An updated systematic review and meta-analysis of the effect of medications with anticholinergic activity on the risk of dementia, mild cognitive impairment and cognitive decline

Nina Pieper¹, Carlota M Grossi², Wei-Yee Chan¹, Clara Harouli³, Yoon Loke¹, George M Savva³, Chris Fox¹, Toby Smith¹, Antony Arthur¹, Nicholas Steel¹, Ian Maidment¹, Phyo K Myint⁴, Louise Robinson⁵, Fiona Matthews⁶, Carole Brayne⁷, Kathryn Richardson¹

¹University of East Anglia, ²James Paget Hospital, ³Aston University, ⁴University of Aberdeen, ⁵Newcastle University, ⁶University of Cambridge
Email: c.grossi-sampedro@uea.ac.uk

Summary

- Dementia is a global health issue
- Anticholinergic medications are widely used and may contribute to cognitive decline
- Results from this review suggest an association between anticholinergic use and incident dementia and MCI
- More work is needed, however, as studies to date have substantial risk of bias

Introduction

- Dementia affects 46.8 million people worldwide and costs $818 billion in healthcare annually (1)
- No treatment exists to reverse dementia and so dementia prevention is a priority
- Medications with anticholinergic properties are commonly used and may contribute to cognitive decline and dementia incidence if used long-term, but research to date has been conflicting (2)
- Here we review the evidence for an effect of anticholinergic use on dementia risk, mild cognitive impairment (MCI) and cognitive decline

Methods

- This review updates a previous review conducted in 2013 (2)
- Search strategy
  - A new search was undertaken for studies published between 2013 and 2016, with 312 weeks follow-up between ‘definite’ anticholinergic medication exposure and outcomes of dementia, MCI or cognitive decline in participants aged ≥50 years
  - We excluded studies defining exposure via serum sample analysis alone
  - All studies included in our earlier review were also screened against these selection criteria.
- Coding of exposure
  - ‘definite’ anticholinergic use defined as drugs with strong anticholinergic properties measured by established anticholinergic rating scale (ACB, ADS, Chew) (3), expert consensus analysis or direct anticholinergic action
  - Meta-analysis
    - Adjusted odds ratios (OR) were pooled across similar definitions of exposure using random effects meta-analysis separately for outcomes of dementia and MCI. Unadjusted ORs were used when adjusted were unavailable
  - Stratification
    - Analysis was stratified by extent and frequency of anticholinergic use as “any use” and only ‘cumulative or recurrent use’. Cumulative use was defined as use of 90 or more defined daily doses (DDDs) (4). Recurrent use was defined as the repetitive use of one or year longer
    - Study risk of bias was assessed using ROBINS-I (5)

Figure 1. PRISMA Flowchart of study selection

Figure 2. Meta-analysis of odds ratios for dementia by definite anticholinergic medication use, stratified by extent and frequency of exposure. Any use: any anticholinergic use Cumulative: 90 or more defined daily doses of exposure Recurrent: used at least at two time points at least for one-year apart

Discussion

- Studies suggest that cumulative and recurrent use of medications with definite anticholinergic properties is associated with an increased risk of dementia and MCI
- However studies are at risk of considerable bias
- Prescribers should be cautious in prescribing anticholinergics in patients at risk of dementia and MCI
- Better quality observational studies or RCTs with sufficient power needed to further examine this relationship

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References

4. https://www.whoac.nndd