Geriatrics Journal Club

Pravastatin and cognitive function in the elderly. Results of the PROSPER study


Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population, the 3-city study


Background: Evidence is available indicating increased risk of cognitive decline and dementia in users of anticholinergic medications. However, this has not been tested in a prospective study.

Objectives: This study aims to examine the effect of anticholinergic medications on cognitive function and dementia in a large prospective study. The authors also sought to look at several other factors which have not been extensively reported on in the past. These include the affect of stopping anticholinergic therapy and the affects of sex, genetics, and hormone therapy.

Methods: The study enrolled community-dwelling adults ≥65 years of age in 3 French cities between 1999 and 2001 (4128 women, 2784 men). The mean age of the sample was 73.6 years for men and 73.8 years for women. Follow-up was conducted at 2 years and 4 years. Cognitive tests used included the Isaacs Set Test to measure verbal fluency and semantic access, the Benton Visual Retention Test (BVRT) to assess visual memory, the Trail
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Making Tests A and B (TMT A and TMT B) to assess psychomotor speed and executive function, and the Mini Mental State Examination (MMSE) to assess global cognitive function. The tests were conducted at baseline and at the 2 and 4 year follow-ups with the exception of the TMT A and TMT B which were done only at baseline and 4 years. A diagnosis of dementia was made per the clinical investigator according to DSM-IV criteria at each follow-up visit and was confirmed by an independent panel of neurologists. An interview was conducted to determine a list of all prescription and over-the-counter drugs used in the last month. Prescriptions, and when possible, the medications themselves were checked by the interviewer. Other information gathered included demographics, educational level, marital status, mobility, height, weight, alcohol, tobacco, and caffeine consumptions, and hormone therapy for women. History of stroke, angina, myocardial infarction, cardiovascular surgery, recent asthma exacerbation, hypertension, hypercholesterolemia, and diabetes were determined. Fasting blood samples were gathered to determine cholesterol levels and apolipoprotein E genotype. Univariate and multivariate logistic regression was used to determine whether anticholinergic drug use at baseline was associated with the odds of cognitive decline. There were two models used for the multivariate logistic regression analysis each adjusting for various confounders. Model 1 adjusted for center, age, education, baseline cognitive performance, BMI, alcohol, tobacco, caffeine, mobility, hypercholesterolemia, apolipoprotein E, diabetes, asthma, and hormone therapy. Model 2 further adjusted for depression, ischemic disease, Parkinson’s, and hypertension. Chi-squared test was used to identify sex related differences. A Cox model was used to look at incidence of dementia.

Results: At total of 7.5% of the study population reported anticholinergic drug use at baseline. The anticholinergic classes used included antidepressants, digestive antispasmodics, genitourinary antispasmodics, H-1 antihistamines, anxiolytics, cardiovascular medications, antiepileptics, antipsychotics, antiasthmatics, and anti-Parkinson’s drugs. Women were more likely to report anticholinergic drug use than men (9.6% vs. 4.4%, p<0.001). Men and women differed on all baseline characteristics except APOE*E4. For the univariate analysis in women, anticholinergic use was significantly associated with decline in the Isaacs Set Test score (OR 1.47, 95% CI 1.16-1.86, p=0.002) and borderline significant decline in MMSE (OR 1.26, 95% CI 1.00-1.60, p=0.05). Significant associations were not found for the other cognitive tests in women. For the univariate analysis in men, use of anticholinergics was associated with decline on the BVRT (OR 1.70, 95% CI 1.13-2.56, p=0.01), but not on the other cognitive tests. In the multivariate analysis (model 1) similar results were found. In women, anticholinergic use was associated with significant decline on the Isaacs Set Test (p=0.03) and in men with a decline in the BVRT (p=0.01). The same tests remained significantly associated in model 2 as well, Isaacs Set Test for women (OR 1.41, 95% CI 1.11-1.79, p=0.006) and the BVRT for men (OR 1.63, 95% CI 1.08-2.47, p=0.02). In women there was an interaction on the MMSE for
anticholinergic use and age (risk increases with age, p=0.002) and apolipoprotein E (risk increase for APOE*E4 carriers, OR 2.05, 95% CI 1.24-3.40, p=0.005, but not for non-carriers, OR 1.07, 95% CI 0.81-1.40, p=0.65). In women, it was also found that risk of cognitive decline in anticholinergic users was greater for those than never used hormone therapy (OR 1.44, 95% CI 1.07-1.94, p=0.02) as compared to current users (OR 0.51, 95% CI 0.25-1.05, p=0.07). Compared with women reporting no anticholinergic use at any point in the study, continuous users were at higher risk of decline on the Isaacs Set Test and on the MMSE. In men, the continuous use group was more likely to show decline on the BVRT and TMT B. Risk was not increased in those who discontinued use of anticholinergics during the study. An increased risk for dementia or Alzheimer’s disease was noted for those that used anticholinergics continuously (HR 1.65, 95% CI 1.00-2.73, p=0.05 for dementia, HR 1.94, 95% CI 1.01-3.72, p=0.05 for Alzheimer’s disease). There was no increase in risk for those who discontinued anticholinergic treatment.

