Epilepsy Research 140 (2018) 90–94

Contents lists available at ScienceDirect

Epilepsy Research

journal homepage: www.elsevier.com/locate/epilepsyres

Epilepsy in an elderly population: Classification, etiology and drug resistance

Lizbeth Hernández-Ronquillo*, Scott Adams, Stephanie Ballendine, Jose F. Téllez-Zenteno*

Department of Medicine, Division of Neurology, University of Saskatchewan, Saskatoon, SK, Canada

ARTICLE INFO

Keywords:
Epilepsy
Elderly
Classification
Etiology
Drug resistance
Drug resistant epilepsy

ABSTRACT

Purpose: To characterize epilepsy in an elderly population and describe the prevalence of drug resistant epilepsy (DRE) using recently validated International League Against Epilepsy (ILAE) criteria.

Methods: Using a case-control design, 72 patients aged 60 years and older (cases) and 223 patients under age 60 (controls) were identified from the Saskatchewan Epilepsy Program database. Patients' charts were retrospectively reviewed. Bivariate and multiple logistic regression analyses were performed to identify variables that were associated with epilepsy in elderly patients.

Results: Forty-seven elderly patients (65%) had focal epilepsy, while 9 (13%) had generalized epilepsy. The most common etiology in elderly patients with epilepsy was unknown in 30 (48%) patients. Other identified etiologies included brain tumors in 14 (19.4%), genetic in 6 (8%), degenerative disease in 4 (5%), stroke in 6 (8%) and head injury in 3 (4%). Significantly fewer elderly patients met criteria for DRE compared to non-elderly patients (26% vs. 51%, $p = 0.001$). In the multiple logistic regression analysis, elderly patients with epilepsy were more likely to have the presence of stroke, psychiatric comorbidity and to be on monotherapy.

Conclusion: In our sample, elderly patients with epilepsy were more likely to have seizures resulting from brain tumors and stroke, and less likely to have DRE than non-elderly patients. These unique features of elderly patients strongly suggest that clinical practice guidelines are needed to facilitate the highest quality of care in elderly patients with epilepsy.

1. Introduction

The bimodal age distribution of epilepsy is well established, with incidence shown to be highest in children and the elderly (Kotsopoulos et al., 2002). Despite the high prevalence of epilepsy in elderly patients (Tellez-Zenteno et al., 2004; Hauser et al., 1993), the unique features of epilepsy in this age group have not been extensively studied. Initial investigations have found that the etiological risk factors for seizures in elderly patients are often different from those in children and younger adults (Ferlazzo et al., 2016). Elderly patients also face specific treatment challenges due to their high rate of somatic and psychiatric comorbid conditions, metabolic changes, and increased risk of drug–drug interactions (Werhahn et al., 2015). These unique features of elderly patients have prompted calls to consider this population separately in future investigations and clinical practice guidelines (Krumholz et al., 2007; Sauro et al., 2016).

There is currently no standard age threshold used to define epilepsy in the elderly. Previous studies have used definitions ranging from patients older than 50–70 years of age (Ruggles et al., 2001; Stefan et al., 2014; Josephson et al., 2016). While prior studies have focused on only elderly-onset epilepsy (Josephson et al., 2016; Besocke et al., 2013; Lühdorf et al., 1986; Pugh et al., 2009) or investigated epilepsy in the elderly without non-elderly controls (Hiyoshi and Yagi, 2000; Huang et al., 2016), few studies have investigated the entire population of elderly patients with epilepsy—that is, not selected based on age of onset of epilepsy—in comparison to non-elderly epilepsy patients. Furthermore, despite evidence that drug resistance is affected by age (Voll et al., 2015), the prevalence of drug resistant epilepsy (DRE) in elderly patients has not been extensively studied.

The goals of our study were to identify the profile of epilepsy in elderly patients, including seizure classification and etiology, and to describe the prevalence of DRE as defined by the International League Against Epilepsy (ILAE) (Kwan et al., 2010). A single-centre case-control study design was employed. Elderly patients were compared with a cohort of non-elderly control patients that was previously described by our group (Téllez-Zenteno et al., 2014).

* Corresponding authors at: Royal University Hospital.103 Hospital Drive. BOX 26, Room 1622, Saskatoon, SK S7N OW8, Canada.
E-mail addresses: liztellez33@yahoo.com (L. Hernández-Ronquillo), jose.tellez@usask.ca (J.F. Téllez-Zenteno).

https://doi.org/10.1016/j.eplepsyres.2017.12.016
Received 14 July 2017; Received in revised form 4 December 2017; Accepted 30 December 2017
Available online 03 January 2018
0920-1211/

2. Methods

2.1. Study population

The Saskatchewan Epilepsy Program (SEP) is the only epilepsy centre in the province of Saskatchewan, Canada. The centre serves as a catchment for 1.1 million people and is utilized to assess new onset epilepsy and complex cases. A database of 1000 patients from the program was queried to identify all epilepsy patients aged 60 years and older at the time of their last assessment by an epileptologist. All consecutive patients assessed at the SEP since 2007 were included in this study. Cases were defined as patients aged 60 or older with a diagnosis of epilepsy. Control subjects were patients younger than 60 who were part of a cohort previously published by our group (Téllez-Zenteno et al., 2014). In this previous study, 223 patients were randomly selected from the same database of 1000 patients in order to validate the ILAE definition or DRE and assess DRE rates in our institution (Téllez-Zenteno et al., 2014). All diagnoses of epilepsy were established by an epileptologist using ILAE criteria (Fisher et al., 2014). This study was approved by our institution's research ethics board.

