Epilepsy & Behavior 27 (2013) 29–35

Contents lists available at SciVerse ScienceDirect

Epilepsy & Behavior

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

Outcome of newly-diagnosed epilepsy in older patients

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ARTICLE INFO

Article history:
Received 25 July 2012
Revised 14 November 2012
Accepted 17 November 2012
Available online 29 January 2013

Keywords:
Epilepsy in older people
Outcome of epilepsy
Epilepsy prognosis in older people

ABSTRACT

Introduction: The annual incidence of seizure disorders rises sharply after the age of 60. Treatment is complicated by the normal physiological changes of aging, comorbid diseases, and polypharmacy. Despite this, approximately 80% of the patients become seizure-free.
Objectives: The objectives of this study were to (1) analyze the outcome of a cohort of patients with newly-diagnosed epilepsy over the age of 65, (2) describe epilepsy etiology and seizure type, and (3) classify the outcome according to the latest ILAE classification proposal for drug-resistant epilepsy (2010).
Methods: All patients with newly-diagnosed epilepsy over the age of 65 who were evaluated in two different institutions were included. Seizures and epilepsy syndromes were classified according to the International League Against Epilepsy proposal (2010). Epilepsy outcomes were also analyzed according to the proposal of the ILAE Commission on Therapeutic Strategies (2010).
Results: One hundred and twenty-two patients were included with a median follow-up time of 15 months. Median age of diagnosis was 78 years. Seventy-seven patients (55%) had epilepsy of unknown cause, and 55 (45%) had structural–metabolic epilepsy. The proportions of seizure-free patients at 6, 12, 18, and 24 months were 90%, 77%, 74%, and 67%, respectively. Thirty percent of patients experienced adverse effects (AEs). We found a statistically significant trend toward a higher frequency of AEs as the number of concomitant medications rose and in younger patients. According to the 2010 ILAE classification proposal for drug-resistant epilepsy criteria, 55.8% of the patients were seizure-free, 12.3% had treatment failure, and 32% had undetermined seizure outcome.
Conclusion: Patients with newly-diagnosed epilepsy after the age of 65 have very good chances of achieving seizure control with AED treatment. It seems that fulfilling the ILAE classification proposal for drug-resistant epilepsy (2010) criteria for seizure freedom was more difficult in our cohort. Older patients also seem to be more prone to suffering from AEs.

1. Introduction

The annual incidence of seizure disorders rises sharply after the age of 60 years old (yo), from 40 per 100,000 for people between 40 and 45 yo, to 80 per 100,000 for people between 60 and 65, to more than 150 per 100,000 in those older than 80 [1,2]. The clinical presentations of seizures in the elderly differ from those in other age groups, and underdiagnosis and misdiagnosis occur very frequently in this population [3,4].

Epilepsy can have profound physical and psychological consequences in older patients. The stigma surrounding the diagnosis can be hard to address at this time of life. Elderly people are particularly vulnerable to physical injury as a consequence of seizures. The situation may be complicated by a range of neurodegenerative, cerebrovascular, and neoplastic comorbidities; furthermore, problems with concomitant medications are common. Quality of life can be adversely affected, and the unpredictable nature of the seizures can lead to social withdrawal. Loss of confidence and reduced independence can result in premature admission to nursing homes and residential care facilities. Despite this, approximately 80% of patients with new onset epilepsy beyond the age of 65 yo become seizure-free during a period of at least 12 months after being treated with one or two drugs in monotherapy [5].

Adverse effects (AEs) of antiepileptic drugs (AEDs) are causes for concern in the elderly population because they are common and can occur at lower blood levels than in younger patients [6]. Treatment is complicated by the normal physiological changes of aging, comorbid diseases, and polypharmacy.

We describe the characteristics of a cohort of patients with newly-diagnosed epilepsy over the age of 65 yo, with a special focus on their outcome, treatment, and tolerability of AEDs.

1.1. Objectives

The objectives of this study were to analyze the outcome of a cohort of patients with newly-diagnosed epilepsy over the age of

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http://dx.doi.org/10.1016/j.yebeh.2012.11.041

65 yo in two different neurology departments, describe epilepsy etiology and seizure type, and compare a classical clinical approach of defining epilepsy outcome with the latest ILAE classification proposal for drug-resistant epilepsy (2010) [7,8].

2. Methods

2.1. Patients

We retrospectively included all the patients with newly-diagnosed epilepsy over the age of 65 yo evaluated in two neurology departments from two different institutions: Hospital Privado de Comunidad de Mar del Plata, Argentina (November 1st, 2007 to June 30th, 2009) and Hospital Italiano de Buenos Aires, Argentina (November 1st, 2006 to June 30th, 2009). Patients with acute provoked seizures were not included in this cohort. Patients were interviewed by a neurologist every 6–8 weeks, until seizure freedom was achieved. Subsequently, patients were monitored every 3–6 months. Seizure outcome was established on the last visit to the neurologist's office. If no seizures were reported after one year of seizure freedom, the patient was assumed to be seizure-free. Furthermore, we classified outcomes according to the 2010 ILAE classification proposal for drug-resistant epilepsy, to compare the most recent definition with a classical, widely used clinical definition. All patients were initially treated with monotherapy. The objective of the treatment was to control seizures with the lowest drug dose necessary. Treatment was modified according to clinical response and tolerability. A second drug was prescribed if patients did not tolerate the first drug or if it was not effective. When there was a lack of efficacy after two drugs in monotherapy, combined treatment was established.

