ELSEVIER

Alzheimer's & Dementia ■ (2018) 1-8

Alzheimer's & Dementia

Featured Article

Acetylcholinesterase inhibitors and risk of stroke and death in people with dementia

Edwin C. K. Tan[a,b,*], Kristina Johnell[b], Sara Garcia-Ptacek[c,d], Miriam L. Haaksma[b,e], Johan Fastbom[b], J. Simon Bell[a], Maria Eriksdotter[c,f]

[a]*Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Australia*
[b]*Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden*
[c]*Division of Clinical Geriatrics, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden*
[d]*Department of Internal Medicine, Section for Neurology, Södersjukhuset, Stockholm, Sweden*
[e]*Department of Geriatric Medicine, Radboudumc Alzheimer Center, Radboud University Medical Center, Nijmegen, the Netherlands*
[f]*Theme Aging, Karolinska University Hospital, Huddinge, Sweden*

Abstract

Introduction: The aim of this study was to investigate the association between acetylcholinesterase inhibitor (AChEI) use and risk of ischemic stroke and death in people with dementia.
Methods: A cohort study of 44,288 people with dementia registered in the Swedish Dementia Registry from 2007 to 2014. Propensity score-matched competing risk regression models were used to compute hazard ratios and 95% confidence intervals for the association between time-dependent AChEI use and risk of stroke and death.
Results: Compared with matched controls, AChEI users had a lower risk of stroke (hazard ratio: 0.85, 95% confidence interval: 0.75–0.95) and all-cause death (hazard ratio: 0.76, 95% confidence interval: 0.72–0.80). After considering competing risk of death, high doses (≥1.33 defined daily doses) of AChEI remained significantly associated with reduced stroke risk.
Discussion: The use of AChEIs in people with dementia may be associated with reduced risk of ischemic stroke and death. These results call for a closer examination of the cardiovascular effects of AChEIs.
© 2018 the Alzheimer's Association. Published by Elsevier Inc. All rights reserved.

Keywords: Cholinesterase inhibitors; Stroke; Dementia; Alzheimer disease; Cohort studies; Registries

1. Introduction

Worldwide, there are more than 46.8 million people with dementia, and this number is projected to increase to 131.5 million by 2050 [1]. In Sweden, an estimated 160,000 individuals have a diagnosis of dementia [2]. Cardiovascular disease (CVD) and its risk factors have been associated with both cognitive impairment and dementia [3]. In particular, people with dementia are at an increased risk of ischemic stroke, with previous studies indicating a twofold greater risk of stroke in people with dementia compared with those without [4–6]. People with dementia who experience a stroke have accelerated functional decline, decreased daily activities, and poorer survival [7–9]. The presence of coexisting stroke in dementia also increases the use and cost of health-care services and increases the burden of care placed on carers and families [10]. In 2015, the total estimated worldwide costs of dementia were US $815 billion [1].

Acetylcholinesterase inhibitors (AChEIs) are indicated for the symptomatic treatment of mild-to-moderate Alzheimer's disease (AD). They inhibit acetylcholinesterase, an enzyme responsible for the breakdown of acetylcholine, a neurotransmitter associated with memory function [11].

Conflicts of interest: The authors have declared that no conflict of interest exists.

*Corresponding author. Tel.: +46 8 690 5823; Fax: +46 8 690 6889.
E-mail address: edwin.tan.@monash.edu

https://doi.org/10.1016/j.jalz.2018.02.011
1552-5260/© 2018 the Alzheimer's Association. Published by Elsevier Inc. All rights reserved.

ARTICLE IN PRESS

Experimental studies in both animals and humans suggest that these medications have additional endothelial protective effects and anti-inflammatory properties [12,13]. It has been postulated that AChEIs may thus lower the risk of stroke through benefits on endothelial function and inflammatory processes associated with atherosclerosis and ischemic stroke development [8,14].

Our research group has reported that AChEIs reduce the risk of myocardial infarction in people with AD [14]. The aim of this study was to investigate whether AChEIs reduce the risk of ischemic stroke and mortality in people with dementia.

