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Selección de artículos

DRUGS AND AGING

Association of Anticholinergic Drug Burden with Cognitive and Functional Decline Over Time in Older Inpatients: Results from the CRIME Project

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Abstract

Background
Medications with anticholinergic properties, although widely used, may negatively affect cognitive and functional status in older patients. To date there is still no standardized method to quantify anticholinergic exposure. We analyzed the relationship of two different tools for the evaluation of the anticholinergic drug burden with cognitive and functional impairment in a sample of older hospitalized patients.

Methods
A retrospective and longitudinal analysis with 1-year follow-up of 1123 older hospitalized patients enrolled in seven Italian acute care wards was conducted. We assessed anticholinergic burden with the Anticholinergic Cognitive Burden (ACB) and Anticholinergic Risk Scale (ARS). Cognitive and functional status were evaluated at hospital discharge and during follow-up (3, 6, 12 months) using the Mini Mental State Examination (MMSE) and five basic activities of daily living (ADLs). Associations between anticholinergic burden and cognitive decline and incident disability were estimated using linear regression models for repeated measures and logistic models, respectively.

Results
The mean age of the study population was 81 ± 7.5 years. ACB and ARS classifications showed low correlation (Spearman's rho = 0.39–0.43). Anticholinergic burden increased during hospitalization and was associated with cognitive and functional status. Patients with an ARS of ≥ 1 at discharge had significantly lower baseline MMSE scores (ARS = 0: 23.1; ARS ≥ 1: 20.8; $p = 0.002$) and during follow-up presented a significantly steeper MMSE score decline (− 0.15/month). Moreover, patients with an ACB of ≥ 1 at discharge had an almost threefold increased risk of developing disability (odds ratio 2.77, 95% confidence interval 1.39–5.54).

Conclusions
ACB and ARS have only a moderate degree of correlation. Use of drugs with anticholinergic properties in elderly patients is independently associated with cognitive and functional decline.

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EUROPEAN GERIATRIC MEDICINE

Characteristics and outcomes of older adults presented to Spanish emergency departments after a fall

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Abstract

Purpose
To study patient profile, fall-related characteristics and immediate outcomes according to age and to determine the effect of age in the outcomes among older patients presenting to ED after a fall.

Methods
Cross-sectional analysis of the FALL-ER registry that included patients aged ≥ 65 years old that presented to five Spanish EDs after a fall. Patients were classified into three age categories, and demographic, comorbidity, chronic medication, fall-related characteristics, health care resources and immediate outcomes data were analysed.

Results
We included 1610 patients, 541 (28%) aged 65–74, 647 (40.2%) aged 74–84 and 512 (31.8%) aged ≥ 85 years old. Indoor falls, with no witnesses, at night and due to non-identified causes were significantly more likely among the oldest old. Medications related to risk of falling and antithrombotic therapy significantly increased with age category. Physical, functional and psychological consequences and healthcare resource use increased significantly with age group. Age was independently associated with severe injury (adjusted OR 1.02; IC 95% 1.01–1.04), fear of falling (adjusted OR 1.02; IC 95% 1.01–1.04) and acute functional impairment (adjusted OR 1.02; IC 95% 1.00–1.04).

Conclusions
Indoor falls, with no witnesses, at night and due to non-identified causes were significantly more likely among the oldest old. The probability of presenting with severe injury, fear of falling and acute functional impairment increases with age.

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JOURNAL OF THE AMERICAN GERIATRICS SOCIETY

Cumulative Antidepressant Use and Risk of Dementia in a Prospective Cohort Study

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Abstract

Objectives
To determine whether antidepressant use is associated with dementia risk.
Design
Prospective cohort study.
Setting
Kaiser Permanente Washington (KPWA), an integrated healthcare delivery system.
Participants
Community-dwelling individuals aged 65 and older without dementia and with 10 years or more of KPWA enrollment at baseline (N=3,059).
Measurements
Primary exposures were selective serotonin reuptake inhibitors (paroxetine vs other), tricyclic antidepressants, and serotonin antagonist and reuptake inhibitors. Using health plan pharmacy data, we calculated cumulative medication exposure, defined as total standardized daily doses (TSDDs), over rolling 10-year windows. Exposure in the most recent year was excluded to avoid use related to prodromal symptoms. The Cognitive Abilities Screening Instrument was administered every 2 years; low scores triggered clinical evaluation and consensus diagnosis procedures. Dementia risk was estimated according to medication use using Cox proportional hazards models.
Results
During a mean follow-up of 7.7 years, 775 participants (25%) developed dementia; 659 (22%) developed possible or probable Alzheimer's disease. Individual antidepressant classes were not associated with differences in dementia risk, although paroxetine use was associated with higher risk of dementia for all TSDD categories than no use (0–90 TSDDs: hazard ratio (HR)=1.69, 95% confidence interval (CI)=1.18–2.42; 91–365 TSDDs: HR=1.40, 95% CI=0.88–2.23; 366–1095 TSDDs: HR=2.13, 95% CI=1.32–3.43; ≥1095 TSDDs: HR=1.42, 95% CI=0.82–2.46).
Conclusion
Most commonly prescribed nonanticholinergic depression medications used in late life do not appear to be associated with dementia risk. Paroxetine and other anticholinergic antidepressants may be exceptions in older individuals. Future studies are warranted to improve scientific understanding of potential associations in other settings and populations.

