including OAB, than their younger counterparts.^{2,4} For older sufferers with OAB, bladder sensation appears to be heightened, bladder capacities much lower, and urethral resistance rises in association

with the onset of the condition, although the mechanism underlying this is unknown.

Underlying mechanisms

Urinary urgency in older people may be a result of both bladder and intracerebral lesions. Severity of urinary urgency and of incontinence *per se* have been associated with increased white matter hyperintensities (WMH) on MRI scanning of older people, suggesting that increasing ischemic insults in association with aging may impair higher centres of influence on the maintenance of continence, manifesting as severe urge, urgency and urgency incontinence.^{5,6}

Treatment of OAB in older patients

Conventional treatment for OAB with conservative and lifestyle measures in combination with antimuscarinic pharmacotherapy is effective in older people. In direct contradiction to the usual geriatric paradigms of prescribing, older people are more likely than young to require, and ask for, medication for their bladder problem;⁷ appear to require higher doses of medication;^{8,9} and, despite higher reported rates of adverse events, are more adherent to their medication than younger users.¹⁰

Antimuscarinics: efficacy

In a study published in 2000, investigators examined the effects of combining behavioural treatment and drug treatment for urge incontinence in community-dwelling older women.¹¹ A total of 197 ambulatory, nondemented, community-dwelling women (age 55 years or older) with persistent urge urinary incontinence were enrolled. Of these, 34 participated in combined treatment. Eight patients started on conservative measures (biofeedback-assisted behavioural training) and then had eight weeks of combined behavioural training and drug treatment with oxybutynin, titrated from 2.5 mg to 15 mg daily. The second group received the anti-

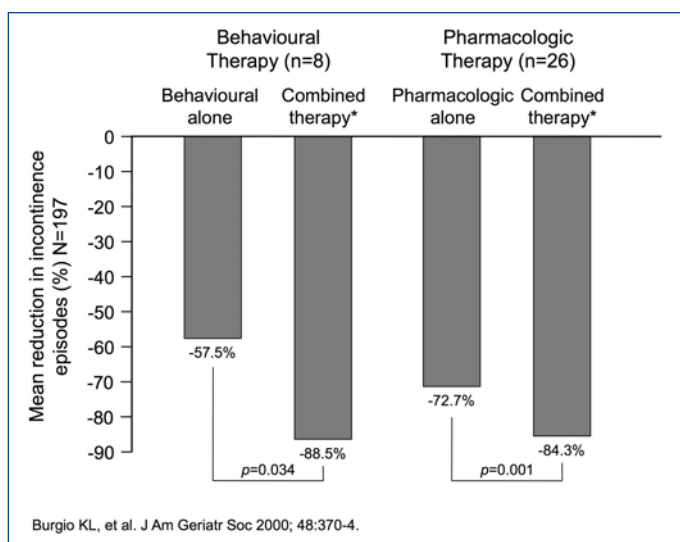


Fig. 1. Benefits of combined pharmacologic and behavioural therapy in older people. *Behavioural therapy and pharmacotherapy (oxybutynin 2.5-15 mg daily)

muscarinic therapy first, followed by eight weeks of this drug therapy combined with behavioural training. As shown in Figure 1, the combination of behavioural training and pharmacotherapy was superior to either element alone. Although a small group, this finding is worthy of further exploration.

Several antimuscarinic agents have subsequently been evaluated in older patients, although these are mostly subgroup or pooled analyses from more inclusive study populations.

In a 12-week planned placebo-controlled study of darifenacin in 400 older patients (≥ 65 years) with OAB, the active therapy did not achieve a statistically significant separation from placebo for the primary endpoint of change in weekly urge urinary incontinence episodes.¹² However, a significantly greater proportion of darifenacin-treated patients achieved at least a 50% reduction in episodes compared to placebo (70% vs. 58%, respectively, $p = 0.021$). This was accompanied by significant differences between groups in reductions in micturition frequency (-25.3% with darifenacin vs. -18.5% placebo; $p < 0.01$). QoL assessments revealed significant improvements in the OAB-q, Patient Perception of Bladder Condition, and patient and physician assessments of treatment benefit.

