

Association between benzodiazepine use and dementia: nested case-control study

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Introduction Benzodiazepines can have short term adverse effects on cognition but there are conflicting findings regarding risk of serious long-term harm e.g. dementia. We aimed to evaluate the association between long-term use of benzodiazepines (including benzodiazepine derivatives) and dementia.

Methods We conducted a nested case-control study using the UK Clinical Practice Research Datalink. We selected participants of age 65-99 years (time period 2006-2015) based on new dementia diagnosis or prescription for a dementia drug and subsequent dementia diagnosis, with up to 7 controls matched on gender, age, deprivation index and data history. We considered the relevant exposure period to be 4-20 years prior to incident dementia, and we assessed dose-response using Defined Daily Doses for benzodiazepines and z-drugs. We used conditional logistic regression to estimate adjusted odds ratios (aOR) and 95% Confidence Intervals (CI) for dementia and drug use, adjusted for potential confounders.

Results We selected 40,770 dementia cases and 283,933 controls, median age 74 years, 60% female. Mean drug exposure period was 7.8 years. When comparing new users to non-users (adjusted for baseline covariates), benzodiazepine use was not associated with a significant risk of dementia (aOR 1.03, 95% CI 1.00 -1.07) whereas Z-drugs had a small association with dementia (aOR 1.07, 95% CI 1.02 - 1.12). Residual confounding is a potential limitation and we did not identify a plausible cumulative dose relationship for the link between dementia and defined daily doses of benzodiazepines or Z-drugs.

Conclusions Despite the findings of our nested case-control study, benzodiazepines can cause a wide range of other adverse effects, and clinicians should continue to follow guidelines on avoiding potentially inappropriate prescription of long-term benzodiazepines, even in the absence of a definitive evidence of any association with dementia. Interestingly, the results of this study conflict with recent systematic review findings. This research was supported by funding from Alzheimer's Society (AS-PG-2013-017).