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JOURNAL OF GERONTOLOGY

Associations Between Vitamin D Levels and Depressive Symptoms in Later Life: Evidence From the English Longitudinal Study of Ageing (ELSA)

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Abstract

Background

A possible role of vitamin D in depression has received considerable attention, especially given the significant disability, mortality, and healthcare costs associated to depression and the high prevalence of vitamin D deficiency.

Methods

We investigated the cross-sectional associations between serum 25-hydroxyvitamin D (25OHD) levels and depressive symptoms (CES-D) in 5,607 older adults from the English Longitudinal Study of Ageing (ELSA).

Results

Overall, there was a significant association between low 25OHD levels and elevated depressive symptoms (odds ratio [OR] = 1.58, 95% confidence interval [CI] = 1.20–2.07 for the lowest quartile; OR = 1.45, 95% CI = 1.15–1.83 for <30 nmol/L cut-off and OR = 1.34, 95% CI = 1.10–1.62 for the ≤50 nmol/L cut-off) after adjustment for a wide range of covariates of clinical significance. Fully adjusted models showed that women in the lowest (OR = 1.67, 95% CI = 1.20–2.34) and second lowest (OR = 1.68, 95% CI = 1.20–2.35) quartiles of 25OHD as well as those with 25OHD levels <30 nmol/L (OR = 1.40, 95% CI = 1.06–1.86) and ≤50 nmol/L (OR = 1.35, 95% CI = 1.07–1.72) were more likely to report elevated depressive symptoms. For men, however, this association only remained significant for those with 25OHD levels of <30 nmol/L (OR = 1.60, 95% CI = 1.06–2.42) in the fully adjusted models.

Conclusions

The independent and inverse association found between low 25OHD levels and elevated depressive symptoms suggests that vitamin D deficiency may be a risk factor for late-life depression, particularly among women. Whether our findings have any clinical meaning or not, additional data are needed from well-designed randomized controlled trials of vitamin D for the prevention and treatment of late-life depression.

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Antidepressant Use and Cognitive Outcomes in Very Old Women

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Abstract

Background
Antidepressant use is very common in the elderly, but the effects of antidepressants on cognition in the elderly are controversial with some studies suggesting harm and others protection. We aimed to investigate the association between different antidepressant use and change in cognition and risk of mild cognitive impairment (MCI) or dementia in very old women.

Methods
We examined 1,234 community-dwelling women (mean age 83.2 years) from the Study of Osteoporotic Fractures. Baseline antidepressant use was reported and verified by medication containers, and medications were coded with computerized dictionary. Cognitive status (normal, MCI, or dementia) was adjudicated by an expert clinical panel 5 years later. Change in a short-form Mini-Mental State Examination and Trails B were evaluated over 5 years.

Results
Eleven per cent of the women were taking antidepressants. Users of selective serotonin reuptake inhibitors (SSRIs) had the greatest cognitive decline over 5 years, after adjustment for demographics, medical comorbidities, benzodiazepine use, and baseline cognition. Multivariable logistic regression shows that the users of SSRIs were more than twice (OR = 2.69, 95% CI = 1.64–4.41) and trazodone users more than three times (3.48, 1.12–10.81) as likely to develop MCI or dementia compared with the nonusers. Further adjustment for baseline cognition or depressive symptoms did not appreciably alter the results, and the association remained after excluding women with high depressive symptoms. The use of tricyclic antidepressants or other antidepressants was not significantly associated with cognitive outcomes.

Conclusions
The use of antidepressants, especially SSRIs and trazodone, was associated with an increased risk of cognitive impairment 5 years later among the oldest old women.

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The Impact of Antipsychotic Drugs on Long-term Care, Nursing Home Admission, and Death in Dementia Patients

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Abstract

Background
Behavioral and psychological symptoms of dementia are commonly treated with antipsychotic drugs (APDs), which have been associated with adverse health effects. We examine the effect of APDs on long-term care (LTC), nursing home (NH) admission, and death of dementia patients.