In an *a priori* study presented at the 2011 European Association of Urology congress, fesoterodine demonstrated a significantly significant improvement in the primary endpoint of change in daily urgency episodes (-3.47 , vs. -1.92 with placebo, $p < 0.0001$).¹³

Notably, studies with both fesoterodine and solifenacin have demonstrated that a large proportion of elderly patients require higher doses for optimal efficacy.^{8,9} Older people do complain of more adverse events from therapy but, as

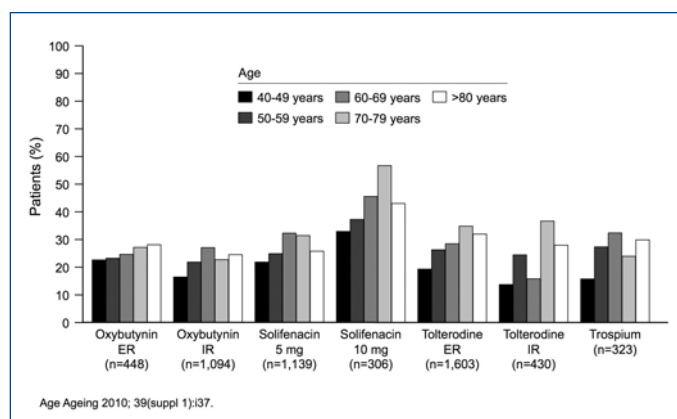


Fig. 2. Elderly patients are more likely to be persistent with therapy.

previously noted, older patients appear to be more adherent to their therapies than younger patients (Figure 2).¹⁰

Antimuscarinics: effect on cognition

Many clinicians are wary of prescribing antimuscarinic medication to older people and are fearful of adverse events, particularly cognitive impairment. This has perhaps led to the vast underuse of antimuscarinic medications reported for the elderly. Are such concerns about cognition without foundation? Theoretically, no; the aging brain is, overall, deficient in cholinergic neurotransmission and muscarinic mechanisms are required for a number of cognitive processes, including short-term memory. M2 receptors in particular, are known to mediate cognitive processes.

It is well-established that the use of medications with antimuscarinic properties (e.g., antidepressants, antipsychotics) is associated with impairment of cognition in community-dwelling older people.^{14,15} Cholinergic mechanisms are implicated in the neuropathology of Alzheimer's disease and the continued use of anticholinergic medication over a four-year period appears to be associated with cognitive impairment and an increased risk of incident dementia.^{16,17} In the 3-City Study, 520 of the 6,912 participants (7.5%) were taking anticholinergic drugs at baseline. In this study, women who were taking anticholinergic drugs at baseline showed greater decline over 4 years in verbal fluency scores and global cognitive functioning than women not using anticholinergic drugs. In men, anticholinergic drugs were associated with a decline in visual memory. There was also a trend towards a reduction in executive function with anticholinergic medication in men.

As far as bladder medications are concerned, immediate release oxybutynin has been shown to adversely affect cognition in the cognitively intact elderly. The newer antimuscarinics for OAB – darifenacin, fesoterodine, solifenacin, tolterodine, and the quaternary ammonium compound,

trospium chloride – do not appear to adversely affect cognition.¹⁸⁻²² Oxybutynin transdermal gel similarly appears to have no demonstrable adverse effect on cognition.²³

There are, as yet, no data on the use of these medications in older people who are cognitively at risk, those with mild cognitive impairment, dementia, Parkinson's disease and the like.²⁴ These patients should be only given medication if conservative measures fail or are impractical, and then started at the lowest possible dose and carefully monitored.

The risk of delirium is often cited as a reason not to give these medications. Delirium appears to be an idiosyncratic reaction and uncommon. In a randomized controlled study of extended-release oxybutynin in nursing-home residents with mild to severe dementia, there was no incidence of delirium over the duration of the study.²⁵

Conclusions

The frequency and severity of urinary symptoms increases with age. OAB in older people may be characterized more by a severe, irresistible "urge," rather than urgency. It is thought that one of the key underlying pathologic mechanisms in the generation symptoms is the accrual of white matter lesions in the brain. Evidence gathered to date has shown that pharmacotherapy is effective in improving urinary symptoms. Paradoxically, older people tend to require higher doses of medication and are more likely to adhere to therapy than younger people. And although there is a theoretical potential for cognitive impairment with antimuscarinic agents, the newer antimuscarinics are cognitively safe in cognitively intact older people.

Competing interests: Dr. Wagg has received speaker fees or honoraria from Astellas, Orion, Pfizer and SCA.

This paper has been peer-reviewed.

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Correspondence: Dr. Adrian Wagg, Division of Geriatric Medicine, Department of Medicine, University of Alberta, 300 Campus Tower, 8625 – 112 St, Edmonton, AB T6G 1K8; Adrian.Wagg@ualberta.ca