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Original Study

Mortality and Antipsychotic Drug Use in Elderly Patients With Parkinson Disease in Nursing Homes

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A B S T R A C T

Objectives: To evaluate mortality rate in elderly and very elderly (≥85 years) residents with Parkinson disease (PD) in nursing homes (NHs) with and without antipsychotic drugs.
Design: Cross-sectional study.
Participants: All residents with PD from the 6275 NH residents participating in the Impact d'une démarche QUAlité sur l'évolution des pratiques et le déclin fonctionnel des Résidents en Etablissement d'hébergement pour personnes âgées dépendantes (IQUARE) study.
Setting: A total of 175 NHs in Midi-Pyrénées region, South-Western France.
Exposure: Patients with PD taking antipsychotic drugs.
Outcome Measurements: All-cause mortality between baseline and 18 months.
Statistical Methods: Logistic regression was used to explore baseline characteristics associated with mortality rate and with antipsychotic use at 18 months.
Results: At baseline, among 452 residents with PD, 72 (15.9%) received at least 1 antipsychotic drug. Mortality rates at 18 months in residents with PD with and without antipsychotic use were similar (34.3% and 38.2%, respectively, $P = .58$). Among factors associated with mortality, a statistically significant increase in mortality rate was found in very old residents (≥85 years of age) [odds ratio (OR) 2.0; 95% confidence interval (CI) 1.3−3.1] or in those with chronic pulmonary disease (OR 3.6; 95% CI 1.5−8.5). Among residents ≥85 years of age, we also found a statistically significant increase in mortality rate in individuals with arterial hypertension (OR 2.8; 95% CI 1.3−5.8). Moreover, a statistically significant increase in prescription of antipsychotic drugs was found in residents who tried to elope (OR 3.8; 95% CI 1.4−10.7) and in those with severe psychiatric diseases (excluding depression) (OR 7.5; 95% CI 4.1−13.6).
Conclusions: In this study investigating factors associated with mortality in old and very old residents with PD in NHs, no significant association was observed with the use of antipsychotics. However, our study suggests that age (≥85 years) or chronic pulmonary disease could be associated with mortality among patients with PD, as well as arterial hypertension in very old patients (≥85 years of age).

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Psychotic disorders are one of the most common nonmotor complications in Parkinson disease (PD), with a prevalence of 40%–60% patients affected.[1] Benign psychotic disorders, such as slight visual hallucinations, do not require drug therapy in contrast to serious ones, such as schizophrenia, dementia, delirium, psychosis, agitation, or affective disorders. Management of these disorders usually includes reduction of antiparkinsonian drugs and addition of atypical antipsychotics (AAPs).[2] Clozapine was the only medication approved for the treatment of psychosis in patients with PD until April 2016 when pimavanserin was first approved by the US Food and Drug Administration to treat hallucinations and delusions in people with PD. For other antipsychotics, there is insufficient evidence to make adequate conclusions on their efficacy.[3,4] Nevertheless, other antipsychotics (APs) at risk of worsening parkinsonism [conventional antipsychotics (CAPs) and AAP] are also used in this population.

Several studies performed in nonparkinsonian patients with dementia and exposed to CAP/AAPs showed an increased mortality rate.[5–8] This association was also found for elderly adults, particularly for residents in NHs.[9–13] A recent systematic review concluded to an increase in the risk of death for the use of CAP/AAPs vs nonuse in residents with dementia.[14]

For patients with PD, psychotic disorders but also age or dementia are additional factors associated with prescriptions of CAP/AAPs in NHs.[15–17] Residents aged 85 years or older in NHs are particularly at risk of inappropriate prescriptions of CAP/AAPs.[18] Because of the vulnerability of elderly and very elderly residents with PD, it is important to assess the safety of the use of APs in this population.

As far as we know, only 4 studies investigated the safety of APs in elderly patients with PD. A nested case-control study in patients with PD aged 70 years or over has shown a double risk of death after a new AAP prescription [odds ratio (OR) 2.0; 95% confidence interval (CI) 1.4–2.7).[19] Another study also suggested that psychosis in patients with PD requiring APs is frequently associated with death and nursing home placement.[20] A recent open-label study of people with PD psychosis found a significant increase in the mortality rate for participants with AAPs (relative risk 4.2; 95% CI 2.1–8.0).[21] This result is in accordance with the latest study in which risk of death was increased by more than double with the use of CAP/AAPs (HR 2.4, 95% CI 2.1–2.7).[22] However, none of these studies investigated factors associated with mortality in elderly residents with PD in NHs, which is crucial for this fragile population.