Methods
We used health claims data of the largest German health insurer from 2004 to 2010 and followed newly-diagnosed dementia patients aged 60 years and older into LTC, NH, and until death. Cox proportional hazards models were estimated to explore whether the risk of these outcomes differed between patients receiving haloperidol, melperone, risperidone, or quetiapine.

Results
In a cohort of 6,930 dementia patients who were initially free of LTC dependency, APD users generally faced a twofold increased risk of LTC relative to nonusers. Quetiapine was the exception, showing a comparatively lower risk (HR = 1.64; CI = 1.35–1.98). Among 9,950 dementia patients initially living in private homes, the risk of moving into a NH was generally increased by about 50% among APD users relative to nonusers. Risk of death (N = 10,921) was significantly higher for haloperidol-, melperone-, and risperidone- but not for quetiapine users (HR = 0.91; CI = 0.78–1.08). The excess mortality associated with haloperidol and melperone was greater among patients living in private households.

Conclusions
In our study, APDs appeared to accelerate adverse health outcomes in German dementia patients. Differentiating between the effect of antipsychotic drug use among dementia patients residing in private households and in NHs, we found that excess mortality for haloperidol and melperone users was higher in private settings.

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The Impact of Dementia Diagnosis on Patterns of Potentially Inappropriate Medication Use Among Older Adults

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Abstract
Background
Use of potentially inappropriate medications (PIM) among people with dementia is common. We assessed the patterns of medication use from 1-year before dementia diagnosis, to 1-year after dementia diagnosis, compared with patterns of medication use in people without dementia.

Methods
We conducted longitudinal study using the National Alzheimer's Coordinating Center data. Adults aged 65 years and older newly diagnosed with dementia (n = 2,418) during 2005–2015 were year, age, and sex matched 1:1 with controls. Generalized estimating equation models weighted for missingness and adjusted for 15 participant characteristics were fit.

Results
Among participants with dementia, number of medications reported 1-year prediagnosis was 8% lower than at diagnosis year ($p < .0001$) and 11% higher 1-year postdiagnosis compared

with year of diagnosis (p < .0001). Among participants with dementia, the odds of PIM exposure, assessed using the 2015 Beers Criteria, was 17% lower 1-year prediagnosis (p < .0001) and 17% higher 1-year postdiagnosis (p = .006) compared with year of diagnosis. Among controls, there were approximately 6% more medications reported between consecutive years (p < .0001 each comparison) and the odds of PIM exposure increased 11% between consecutive years (p = .006 and p = .047). At each annual follow-up, participants with dementia had lower odds of PIM exposure than their controls (prediagnosis p < .0001, at diagnosis p = .0007, postdiagnosis p = .03, respectively). There were no differences in exposure to anticholinergic medications

Conclusions
Number of medications and PIM use increased annually for participants with and without dementia. Persistent challenge of increasing PIM use in this group of older adults is of major concern and warrants interventions to minimize such prescribing.

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BRITISH JOURNAL OF CLINICAL PHARMACOLOGY

New-onset epilepsy in the elderly

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Abstract

People who are 60 years old and older have the highest incidence of developing new-onset epilepsy. The increase of the ageing population has resulted in a greater number of patients with new-onset epilepsy or at risk of developing the condition. Previously published review articles regarding epilepsy in older patients have had a broad focus, including people who were diagnosed with epilepsy in their childhood or middle age. The present review focuses on the causes, treatment, prognosis and psychosocial impact of new-onset epilepsy in people aged ≥60 years. Following a search of the medical electronic databases and relevant references, we identified 22 studies overall that met the inclusion criteria. Only four randomized clinical trials (RCTs) were identified that compared different antiepileptic drug treatments in this population, demonstrating that newer-generation antiepileptic drugs (e.g. lamotrigine and levetiracetam) were generally better tolerated. One uncontrolled study provided promising evidence of good outcomes and safety for surgical resection as a treatment for people with uncontrolled seizures. Five studies reported that people ≥60 years with new-onset epilepsy have significant cognitive impairments (e.g. memory loss) and psychological issues including depression, anxiety and fatigue. We found that there is limited evidence to guide treatment in people with Alzheimer's disease and epilepsy. The specific features of new-onset epilepsy in this target population significantly influences the choice of treatment. Cognitive and psychiatric screening before treatment may be useful for management. Two studies with proposed guidelines were identified but no formal clinical practice guidelines exist for this special population to assist with appropriate management. There is a need for more RCTs that investigate effective

treatments with limited side effects. More research studies on the psychosocial effects of new-onset epilepsy, and long-term outcomes, for people aged ≥60 years are also required.

