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Antiepileptic drug use and epileptic seizures in nursing home residents in the Province of Pavia, Italy: A reappraisal 12 years after a first survey

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ABSTRACT

Purpose: To assess the prevalence of epileptic seizures, and antiepileptic drug (AED) use among nursing home elderly residents; to evaluate demographics, seizure characteristics, and seizure-related comorbidities associated with institutionalization; and to compare findings with a previous survey conducted 12 years earlier.
Methods: Data on demographics, age at institutionalization, diagnoses, functional and cognitive status (Barthel Index and Mini Mental State Examination) and drug treatment were obtained by review of medical records of all individuals aged ≥60 years at 21 nursing homes. Data from individuals with a diagnosis of epileptic seizures and AED users were compared with non-seizure, non-AED individuals.
Results: Among the 2163 individuals surveyed (79% females, age at observation 84.9 ± 7.8 years, mean ± SD), 278 (12.8%, vs 4.3% in the previous survey) received chronic AED treatment, including 174 who did not have a diagnosis of seizures. Of the 116 residents with a diagnosis of seizures (5.4%, vs 2.9% in the previous study), 104 were on AED treatment and were younger and had lower cognitive abilities, and a higher number of comorbidities and co-medications compared with non-AED-users. The most commonly prescribed AEDs in seizure individuals were phenobarbital (43.3%, vs 70% in the previous survey) and levetiracetam (27.9%, not available at the time of previous survey). At multivariate analysis, a diagnosis of seizures was found to be associated with younger age at the time of the survey, a history of neurological (cerebrovascular events, meningiomas) and non-neurological conditions (psoriasis and chronic bronchitis), and a lower MMSE score.
Conclusions: The prevalence of seizures and AED use was higher than in our previous survey and more aligned with data from other countries. Seizures, AED use and co-morbidities were associated with earlier institutionalization. There were indicators of treatment being suboptimal in many cases.

1. Introduction

The prevalence of epilepsy in nursing home elderly residents is higher than in the general population (de la Court et al., 1996; Olafsson et al., 2005; Schachter et al., 1998). The use of antiepileptic drugs (AEDs) in this setting is also greater than in community dwelling elderly people, and varies from 4 to 17% in surveys conducted in Europe and North America, with considerable differences across studies in patterns of AED use (Leppik et al., 2012; Leppik and Birnbaum, 2010; Tallis et al., 2002). The frequent utilization of AEDs in elderly individuals raises concerns because of their greater susceptibility to adverse drug effects and drug interactions (Leppik et al., 2012), and does not necessarily reflect the prevalence of seizure disorders because AEDs are also used to treat a variety of diseases other than epilepsy (Garrard et al., 2003; Schachter et al., 1998). As a result, drug therapy patterns in elderly patients with seizures are not easily identifiable in database-based surveys, due to confounders such as diagnostic uncertainties and prescription of AEDs for different indications. Moreover, it is generally unclear to what extent occurrence of seizures and AED treatment impact

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on the likelihood of institutionalization and on the health status of institutionalized elderly people.

2. Objectives

This observational study was aimed at (i) assessing the prevalence of epileptic seizures and AED use in a population of nursing home residents aged ≥60 years in the province of Pavia, Italy; (ii) determining the demographic, clinical and functional characteristics, comorbid conditions, and pattern of AED use in the same population; (iii) exploring the role of potential factors associated with epileptic seizures; (iv) evaluating changes over time in the prevalence of epileptic seizures and AED use by comparing the findings with those obtained in a survey conducted 12 years earlier in the same setting (Galimberti et al., 2006).

3. Methods

3.1. Study population and clinical assessments

Twenty-one nursing homes (median size 85 beds; range 40–264) located in the Province of Pavia, identical to those included in our previous survey (Galimberti et al., 2006), were visited over a 7-month period in 2012. Through collaboration with local physicians and administrative and health managers, the medical records of all residents aged ≥60 years were reviewed and anonymized demographic and clinical data were recorded in pre-designed study forms. Ethics Committee approval was obtained.

Information collected for each resident included (i) demographic data; (ii) age at institutionalization; (iii) clinical diagnoses, including "epilepsy" or "epileptic seizures", as reported in the medical records; (iv) functional status as measured by the modified Barthel Index (MBI, Shah et al., 1989) and cognitive functioning as measured by the Mini Mental State Examination (MMSE, Folstein et al., 1983), both of which are updated regularly for each resident by the nursing home health personnel for reimbursement purposes; (v) all drugs prescribed on a regular basis, both at institutionalization and at the time of the survey.

