New evidence suggests that prescribers should be cautious when prescribing any medication with anticholinergic effects

**Risks linked to drugs with anticholinergic effects**

**In this article...**

- Adverse events associated with drugs with anticholinergic effects in people aged 65 or older
- Use of anticholinergic risk scales with older or frail people

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Drugs with anticholinergic effects block the neurotransmitter acetylcholine to inhibit smooth muscle function, such as in the lungs, gastrointestinal tract and urinary tract. These drugs are prescribed for a wide range of conditions, including Parkinson’s disease, overactive bladder, chronic obstructive pulmonary disease, nausea and vomiting, depression and psychosis. Drugs with anticholinergic effects can cause a broad range of adverse events, including constipation, dry mouth, dry eyes, urinary retention, confusion, falls and agitation. A recent prospective cohort study suggested an increased risk of dementia with long-term exposure to drugs with anticholinergic effects (Gray et al, 2015).

**New evidence**

A systematic review and meta-analysis assessed the effect of drugs with anticholinergic effects on cognitive impairment, falls and all-cause mortality in older people (Ruxton et al, 2015). The investigators examined drugs with anticholinergic effects as a class, compared individual drugs and assessed different scoring systems that measure exposure to drugs with anticholinergic effects.

The authors included 18 studies in the systematic review, with the results of 11 studies included in the meta-analysis. The majority of the studies were of people aged 65 years and over, and follow-up ranged from one month to six years.

The systematic review found that the individual studies had conflicting results on the effects of drugs with anticholinergic effects as a class. Meta-analysis of three studies showed that exposure to drugs with anticholinergic effects as a class was associated with a significant increase in cognitive impairment. Details of risks associated with specific drugs were not reported. Four studies that assessed risk of falls were included in the meta-analysis, which examined the effects of five drugs — amitriptyline, olanzapine, paroxetine, risperidone and trazodone. The risk of falling was significantly increased with olanzapine and trazodone, with some heterogeneity present in the trazodone analysis. Exposure to amitriptyline, paroxetine and risperidone was not associated with an increased risk of falls.

The authors did not report the effect on all-cause mortality of drugs with anticholinergic effects as a class or of individual drugs. They did report on all-cause mortality relative to scores on the Anticholinergic Cognitive Burden (ACB) scale, a system that scores drugs with anticholinergic effects from one (possible anticholinergic effects based on in vitro data) to three (known anticholinergic effects that may cause delirium). This analysis showed a significant association between ACB scale and all-cause mortality, with an increase of one point on the scale approximately doubling risk.

This study has a number of limitations. The majority of studies included were observational, with only two randomised controlled trials included. Significant heterogeneity was observed in the meta-analysis of some drugs or scoring systems. Limited data was available on the relative risks associated with specific drugs.

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**BOX 1. COMMENTARY**

**By Dr Martin Duerden, GP and clinical senior lecturer, Centre for Health Economics and Medicines Evaluation, Bangor University**

“The evidence is not very strong, but there does appear to be an association between some drugs and these harms. There also seems to be a correlation between overall anticholinergic burden and mortality. Taken alongside the other known adverse effects of these drugs, it seems sensible to be cautious when prescribing. The catch is that there is little evidence to show that using measures of anticholinergic burden to reduce exposure, reduces the harm from these drugs. Researching this area is difficult, and it may be that we have to continue hoping this process is beneficial. Anticholinergic risk scales are contained in various toolkits for polypharmacy; the Ruxton et al (2015) study provides reasonable support to continue using these tools when reviewing treatments for older or frail people, or those with multimorbidities.”

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**References**


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**Keywords:** Anticholinergic drugs/side effects/risk scores

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**Gareth Franklin, medicines advisor, Medicines and Prescribing Programme, National Institute for Health and Care Excellence**

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