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Original Study

Association Between Psychotropic and Cardiovascular Iatrogenic Alerts and Risk of Hospitalizations in Elderly People Treated for Dementia: A Self-Controlled Case Series Study Based on the Matching of 2 French Health Insurance Databases

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A B S T R A C T

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Background: Elderly people are at risk of repeated hospitalizations, some of which may be drug related and preventable. In 2011, a group of French healthcare experts selected 5 iatrogenic alerts (IAs), based on criteria identified in a literature search and from their professional experience, to assess the appropriateness of medication in elderly patients.

Objectives: Our objective was to examine the association between hospitalizations and IAs in elderly patients treated for Alzheimer disease who are particularly sensitive to adverse drug events.

Design: A 2-year (January 1, 2011, to December 31, 2012) longitudinal national database study, with a study design similar to self-controlled case series, was performed to analyze data on drug prescriptions and hospitalization. IAs were defined as (1) long half-life benzodiazepine; (2) antipsychotic drugs in patients with Alzheimer disease; (3) co-prescription of 3 or more psychotropic drugs; (4) co-prescription of 2 or more diuretics; and (5) co-prescription of 4 or more antihypertensive drugs. Data were obtained by matching of 2 French National Health Insurance Databases.

Setting: France.

Participants: All affiliates, aged ≥ 75 years, receiving treatment for Alzheimer disease, alive on January 1, 2011 were included.

Measurements: We calculated the relative increase in the number of hospitalizations in patients with IAs. The analysis was performed over four 6-month periods.

Results: A total of 10,754 patients were included. During the periods with IAs, hospitalization rates increased by 0.36/year compared with 0.23/year in the periods without for the same patient, and the number of hospitalizations doubled [proportional fold change = 1.9, 95% confidence interval (1.8, 2.1)]. We estimated that 22% [95% confidence interval (20%, 23%)] of all hospitalizations were associated with IAs, 80% of which were due to psychotropic IAs.

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The authors declare no conflicts of interest.

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Conclusions: The IAs could be used as a simple and clinically relevant tool by prescribing physicians to assess the appropriateness of the prescription in elderly patients treated for Alzheimer disease.

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Older age has been reported to be associated with an increase in repeated hospital admissions.^{1–3} Reducing unnecessary hospitalizations is a priority for hospitals and national health plans. Identifying the modifiable factors that are associated with the risk of hospitalization in elderly people is essential for the development of risk minimization strategies. Between 5% and 20% of all hospital admissions are known to be related to adverse drug events (ADE) in people aged ≥ 65 years, and 40% to 70% of these ADE-related admissions could be preventable.^{4–9} This has prompted the development of criterion-based tools, based on explicit measures, to assess and correct inappropriate prescription in elderly people.^{10–15} However, the evidence that inappropriate prescription, as defined by the explicit measures, is associated with adverse patient outcomes and notably hospitalizations, is mixed and contradictory.^{11,16,17} This could be due to the studies being performed in populations with a heterogeneous risk for hospitalization or the heterogeneous risk for serious ADE associated with the criteria, even within the same tool.

In 2011, the French National Authority for Health commissioned a panel of French health professionals to determine the most important criteria for cardiovascular and psychotropic drugs known to be involved in ADE-related admissions, to inform a national health plan to improve medication in elderly people.^{4–7,9–12,14,15,18} Five iatrogenic alerts (IAs) were identified which were easy to assess and clinically relevant for the prevention of serious ADE in the elderly, based on a literature search and the panel members' clinical experience.¹⁹ There were 3 psychotropic IAs corresponding to (1) the prescription of a long half-life benzodiazepine; (2) the prescription of antipsychotic drugs in Alzheimer patients; and (3) the co-prescription of 3 or more psychotropic drugs; and 2 cardiovascular IAs corresponding to (4) the co-prescription of 2 or more diuretics and (5) the co-prescription of 4 or more antihypertensive drugs.

The aim of our study was to validate this new screening tool for inappropriate prescriptions in elderly people, by measuring the association between these IAs and the risk of hospitalizations. We focused on patients treated for Alzheimer disease because they are at high risk of hospitalizations and because one of the IAs is specific for this population.^{19–22} Our main objective was to examine the association between all-cause hospitalizations and IAs in elderly people treated for Alzheimer disease, using a self-controlled case series design. We also examined the association between ADE-related hospitalizations and IAs in this population.

Methods

Between January 1, 2011 and December 31, 2012 a longitudinal, national database study using based on the “self-controlled case series” methodology^{23,24} was performed. The study is reported according to the Reporting of Studies Conducted Using Observational Routinely Collected Health Data (RECORD) recommendation.²⁵ The period was divided into 4 consecutive 6-month periods, enabling sufficient data to be available for a sequential analysis for each patient. The 6-month analysis periods were a compromise between a monthly analysis period, which would have provided 24 periods for each patient, but with more complex analyses, and an annual analysis period, with only 2 periods for each patient making detailed analysis impossible.

Databases

Data were obtained from 2 French National Health Insurance databases. One was the database for the social security scheme for self-employed individuals, Régime Social des Indépendants (RSI) database, which contributed data from 6 million self-employed people. The database included data such as age, sex, social security number, all ambulatory prescriptions, the prescriber identity, and all hospitalizations in private hospitals [with major diagnosis category (MDC), corresponding to the primary reason for hospital admission,²⁶ Appendix 1]. The second was the French National Health Insurance Information System database, the Système National d'Information Inter-Régimes de l'Assurance Maladie (SNIIRAM), which collects all individualized and anonymous healthcare claims reimbursed by the French National Health Insurance covering the whole French population.²⁷ This database contains data such as sex, vital status, eligibility for 100% health insurance cover for serious and costly long-term diseases, coded using the *International Classification of Diseases, 10th Revision* (ICD-10)²⁸ and all hospitalizations in public hospitals with their MDC.²⁶

Population Selection

In the RSI database, all individuals aged ≥ 75 years on January 1, 2011 with a diagnosis of Alzheimer disease (ICD-10: F00-F03*) receiving Alzheimer-specific drugs [anatomic therapeutic chemical (ATC) code: NO6D] were included^{26,29} (Figure 1). All patients undergoing a dementia-specific treatment had the specific ICD-10 code. The Charlson comorbidity index (CCI) was calculated for each patient; any missing information was replaced by the default value (ie, least severe) (Appendix 2).^{28,30,31}

Database Matching

The SNIIRAM and RSI databases (Figure 1) have restricted access under French privacy laws.²⁷ We obtained authorization to match the 2 databases anonymously (CNIL authorization no.: 1537081). In the absence of a unique patient identifier, the matching was performed using criteria such as sex, year of birth, social security number, prescriber and the Alzheimer-specific drugs refunded during the first 6-month period (inclusion criteria).

Exposure

The ATC class of each of the prescribed drugs was available with a precision ranging from 3 to 5 digits.²⁹

We determined the following for each patient and for each 6-month period.

- (1) Presence of an IA. The algorithm for identifying IAs, developed from the ATC codes proposed by French National Authority for Health, is described in Appendix 3.¹⁹ Co-prescription IAs was defined as the delivery of ≥ 2 different drugs over the course of the same 6-month period.
- (2) The delivery of a drug known to increase the risk of ADE-related hospitalization and not included in IAs.^{4,6} We included antiplatelet agents or anticoagulants (ATC: B01); nonsteroidal anti-inflammatory drugs (NSAIDs) (ATC: M01);

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