2.2. Definitions

Seizures and epilepsy syndromes were classified according to the International League Against Epilepsy proposal (2010). Epileptic seizures were classified as focal seizures (FS), generalized seizures (GS), or unclassified seizures (US). FS are conceptualized as originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed, and they may originate in subcortical structures. FS are further subdivided into FS with or without impairment of consciousness or awareness; FS evolving to a bilateral, convulsive seizure; and generalized seizures (involving tonic, clonic, or tonic and clonic components). GS are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed networks that can include cortical and subcortical structures but do not necessarily include the entire cortex. Although individual seizure onsets can appear localized, the location and lateralization are not consistent from one seizure to another [9].

Epilepsy syndromes were classified into the following:

(1) "Genetic": epilepsy as the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder. The knowledge regarding the genetic contributions may derive from specific molecular genetic studies that have been well replicated and have even become the basis of diagnostic tests.
(2) "Structural/metabolic" (SE): epilepsy as the direct result of a distinct structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy in appropriately designed studies. SE syndromes include acquired disorders such as stroke, trauma, and infection. They may also be of genetic origin (e.g., tuberous sclerosis, many malformations of cortical development).
(3) "Unknown cause" (UE): the nature of the underlying cause is currently unknown; it may have a fundamental genetic defect at its core or it may be the consequence of a separate unrecognized disorder [9].

Seizure freedom was defined as freedom from seizures or auras for a minimum of three times the longest pre-intervention inter-seizure interval, or 12 months, whichever was longer. Treatment failure was defined as recurrent seizure(s) after the intervention had been adequately applied. Both instances were further classified according to the presence or absence of adverse events. Undetermined seizure outcome was applied when the treatment had not been adequately established for a valid assessment of the outcome, or information was lacking to make the assessment [7].

Adverse effects (AEs) were defined as any harmful, unwanted effect of a medication used at therapeutic recommended doses [10,11].

2.3. Statistical analysis

Patients were divided into two groups according to the seizure freedom criteria. Categorical data were analyzed using the chi-square test and Fisher exact test. The Mann–Whitney test was used to compare ordinary and intervallic variables without normal distributions. The Kaplan–Meier method was applied to assess the proportion of seizure-free patients. The Wilcoxon (Peto–Prentice) method was used to compare two or more survival curves. All statistical tests were two-tailed. We used the 2008 version of STAT 2.7.2 for all statistical analyses.

3. Results

3.1. Patients

One hundred and twenty-two patients were included, and all of them received their first AEDs. None of them had been previously treated with AEDs. The median follow-up time was 15 months (inferior quartile: 12–superior quartile: 24). Twenty-six patients (21%) died during the study period.

The median age of diagnosis was 78 yo; 66% were female. Seventy-seven patients (55%) had UE, and 55 (45%) had SE. In the latter group, 50% (n = 28) of the cases were related to cerebrovascular disease (ischemic or hemorrhagic), 20% (n = 11) to brain tumors, 7.2% (4) to subdural hematomas, and 20% were associated with different causes (cerebral infections, previous neurosurgery, cavernous angioma, mesial temporal sclerosis).

3.2. Seizure type

Seventeen patients (14%) suffered from focal seizures without impairment of consciousness, 41 (33.5%) had focal seizures with impairment of consciousness, 37 (30.3%) had focal seizures evolving to bilateral convulsive seizures, and 27 (22.2%) suffered from generalized tonic-clonic seizures. None of the patients had absences or myoclonic seizures.

We performed an interictal electroencephalogram (EEG) in 95 patients (78%); 52% were normal, 14.4% had non-specific changes (mostly focal or generalized slowing), and 33.6% evidenced epileptiform abnormalities (Table 1).

3.3. Outcome

The proportions of patients who attained remission for 6, 12, 18, and 24 months were 90%, 77%, 74%, and 67%, respectively (Fig. 1). Of the patients who attained a period of 12 months of seizure freedom (n = 76), 62 received one lifetime AED, 11 received two lifetime AEDs, and 3 received 3 or more lifetime AEDs.

There were no statistically significant differences when comparing seizure freedom survival curves between the two neurology departments, sex, age at diagnosis, or seizure type (Table 2 and Fig. 2). However, we identified a trend toward higher seizure freedom in the SE group compared to the UE group, and in the normal EEG