2.2. Variables and definitions

All patient charts, including referral and consultation letters and available investigation results (routine and ambulatory EEG; video EEG telemetry; neuropathology; CT, MR, and PET/CT imaging) were manually reviewed. Age at diagnosis of epilepsy, years of evolution, frequency of seizures per month, duration of inter-seizure intervals, history of status epilepticus, first anti-epileptic drug (AED) used, response to first AED, family history of epilepsy, past medical history, diagnosis of developmental delay and psychiatric comorbidities were recorded for each patient.

Seizure profiles were classified and recorded as per the 1985 ILAE criteria (Commission, 1985). Etiology of epilepsy, when known, was categorized as the following: genetic (familial epilepsy), perinatal insult (i.e. asphyxia during birth, intrauterine viral infections, or other pregnancy complications), congenital malformation, cranial trauma, malignant or benign cerebral neoplasm, toxic or metabolic disorder, stroke, primary degenerative lesion, cerebral infection, cortical dysplasia, mesial temporal sclerosis (MTS), or idiopathic.

Epileptic syndromes were classified as idiopathic, symptomatic or cryptogenic (Commission, 1985). Specific epileptic syndromes including, but not limited to West syndrome, Lennox–Gastaut syndrome, childhood absence epilepsy, juvenile myoclonic epilepsy, mitochondrial disease, and Rasmussen encephalitis were documented.

All current and previous AEDs were recorded, noting dose, frequency, duration of use, and reasons for discontinuation (including, but not limited to adverse effect, unsatisfactory seizure control, long-term seizure freedom, pregnancy, loss to follow-up, financial issues, or patient/caregiver preference). ILAE criteria for DRE were applied to each patient based on status at their most recent follow up appointment as follows: failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom (Kwan et al., 2010). All patients that were included had at least 12 months of follow up, so that the ILAE definition could be applied.

2.3. Statistical analysis

All analyses were performed using SPSS Statistics version 24.0 (IBM, Armonk, NY). Descriptive statistics, including means, frequencies and distributions, were determined. Bivariate analysis was used to determine variables associated with epilepsy in elderly patients. Comparisons between elderly and non-elderly patients were tested using Student's T-tests/Mann Whitney *U* test or Chi-squared tests for continuous and categorical variables, respectively. A *p*-value of less than 0.05 was regarded as significant throughout our analysis.

A multiple logistic regression analysis was performed. The dependent variable was DRE status. Independent variables included in the model were age at diagnosis of epilepsy, number of AEDs tried, monotherapy, presence of psychiatric comorbidity and developmental delay, diagnosis of stroke, tumor, or MTS; epilepsy type; and diagnosis of DRE. Independent variables that reached statistical significance were included in the multivariate analysis. A purposeful selection modeling strategy was used, with consideration of past evidence and theory, as well as statistical criteria (likelihood ratio test), in the selection of covariates. Presented estimates of effect included adjusted odds ratios with 95% confidence intervals.

3. Results

3.1. Description of elderly patients (cases)

The elderly patient group consisted of 72 patients, 38 (53%) of whom were male and 34 (47%) of whom were female. Mean age was 70.7 (+6.8) with a median age at diagnosis of epilepsy of 61 years (2–81) and median years of evolution of eight years (0–84). Twenty-eight patients (39%) were on monotheraphy. The first AED prescribed to 35 (48%) of the patients was phenytoin, while 13 (18%) patients were first prescribed lamotrigine. Thirty-seven (60%) had a good response to the first AED they were prescribed. Overall, 15 elderly patients met the criteria for DRE, giving a prevalence for DRE in the elderly of 20.8% (95% CI: 12.9-31.7).

Regarding seizure etiology, the most common etiology was unknown in 30 (48%) patients. Other identified etiologies included brain tumors in 14 (19.4%), genetic in 6 (8%), degenerative disease in 4 (5%), stroke in 6 (8%) and head injury in 3 (4%); other etiologies are displayed in Table 1. Forty-seven (65%) elderly patients had focal epilepsy, 9 (13%) had generalized and 16 (22%) were unknown.

3.2. Description of younger patients (controls)

The younger patient group consisted of 223 patients, 106 (47.5%) of whom were female. Mean age was 33.4 (± 11.5) years and mean age at diagnosis of epilepsy was 16.9 (13.6). Forty-one patients (18%) were on monotheraphy. Overall, 114 (51%) control patients met the criteria for DRE.

Regarding seizure etiology, the most common etiology was unknown in 125 (56%) patients. Other identified etiologies included MTS in 27 patients (12%), cortical dysplasia in 21 patients (9.4%) and brain tumor in 12 patients (5%); other etiologies are displayed in Table 2. One hundred and twenty-one control patients (54%) had focal epilepsy, 55 (25%) had generalized and 47 (21%) were unknown.

3.3. Bivariate analysis

The mean age of the elderly and non-elderly patient groups was significantly different (70.7 vs. 33.4, $p < 0.001$), as well as the median age at diagnosis of epilepsy (61 vs. 8, $p < 0.001$). Elderly patients were less likely than controls to have developmental delay (4% vs. 20%, $p = 0.001$). However, they were more likely to have seizures resulting from stroke (6% vs. 0.4%, $p = 0.008$) or tumors (18% vs. 6%, $p = 0.001$) than non-elderly patients.

Elderly patients were taking significantly fewer AEDs than non-elderly patients (2.4 vs. 3.6, $p = 0.001$). There were also significantly more elderly patients on monotherapy (n = 28; 39%), compared to non-elderly patients (n = 41; 18%, $p < 0.001$). Significantly fewer elderly patients met criteria for DRE compared to non-elderly patients (26% vs. 51%, $p = 0.001$).

In the bivariate analysis, the following variables were associated with epilepsy in the elderly: median age at diagnosis of epilepsy ($p = < 0.001$), treatment with monotheraphy (OR 2.8, CI 1.5-5,