Seizure 22 (2013) 577–580

Contents lists available at SciVerse ScienceDirect

Seizure

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

Short communication

Risk factors of recurrent seizure, co-morbidities, and mortality in new onset seizure in elderly

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ARTICLE INFO

Article history:
Received 25 November 2012
Received in revised form 11 April 2013
Accepted 11 April 2013

Keywords:
Elderly
Co-morbidity
Recurrent seizure
Thailand

ABSTRACT

Objective: To determine the risk factors of seizure recurrence and the most common comorbidities in elderly patients with epilepsy.
Method: We did a retrospective study of 278 patients older than 65 years with first seizure. We evaluated electrolytes, blood glucose, urea and creatinine levels, and performed electrocardiography (ECG), and routine electroencephalogram (EEG) on all patients. We evaluated seizure recurrence and comorbidities at 2 years.
Results: Univariate analysis found that significant ($P < 0.05$) factors affecting seizure recurrence were etiology of seizure, EEG, and status epilepticus at first presentation. In multivariate regression analysis, etiology of seizure and EEG were significant statistical factors in seizure recurrence at 2 years follow up. Age, sex, duration of time between first seizure and diagnosis of seizure, seizure type, misdiagnosis of non-epileptic seizure, and use of antiepileptic drugs were not significant factors for predicting seizure recurrence. Depression and anxiety were the most common comorbidities in our study, followed by sleep-related disorders and stroke. There were no statistically significantly differences in comorbidities between patients who remained seizure free and patients who had recurrent seizure.
Conclusion: Most of the new onset seizures in our elderly patients were focal onset. Acute symptomatic etiology, remote symptomatic etiology, progressive symptomatic etiology and abnormal EEG features were powerful predictors of seizure recurrence, and mood disorder, sleep disorder and stroke were the common comorbidities.

1. Introduction

Elderly people are the most rapidly growing segment of the population. The incidence and prevalence of epilepsy are higher in this age group than in younger people. Elderly individuals with epilepsy are a unique subpopulation of patients with several important differences from younger people with epilepsy.[1] The literature indicates that epileptic seizures are often difficult to diagnose in the elderly for various reasons, such as difficulty in obtaining an accurate clinical history, a frequently atypical ictal presentation, and difficulty in diagnostically distinguishing between an epileptic and non-epileptic event.[2] Recurrent seizure appears to be common in this population, but the data are largely inconclusive. There also appear to be differences in this patient group in the epidemiology, etiology, and treatment with antiepileptic drugs in developing countries compared to developed countries.[1] Data on epilepsy in the elderly from developing countries are sparse. With the rapid increase in the elderly population in our societies, more attention must be paid to this group of patients when planning future medical services for epilepsy. In this study, we aimed to elucidate the risk factors of recurrent seizure, and describe co-morbidities in older adults who presented with first seizure to a tertiary care hospital in the south of Thailand.

2. Materials and methods

This was a retrospective, hospital-based case-control study conducted on 278 patients older than 65 years with new onset seizure at the Internal Medicine Outpatient Service of Songklanagarind Hospital, a university teaching institute and the major tertiary care referral hospital for medical and neurological cases in

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http://dx.doi.org/10.1016/j.seizure.2013.04.009

southern Thailand. The study was conducted from January 2006 to August 2012. The types of seizure were classified based on the International Classification of Epileptic Seizures.[3] The various data noted related to epilepsy were: demographic characteristics, the clinico-neurological examination findings, initial diagnosis, clinical features including seizure type, duration of epilepsy before adequate treatment, antiepileptic drugs prescribed, and recurrent seizure. Laboratory and other investigations recorded included electrolytes, blood glucose, urea and creatinine levels, and electrocardiography (ECG). Electroencephalogram (EEG) and brain imaging were obtained for all patients (an MRI scan for 120 patients, CT scan for 130 patients, and both for 28). The etiology of seizure was classified as (1) acute symptomatic: seizure occurred within a week of acute central nervous system (CNS) or systemic insult; (2) remote symptomatic: seizure in the presence of a history of CNS insult presumed to result in a static encephalopathy associated with an increased risk for epilepsy; (3) progressive symptomatic: seizure in the occurrence of non static conditions; and (4) unknown: seizure owing to conditions presumed to be symptomatic, but cause unclear. We used standard hospital and anxiety scales for diagnosis of depression and anxiety. We evaluated seizure recurrence and co-morbidities at 2 years.