Previous evidence allows us to address the crucial question of potential association between AP use and mortality among elderly patients with PD. The aim of our study was to compare mortality rate in elderly (and very elderly) patients with PD living in NHs according to their exposure to APs. Factors associated with the use of APs were also investigated.

Methods

Design

Data from the IQUARE study (Impact d'une démarche QUAlité sur Etablissement d'Hébergement pour Personnes Agées Dépendantes [l'évolution des pratiques et le déclin fonctionnel des Résidents en EHPAD]) were collected at baseline (T0) and after an 18-month interval (T18). IQUARE is a nonrandomized controlled multicentric trial of education and professional support for NH staff. All NHs from the Midi-Pyrénées area in France (423 NHs for 2,926,592 inhabitants) were invited to participate in the study in March 2011. One hundred seventy-five NHs were finally enrolled, and data were recorded for 6275 residents. The IQUARE protocol has been fully described elsewhere.[23,24] It followed the principles of the Declaration of Helsinki and complied with ethical standards. The study protocol was approved by the ethics committee of Toulouse University Hospital and the Consultative Committee for the Treatment of Research Information on Health (CNIL 07-438).

Participants

Residents with PD were defined as in a previous analysis conducted in the IQUARE study[18]: all residents with at least 1 prescription of antiparkinsonian drug defined by the anatomic therapeutic chemical class N04B at baseline. Drugs considered as antiparkinsonian drugs were levodopa, amantadine, apomorphine, bromocriptine, cabergoline, piribedil, pramipexole, ropinirole, rotigotine, rasagiline, selegiline, entacapone, and tolcapone.

Data Collection

Information about residents' characteristics and prescriptions was recorded by the coordinating physician or the coordinating nurse of each NH through direct completion of questionnaires on-line on a website developed specifically for the study. In addition, the coordinating physician sent to the research team all drug prescriptions for each resident participating in the study.

Outcomes

The main outcome was mortality rate (whatever the cause), defined by number of deaths that occurred during the IQUARE study period reported to the number of residents enrolled at baseline. Deaths were systematically registered by the coordinating physician and sent to the research team at the end of the study period (18 months). Secondary outcomes included residents' characteristics associated with mortality and with AP prescriptions. All drugs of anatomic therapeutic chemical class N05A were considered as APs except N05AN (Lithium).

Residents' Characteristics

Information on residents' characteristics were recorded using medical charts. They contained age (<85 or ≥85 years), sex, time living in a NH, body mass index, dementia, and behavioral disturbances (wandering, attempts at elopement, aggressive, severe psychiatric disease excepted depression defined as a regular follow-up by a psychiatrist or by repeated hospitalizations in a psychiatric unit). They contained comorbidities: myocardial infarction, peripheral vascular disease, congestive heart failure, arterial hypertension, diabetes, stroke, chronic pulmonary disease, peptic ulcer, hepatic disease, cancer, moderate or severe kidney disease, and epilepsy. Comorbidities were categorized as 0, 1, and ≥2 comorbidities according to the comorbidity Charlson score.[25] Disability was assessed using the Katz activities of daily living (ADLs) and was studied as a categorical variable: (0–2), (2.5–4), and (4.5–6). This scale includes 6 activities: bathing, dressing, toileting, transferring, continence, and feeding. Each activity was scored from 0 to 1: 0 for totally dependent patient, 0.5 for partly dependent patient, and 1 for independent patient.[26]

Statistical Analysis

The mortality rate was compared for residents with at least 1 antiparkinsonian prescription at baseline between those who had been exposed to AP and those who had not. For quantitative variables, we used the Student test under 2 application conditions: normal distribution and equality of variances. If at least 1 of these 2 application conditions was unmet, we transformed the quantitative variables into categorical variables. For categorical variables, we used χ^2 test (if expected values > 5) or Fisher exact test (if expected values ≤ 5).