

Antiepileptic drug use and mortality among community-dwelling persons with Alzheimer disease

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Study objective and summary result

This study tested the hypothesis that patients with Alzheimer disease (AD) who use antiepileptic drugs (AEDs) have elevated relative mortality risks compared to patients not using them, and the results showed that AED users with AD do have elevated mortality rates.

What is known and what this paper adds

The use of AEDs is relatively common in patients with AD, and many patients with AD used older AEDs that are riskier than newer AEDs. This investigation's results provide evidence for an association between AED use and mortality in patients with AD.

Participants and setting

The investigators used data from the Medication Use and AD cohort, which includes all community-dwelling residents of Finland who received AD diagnoses between 2005 and 2011, to identify 5,638 individuals who started using AEDs after AD diagnoses. The investigators matched each AED initiator by age, sex, and time since AD diagnosis to a unique control individual who did not use AEDs.

Design, size, and duration

The investigators obtained AED dispensing data from the Social Insurance Institution of Finland and mortality data from Statistics Finland. The follow-up was limited to 3 years due to the high rate of AED discontinuation. They followed each individual until death, a change in AED usage status, a >90-day hospitalization or institutionalization or the end of 2015, whichever came first. They used Cox proportional hazards models weighted with inverse probability of treatment (IPTW) to analyze the relationship between use of AEDs and mortality.

Primary outcome measures

The primary outcome was the relationship between AED use and mortality.

Main results and the role of chance

In total, 2,182 individuals died within 3 years. Relative to matched control individuals, people who used AEDs had

Table Associations between AED usage and mortality from particular causes

Cause of death	Adjusted hazard ratio (95% confidence interval) for 3-y mortality in AED users vs nonusers
Cardiovascular and cerebrovascular disease	1.01 (0.86–1.19)
Dementia/AD	1.62 (1.42–1.86)
Other causes	0.89 (0.71–1.12)

a greater risk of 3-year mortality (IPTW hazard ratio, 1.23; 95% confidence interval, 1.12–1.36). Risk of death was highest during the first 90 days of AED use (IPTW HR: 2.40, 95% CI: 1.91–3.03).

Bias, confounding, and other reasons for caution

The investigators lacked data concerning the indications for AED usage. Ascertainment of death causes might be biased with overrepresentation of dementia causes. Use of underlying cause of death makes results representative only to intermediate causes where it is possible that immediate deaths were from other causes including cardiovascular and cerebrovascular deaths.

Generalizability to other populations

The present study's exclusion of persons with lengthy institutionalizations may limit the generalizability of the results to such people.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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