Discussion: In general, the authors concluded that anticholinergic medications are associated with increased risk of cognitive decline and dementia. Results remained similar when adjusted for disease states likely associated with anticholinergic treatment suggesting that the drugs themselves rather than the underlying disease states contribute to this increased risk. In addition, risk did not seem to be increased in those who discontinued anticholinergic treatment. Overall, anticholinergic drug use seemed to primarily affect verbal retrieval in women and visual memory in men. Older women seem to be at higher risk of cognitive decline. In addition, APOE*E4 negative status and hormone therapy may protect against the toxicity of anticholinergic medications. The authors noted a higher incidence of dementia at 4 years among continuous anticholinergic users compared with non-uses or those who discontinued anticholinergic use. The authors point out that this may be due to neurotransmitter down regulation, or possibly to a misdiagnosis of dementia when patients are experiencing cognitive decline due to anticholinergic use.

Strengths: This was a large, prospective study and many potential confounding factors were taken into account and adjusted for in the analysis.

Limitations: Much of the data collected, including medication histories were often self-reported which makes it subject to recall bias. Overall, anticholinergic use did not seem particularly high in this population and may have been underestimated. Patients who dropped out of the study were more likely female, older, of lower educational level, more likely to have dementia, had lower baseline cognitive test scores and used anticholinergics more frequently. Data on medication adherence and duration of drug use was generally not available.

Clinical Implications: In general, the results of this study do not significantly alter the clinical approach to anticholinergic drug therapy. Generally, these medications should be avoided if at all possible to avoid any increased risk of cognitive decline or dementia. If patients present to the clinic already on these medications, efforts should be made to discontinue them if possible as this reduces the risk.
Unintentional fall injuries associated with walkers and canes in older adults treated in U.S. emergency departments


Introduction: Falls associated with walkers and canes represent 3% of older adult fall injuries. The National Electronic Injury Surveillance System All Injury Program provides national annual estimates of incidence, rate, location, and circumstances of fall-related injuries associated with walkers and canes in adults 65 and older. Falls are the leading cause of unintentional injuries. Out of 35 million older adults in the U.S. approximately 12% use walking aids. Falls associated with aids are an underrecognized public health problem. Canes are given to people with moderate levels of mobility impairment. Walkers are for people with generalized weakness, debilitating conditions, or poor balance, and poor lower-limb weight bearing.

Purpose: To characterize nonfatal, unintentional, fall-related injuries associated with walkers and canes in older adults.

Methods: Data from National Electronic Injury Surveillance System All Injury Program (NEISS-AIP) was used. The focus of the study was for persons 65 and older treated in emergency departments for nonfatal unintentional injury with walkers or canes that occurred between January 2001 to Dec 2006. The location of fall and circumstance was reviewed. Statistical estimates weighted data for 3932 emergency visits. Forty-four cases unassociated with their own walking aids were excluded. Rates were calculated as cases per 100,000 population.

Results: Based on 3,932 cases, an estimated 47,312 older adults were treated in emergency departments for injuries associated with canes or walkers; 87.3% with walkers, 12.3% with canes, 0.4% with both. Women’s injury rates were greater than men’s, with rate ratio of 2.6 for walkers and like for canes. One-third of the people injured were hospitalized. Men had more head and neck injuries, followed by lower trunk injuries. Women had more lower-trunk injuries, followed by head and neck injuries. Seven times more injuries occurred with walkers. Women suffered more injuries associated with walkers than men (78.2% vs 21.8%), with canes (66.3% vs 33.7%). Increasing age (age over 85) increased injuries with walkers. Walker and cane injuries increased with age. Ratio of walker to cane injuries is 2.9% to 5.3% for men, 6.4% to 10.2% for women. More common injuries are fractures followed by contusions and abrasions. 60% of falls occurred at home, one out of 6 injuries associated with walkers occurred in nursing homes. 8.3% of injuries were with walkers, 12.8% of cane injuries happen in public places. Falls due to intrinsic factors were similar for both walkers and canes.
**Discussion:** An estimated 47,312 older adult injuries associated with walking aids were treated in emergency departments per year, although the extent to which the use of walkers and canes contributed to injuries could not be determined. While more than twice as many older adults use canes than walkers, it was found that 7 times more injuries were with walkers. Limited medical records did not allow the circumstances of the fall events to be characterized precisely. Extrinsic or environmental factors may play a greater role in falls in people using walkers. Some of the problems had to do with using walking aids effectively. Suggestions were made that more time devoted to fitting aids and educating people is beneficial. Women are weaker than men and may have more difficulty using walking aids. It is suggested more information about the circumstances and location of falls to better understand the risks associated with canes and walkers and to develop specific and effective fall prevention strategies is needed.

**Limitations to the study:** Only persons treated in emergency departments were characterized. Fatal injuries that occurred before and after emergency were excluded. Only ICD-9 codes were available at the time and specific injuries could not be identified.

**Conclusion:** 59% are women in population older than 65, 77% of injuries were related to walking aids. 15% are women in population older than 85, 39% sustained injuries. Research is needed to understand the physical and cognitive demands that walking aids place on users. Participants discussed the development and use of a “smart walker.”

Participants were questioning which medications had anticholinergic properties. The following publication provides information about medications with anticholinergic properties.