For those individuals with a recorded diagnosis of epilepsy or epileptic seizures ("seizure individuals"), a subsequent more detailed re-assessment was scheduled, which included a detailed medical history, a general and a neurological examination, and a standard electroencephalographic (EEG) recording whenever possible. Proceeding to re-assessment was conditional on obtaining informed consent from each individual or, when applicable, from his/her legal representative.

3.2. Data analysis

Brand names of each medication and each recorded diagnosis were converted to the corresponding ATC code (Anatomical Therapeutic Chemical Classification) and ICD9 code (International Statistical Classification of Diseases, Injuries and Causes of Death), respectively. When calculating the prevalence of individuals receiving at least one AED, diazepam and clonazepam were considered as AEDs only when there was recorded evidence that they had been prescribed for seizure control.

Data processing included a descriptive analysis followed by an inferential analysis. For descriptive analysis, quantitative variables were reported as mean ± standard deviation (SD), and medians and range, as appropriate. For categorical variables, absolute frequencies and percentages were tabulated.

Seizure individuals and AED users were compared with those with no diagnosis of seizures and no AED use. The prevalence of AED use and a history of seizures were also examined in relation to gender and to age at the time of institutionalization and at the time of the survey by dividing the population into three age subgroups (60–74, 75–84 and ≥85 years). Mean MBI and MMSE values were used to compare degree of functional dependence and cognitive functioning, respectively, for the whole sample and for different subgroups of AED users and seizure individuals. In addition, findings were compared with those obtained in our previous survey.

Inferential analyses were performed to (i) compare seizure- and non-seizure individuals with respect to demographics, comorbidities, and use of drugs other than AEDs and (ii) identify factors associated with a history of seizures. Results were reported as odds ratio (OR) with 95% confidence intervals (CI).

One-way ANOVA (for continuous variables), and Chi-square or Fisher's exact test (for categorical variables) were used for univariate analyses. Multivariate analysis was performed by entering into a logistic regression model variables which emerged as statistically significant ($p < 0.05$) at univariate analysis as well as potential prognostic factors selected from the epidemiological literature. The general principle of one independent variable for every 10 individuals was not exceeded. Statistical analyses were performed using version 9.2 of the SAS statistical software.

4. Results

4.1. Characteristics of the study population

A total of 2163 residents were included in the study (Table 1). Mean age (±SD) at the time of the survey was 84.9 ± 7.8 years (range 60–112 years). Females comprised 79% of the population and, compared with males, were older both at time of institutionalization (81.9 ± 9.7 vs 77.5 ± 12.1 years) and at time of the survey (85.8 ± 7.3 vs 81.3 ± 8.5 years) ($p < 0.0001$, ANOVA).

MBI values indicated a condition of functional dependency (31.8 ± 31.2), which was significantly more severe in females than males (30.6 ± 30.6 vs 36.2 ± 33.2) ($p < 0.0006$, ANOVA). Likewise mean MMSE scores (14.3 ± 9.9) were indicative of severe cognitive decline, without significant gender-related differences.

The median number of medications received by each individual was 4 (range 0–14) (Table 1).

4.2. Prevalence of AED use

Of the 2163 residents surveyed, 278 (12.8%; 73 males, 205 females) were taking at least one AED as chronic treatment, in 90% of cases as AED monotherapy. Phenobarbital, gabapentin and valproate were the most frequently prescribed AEDs (Fig. 1).

Compared with non-AED users and with the entire population, AED users were younger both at institutionalization and at the time of survey, and had lower functional (MBI) and cognitive (MMSE) abilities (Table 1). AED users also had a significantly higher number of morbidities and received a significantly higher number of non-AED medications (Table 1). Individuals in the middle-old age range (75–85 years) accounted for the highest percentage (42.1%) of all AED users ($p = 0.03$), despite the fact that this group included fewer individuals ($n = 750$) than the over 85 group ($n = 1178$).

In 174 individuals (8% of the population), AEDs were prescribed in the absence of a diagnosis of epileptic seizures either in monotherapy ($n = 163$) or as a two-AED combination ($n = 11$): these included 66 individuals on gabapentin, 43 on valproate, 25 on phenobarbital, 18 on pregabalin, 15 on levetiracetam, 14 on carbamazepine and 4 on phenytoin. Of the 174 AED-treated individuals without a seizure diagnosis, 81 had a formal diagnosis of mood disorders and 16 had a peripheral neuropathy, conditions for which some of these AEDs may be indicated.