

## Patient Safety Tip of the Week

February 10, 2015

# The Anticholinergic Burden and Dementia

Anticholinergic drugs commonly contribute to falls, cognitive impairment, and delirium in the elderly. In addition, peripheral anticholinergic effects may cause dry mouth, blurred vision, exacerbation of glaucoma, constipation, urinary retention or difficulty with micturition, and other side effects. Therefore these drugs often appear on lists of drugs to avoid in the elderly, such as Beers' List and the STOPP tool (see list of our prior columns on inappropriate prescribing in the elderly at the end of today's column).

Now a new study used computerized pharmacy dispensing data from a large health plan to assess the impact of **cumulative** anticholinergic drugs on the development of dementia ([Gray 2015](#)). They looked at a cohort age 65 and older (who had no cognitive impairment at the index evaluation) over a 10 year period and found there was a dose-response relationship between use of strong anticholinergic drugs and the development of dementia and Alzheimer's Disease. The most commonly prescribed categories were tricyclic antidepressants, first-generation antihistamines, and bladder antimuscarinic drugs. Those patients in the highest exposure category had a 54% higher risk of developing dementia (63% higher risk for Alzheimer's specifically). Moreover, sensitivity analyses showed that the effect was not dependent upon the class of drug (i.e. the effect was present whether the predominant medications were antihistamines or bladder antimuscarinics rather than just antidepressants).

Keep in mind that this was a retrospective analysis and it is almost impossible to rule out confounding factors, such as the reasons the various drugs were prescribed. And such associations don't necessarily mean cause and effect. Nevertheless, this gives us one more reason to question whether continued use of various drugs with anticholinergic effects is in the individual patient's best interest.

The Gray study assessed the impact of drugs with strong anticholinergic potency. It used drugs taken from the [updated Beers' List](#) of potentially inappropriate drugs (see our November 12, 2013 Patient Safety Tip of the Week "[More on Inappropriate Meds in the Elderly](#)").

However, another timely study from Australia ([Parkinson 2015](#)) assessed the “**anticholinergic burden**” in women born in 1921-1926 and found that almost 60% used at least one medication with anticholinergic properties. But the most salient finding in that study was that high anticholinergic burden, as measured by the Anticholinergic Drug Scale ([Carnahan 2006](#)), was driven not by high potency medications but rather by **multiple medications with low anticholinergic potency**. We previously noted the risks due to additive effects of multiple medications in our January 28, 2014 Patient Safety Tip of the Week “[Is Polypharmacy Always Bad?](#)”. Parkinson et al. note that physicians often readily recognize drugs with high anticholinergic potency but are less likely to recognize when patients are on multiple medications with low anticholinergic potency. Frankly, we were quite surprised at some of the drugs on this list that had some anticholinergic actions (eg. digoxin!, prednisolone!). Also often overlooked are those over-the-counter (OTC) medications that have anticholinergic side effects. Whether the cumulative anticholinergic dose has the same impact on development of dementia as the dose of just high anticholinergic potency medications in the Gray study remains to be seen. However, the potential for an impact of the cumulative dose of all anticholinergic medications on multiple aspects of geriatric care (confusion, delirium, somnolence, falls, etc.) is high.

A previous study ([Rudolph 2008](#)) had used Anticholinergic Risk Scale (ARS), a ranked categorical list of commonly prescribed medications with anticholinergic potential. The objective of this study was to determine if the ARS score could be used to predict the risk of anticholinergic adverse effects retrospectively in a geriatric evaluation and management (GEM) cohort and prospectively in a primary care cohort, both of which were predominantly male cohorts. The study showed that higher ARS scores were associated with statistically significantly increased risk of anticholinergic adverse effects in older patients.

There are actually several different tools measuring “anticholinergic burden” and there apparently is not perfect agreement between them ([Lertxundi 2013](#), [Lampela 2013](#)). Examples are the Anticholinergic Drug Scale, the Anticholinergic Risk Scale, the Anticholinergic Cognitive Burden Scale, and Chew’s list. Not all the lists include the same drugs and the points given for certain drugs differ among them. But rather than argue about which tool is the best measure of anticholinergic burden, it’s the concept that is important – the anticholinergic effects of multiple medications are additive and, thus, more than one drug may be responsible for detrimental effects.

The editorial accompanying the Gray study ([Campbell 2015](#)) discusses the issue of whether the effects of such anticholinergic agents are reversible or not as it pertains to development of dementia. Campbell and Boustani note that it would take a randomized controlled trial of discontinuation of such drugs in a large cohort of patients of substantial duration.

But, risk of dementia aside, we think there are plenty of other reasons to do regular medication reviews on your elderly patients and strongly consider eliminating or

reducing the dose of drugs with anticholinergic activity that may not be absolutely necessary.

In a commentary on the Parkinson et al. study in MJA InSight ([MacKee 2015](#)), Professor Elizabeth Roughead notes “One of the tricks in prescribing [drugs with anticholinergic effects] is to **always note an ‘end-by’ or ‘review-by’ date**, so you really have a solid marker for when you should be asking: Can we cease it? Can we lower the dose? Is there an alternative?” Of course, we would argue those flags for review should be used for any medication. But most medications with anticholinergic effects are not life-long medications so it is particularly important that regular review for potential discontinuation or dose reduction be undertaken.

We’ve done several columns now on “**deprescribing**” (see our Patient Safety Tips of the Week for March 4, 2014 “[Evidence-Based Prescribing and Deprescribing in the Elderly](#)” and September 30, 2014 “[More on Deprescribing](#)”). We’ve obviously long been big advocates of discontinuing medications which no longer have a positive benefit:harm ratio. And anticholinergic drugs are often on that list of agents whose potential benefits are now exceeded by potential or real harms.

One of the barriers to deprescribing noted in our Patient Safety Tip of the Week for September 30, 2014 “[More on Deprescribing](#)” is a **reluctance by physicians to discontinue a medication started by another physician**, especially those started by a specialist. But one equally big barrier we see is **reluctance to discontinue medications that they themselves started**. We’ve previously described an initiative in a health system in which physicians were made aware of the potential adverse effects of amitriptyline in their elderly patients. The number of new prescriptions for amitriptyline decreased but almost never did the physicians discontinue amitriptyline they had already prescribed for their patients.

A 2011 article provides a very practical case example of how to use the Anticholinergic Risk Scale and alter a patient’s medication regimen accordingly ([Bain 2011](#)).

### **Some of our past columns on Beers’ List and Inappropriate Prescribing in the Elderly:**

- January 15, 2008 “[Managing Dangerous Medications in the Elderly](#)”
- June 2008 “[Potentially Inappropriate Medication Use in Elderly Hospitalized Patients](#)”
- October 19, 2010 “[Optimizing Medications in the Elderly](#)”
- September 22, 2009 “[Psychotropic Drugs and Falls in the SNF](#)”
- September 2010 “[Beers List and CPOE](#)”
- June 21, 2011 “[STOPP Using Beers’ List?](#)”
- December 2011 “[Beers’ Criteria Update in the Works](#)”
- May 7, 2013 “[Drug Errors in the Home](#)”
- November 12, 2013 “[More on Inappropriate Meds in the Elderly](#)”

- January 28, 2014 “[Is Polypharmacy Always Bad?](#)”
- March 4, 2014 “[Evidence-Based Prescribing and Deprescribing in the Elderly](#)”
- September 30, 2014 “[More on Deprescribing](#)”

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