Anticholinergic medications, benzodiazepines and long-term cognitive decline in large observational studies

Kathryn Richardson1, Carlota M Grossi1, Chris Fox1, Ian Maidment1, Yoon Loke1, Nick Steel1, Antony Arthur2, Phylo K Myint3, Noll Campbell4, Carol Brayne5, Fiona E Matthews6, Malaz Boustani7, Louise Robinson8, George M Savva9

1 University of East Anglia, 2 Aston University, 3 University of Aberdeen, 4 Purdue University, 5 University of Cambridge, 6 Newcastle University, 7 University of Indiana

Email: kathryn.richardson@uea.ac.uk  Twitter: @ABCD_study  Web: www.uea.ac.uk/drug-safety-and-dementia

**Research questions**

Is there a higher rate of dementia and cognitive decline among people who use certain commonly used medicines for long periods of time?

**Anticholinergic medications** - used for depression, overactive bladder, Parkinson’s disease, allergies, stomach cramps, and psychosis.

**Benzodiazepines** - used for anxiety and sleep disturbance

**Z-drugs** – used for sleep disturbance and similar to benzodiazepines

**Medications and risk of dementia**

We used UK routine primary care data to examine the 20 year medication history of 40,770 patients newly diagnosed with dementia compared to 283,933 age and sex matched patients without dementia.

Dementia patients were 11% more likely to have history of anticholinergic use However associations were inconsistent across drug classes (figure 1).

**Classifying anticholinergic medications**

- The anticholinergic burden scale (ACB) measures the total amount of anticholinergic medication being used by an individual, and the evidence of their anticholinergic activity rated as 0, 1, 2, or 3.
- We classified medications with an ACB score of 3 as anticholinergic (”clinically relevant anticholinergic effects and reported associations with delirium”)
- **ACB scale**: www.agingbraincare.org/tools/abc-anticholinergic-cognitive-burden-scale/

**Medications and cognitive decline**

The Irish Longitudinal Study on Ageing (TILDA)

8,175 participants aged 50+ in Ireland with 2-year follow-up at 2 time points.

**Cognitive recall score**: A list of 10 words read to participants. Participants are asked to recall them immediately, then after 1 minute, and then after 10 minutes.

Greater cognitive decline in those newly taking anticholinergics at 2-year follow-up (figure 2).

**Systematic reviews – findings from other studies**

Two systematic reviews of studies examining benzodiazepine and anticholinergic medication use and cognitive decline and dementia, identified 43 studies examining these topics. The majority reported that greater benzodiazepine and anticholinergic medication use was associated with more cognitive decline and dementia, however studies varied in the size of the effect and in their quality. There are substantial inconsistencies in the overall evidence regarding the association between dementia and use of anticholinergics or benzodiazepines.

**MRC Cognitive Function and Ageing Study**

8,221 participants from England and Wales, aged 67+ with 8-year follow-up

Anticholinergics – recurrent use associated with increased risk of dementia

Benzodiazepines/z-drugs – no association with dementia

**Medications and risk of dementia**

8,221 participants from England and Wales, aged 67+ with 8-year follow-up

Anticholinergics – recurrent use associated with increased risk of dementia

Benzodiazepines/z-drugs – no association with dementia

**Conclusion**

In the largest studies to date, our analyses suggest that benzodiazepines and anticholinergic medications affect cognition over the short-term. We observed no long-term dementia risk with benzodiazepine use, but small associations between certain anticholinergics (antidepressants, antiparkinsons, and urological drugs) and dementia that warrant further research.