2. Methods

2.1. Data source and study population

This was a cohort study based on people with dementia registered in the Swedish Dementia Registry from 2007 to 2014. The Swedish Dementia Registry is a national quality registry for monitoring the diagnosis, treatment, and care of people with dementia in Sweden [15]. It covers 100% of memory clinics and 75% of primary care units in Sweden. It included a total of 48,133 individuals with newly diagnosed dementia from 2007 to 2014. After excluding those with missing data (n = 3845, 8%), a total of 44,288 people were included in the analyses. Compared with excluded participants, included participants were younger (baseline mean age [standard deviation {SD}]: 79.7 [7.8] years vs. 80.4 [8.6] years, $P < .01$) and had a higher baseline Mini–Mental State Examination (MMSE) (20.4 [6.1] vs. 19.8 [6.3], $P < .01$) but similar distribution of the sexes (women: 59.4% vs. 58.6%, $P = .33$).

2.2. Assessment of demographic, medical, and medication data

Demographic data at baseline were obtained from the Swedish Dementia Registry and included age, sex, MMSE, living situation (institutionalized or living alone vs. living at home with a coresident), home care use, and dementia disorder [15]. Dementia diagnoses were made according to the International Classification of Diseases, Tenth Revision, criteria [16] and coded as AD, vascular dementia, mixed dementia, dementia with Lewy bodies, frontotemporal dementia, Parkinson's disease dementia, unspecified dementia, and other dementia types.

Medical diagnoses in the cohort at baseline and during follow-up were obtained from the Swedish National Patient Register. The Swedish National Patient Register contains prospectively collected information from all inpatient and specialized outpatient visits in Sweden and is maintained by the Swedish National Board of Health and Welfare. The coverage of inpatient discharges is >99% [17]. The medical diagnoses of all individuals are classified according to the International Classification of Diseases, Tenth Revision. The primary outcome of ischemic stroke was defined as the first occurrence of International Classification of Diseases, Tenth Revision code 163.x. History of CVD at the time of dementia diagnosis included acute myocardial infarction (I21.x, I22.x, I25.2), ischemic heart disease (I20.x–I25.x), cerebrovascular disease (G45.x, G46.x, H34.0, I60.x–I69.x), congestive heart failure (I09.9, I11.0, I13.0, I13.2, I50.x), atrial fibrillation (I48.x), and diabetes (E1x.x). Data on all-cause death were obtained from the Swedish Total Population Register. This register is maintained by Statistics Sweden and covers 100% of all deaths in Sweden [18].

Information on dispensed drugs was extracted from the Swedish Prescribed Drug Register. This register contains data with unique patient identifiers for all prescriptions dispensed by pharmacies to the whole population of Sweden. The register is maintained by the National Board of Health and Welfare, and the coverage is >99% [19]. All drugs are classified according to the Anatomical Therapeutic Chemical code. AChEIs were defined as Anatomical Therapeutic Chemical code N06DA. Doses were expressed as prescribed daily dose (PDD), that is, the proportion of defined daily dose for the respective AChEI taken. Doses were based on the last AChEI dispensing. If more than one AChEI was used, then their PDDs were summed. Doses were categorized according to tertiles as low dose (<0.67 PDD), medium dose (0.67–1.32 PDD), and high dose (≥1.33 PDD). Data on other drugs dispensed within the previous 3 months of baseline were also extracted and included diuretics (Anatomical Therapeutic Chemical code, C03), β blockers (C07), calcium channel blockers (C08), angiotensin-converting enzyme (ACE) inhibitors and angiotensin II antagonists (C09), other antihypertensives (C02), lipid-modifying agents (C10), antithrombotics (B01AA and B01AC), antidiabetics (A10), antipsychotics (N05 A), antidepressants (N06 A), and nonsteroidal anti-inflammatory drugs (M01 A).

2.3. Statistical analysis

Baseline differences in the cohort for those who did and did not use AChEIs were compared using descriptive statistics. As there were differences in baseline covariates between users and nonusers of AChEIs, we performed 1:1 propensity score matching. Where possible, each AChEI user was matched with an AChEI nonuser with a similar propensity score, based on nearest-neighbor matching without replacement, using a caliper width equal to 0.1 of the SD of the logit of the propensity score. Based on this, a propensity score-matched cohort of 23,144 people (11,572 users and 11,572 nonusers of AChEIs) was generated. Standardized mean differences were used to assess balance between the AChEI user and nonuser cohorts after matching, with a standardized mean difference less than 0.1 taken to indicate

Download English Version:

https://daneshyari.com/en/article/8679906

Download Persian Version:

https://daneshyari.com/article/8679906

Daneshyari.com