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Can doctors identify older patients at risk of medication harm following hospital discharge? A multicentre prospective study in the UK

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Abstract

Aims
Medication-related harm (MRH) is common in older adults following hospital discharge. In resource-limited health systems, interventions to reduce this risk can be targeted at high-risk patients. This study aims to determine whether (1) doctors can predict which older patients will experience MRH requiring healthcare following hospital discharge, (2) clinical experience and confidence in prediction influence the accuracy of the prediction.

Methods
This was a multicentre observational prospective study involving five teaching hospitals in England between September 2013 and November 2015. Doctors discharging patients (aged ≥65 years) from medical wards predicted the likelihood of their patient experiencing MRH requiring healthcare (hospital readmission or community healthcare) in the initial 8-week period post-discharge. Patients were followed up by senior pharmacists to determine MRH occurrence.

Results
Data of 1066 patients (83%) with completed predictions and follow-up, out of 1280 recruited patients, were analysed. Patients had a median age of 82 years (65–103 years), and 58% were female. Most predictions (85%) were made by junior doctors with less than 5 years' clinical experience. There was no relationship between doctors' predictions and patient MRH (OR 1.10, 95% CI 0.82–1.46, P = 0.53), irrespective of years of clinical experience. Doctors' predictions were more likely to be accurate when they reported higher confidence in their prediction, especially in predicting MRH-associated hospital readmissions (OR 1.58, 95% CI 1.42–1.76, P < 0.001).

Conclusions
Clinical judgement of doctors is not a reliable tool to predict MRH in older adults post-discharge.

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EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY

Adequate, questionable, and inadequate drug prescribing for older adults at the end of life: a European expert consensus

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Abstract

Background
Clinical guidance is needed to initiate, continue, and discontinue drug treatments near the end of life.
Aim
To identify drugs and drug classes most often adequate, questionable, or inadequate for older people at the end of life.
Design
Delphi consensus survey.
Setting/participants
Forty European experts in geriatrics, clinical pharmacology, and palliative medicine from 10 different countries. Panelists were asked to characterize drug classes as “often adequate,” “questionable,” or “often inadequate” for use in older adults aged 75 years or older with an estimated life expectancy of ≤ 3 months. We distinguished the continuation of a drug class that was previously prescribed from the initiation of a new drug. Consensus was considered achieved for a given drug or drug class if the level of agreement was ≥ 75%.

Results
The expert panel reached consensus on a set of 14 drug classes deemed as “often adequate,” 28 drug classes deemed “questionable,” and 10 drug classes deemed “often inadequate” for continuation during the last 3 months of life. Regarding the initiation of new drug treatments, the panel reached consensus on a set of 10 drug classes deemed “often adequate,” 23 drug classes deemed “questionable,” and 23 drug classes deemed “often inadequate”. Consensus remained unachieved for some very commonly prescribed drug treatments (e.g., proton-pump inhibitors, furosemide, haloperidol, olanzapine, zopiclone, and selective serotonin reuptake inhibitors).

Conclusion
In the absence of high-quality evidence from randomized clinical trials, these consensus-based criteria provide guidance to rationalize drug prescribing for older adults near the end of life.

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PHARMACOTHERAPY

Association between Development of Dementia and Use of Benzodiazepines: A Systematic Review and Meta-Analysis

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Abstract

Study Objective
The use of benzodiazepines and the development of dementia is controversial, with studies indicating that benzodiazepines could be either a protective factor or a risk factor for dementia, or no association may exist between the two. Our objective was to identify whether such an association exists.

Design
Systematic review and meta-analysis of 12 prospective and retrospective cohort studies and case-control studies.

Participants
A total of 981,133 (in the systematic review) and 980,860 (in the meta-analysis) adults or elderly individuals.

Measurements and Main Results
A search of the PubMed, LILACS, and Cochrane Central Register of Controlled Trials databases, as well as a manual search of the reference lists of the included publications and reviews, was performed. We included studies that reported the incidence of dementia and in ever users of benzodiazepines. Data were analyzed by using a random effects model in R software. Quality of the evidence was assessed with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) certainty ratings system. The results of the main meta-analysis suggest that benzodiazepines can be a risk factor for developing dementia (odds ratio 1.38, 95% confidence interval 1.07–1.77; I2 = 98%; 95% prediction interval 0.58–3.25; very low certainty).

Conclusion
Our results suggest an association between the use of benzodiazepines and the development of dementia. However, the current evidence lacks the power to infer differences between the effects of Alzheimer's disease and vascular dementias, long-acting and short-acting benzodiazepines, and various exposure loads (duration and dose). Future long-term prospective cohort studies are necessary, with adequate adjustments for confounding variables, strategies to minimize reverse causality, reporting of subgroups aimed at greater homogeneity of findings, adequate statistical power to identify high-magnitude effects, and defined daily dose analyses for dose-response gradient.

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