2.1. Statistical analysis

All statistical procedures were performed using R 2.14.2 software and the Epicalc package. Group comparisons between seizure-free and recurrent seizure were made using a two-sample t-test or the Wilcoxon rank sum test. The correlates of recurrent variables were determined using logistic regression models. Each demographic and clinical variable was analyzed for marginal association with seizure recurrence using univariate logistic regression based on the *P*-value. Variables were entered into a single, multivariate, logistic regression model with the backward stepwise entry method, and results were verified using the forced-entry method. For all other analyses, the Bonferroni correction for multiple comparisons was used to maintain at least a 0.05-significance level.

3. Results

278 patients (171 male, 107 female) with a mean ± SD age of 73.32 ± 8.72 years were enrolled in the study, and all were completely followed for a minimum of 2 years. Basic clinical characteristics, clinical data of the seizure and co-morbidities are shown in Table 1. Overall, the seizures were classified as generalized onset in 26 patients (9.4%), focal onset in 195 patients (70.1%), and uncertain in 57 patients (20.5%). The etiology was acute symptomatic in 109 (39.2%) patients, remote symptomatic in 88 (31.7%) patients, progressive symptomatic in 53 (19.1%) patients, and unknown in 28 (10.1%) patients. In the acute symptomatic group, ischemic stroke was the most common cause (45 patients), followed by hemorrhagic stroke (41 patients). There were no statistically significant differences in age, sex, duration of seizure, seizure type, co-morbidity or antiepileptic drug therapy in patients who had or did not have recurrence.

The median duration of time from when the seizure occurred until the patient sought treatment was 13.02 ± 24.29 days. The longest duration of seizure before accurate diagnosis was 18 weeks. The most common incorrect initial diagnosis was syncope, followed by stroke. 11 patients who presented initially with loss of consciousness had an uncertain diagnosis with up to 12 weeks of follow up without definite treatment before the correct diagnosis of seizure activity was made.

Forty five (16.2%) patients died during the study period (24 from ischemic heart, 16 from ischemic stroke, and 5 of undetermined cause). One hundred and twenty (43.2%) patients suffered one or more seizures during the follow up interval. Multivariate analysis for recurrent seizure identified acute symptomatic etiology, remote symptomatic etiology, progressive symptomatic etiology, epileptiform discharge on EEG and non-specific abnormality on EEG to be independent risk factors (Table 2).

The various comorbidities associated with our patients are listed in Table 1. Depression and anxiety were the most common comorbidities, followed by sleep-related disorders and stroke. There were no statistically significant differences in co-morbidities between patients who were seizure-free following the first episode, and patients who had recurrent seizure.

4. Discussion

In the present study, the notable risk factors of recurrent seizure were acute symptomatic etiology, remote symptomatic etiology, progressive symptomatic etiology, epileptiform discharge on EEG and non-specific abnormality on EEG, and the most common co-morbidities were depression and anxiety.

The incidence of seizures in the elderly is at least as high as in the first decade of life. With increasing age, secondary causes of seizure become more frequent and consequently seizures are more likely to be focal onset. In our study, 70.1% of the patients presented with focal onset seizure, most due to ischemic stroke. In a study from India, Thomas et al. found that 12 of 23 patients had focal onset seizure and 56.5% had an identifiable etiology.[4] However, all of the patients in this study were investigated before MRI scanning was available, which would have probably led to a diagnosis of 'unknown etiology' in several of those cases. In a more recent study from Canada, Holt-Seitz et al. found that 88% of their cases presented with focal onset epilepsy and only 55% had an identifiable etiology (acute symptomatic in 49% and remote symptomatic in 6%).[5] In contrast, in our study, all of our patients had neuroimaging (MRI or CT of the brain), and we identified the etiology in 89.9%. Cerebrovascular disease is the single most common pathology underlying epilepsy in elderly people, and in our study, similar to the study of Paradowski and Zagrajek,[6] the most common etiology was ischemic stroke (16.2%) followed by hemorrhagic stroke (14.7%).

The majority of our patients were treated with long-term antiepileptic drugs, even after the first seizure. Unacceptable side effects from the antiepileptic drugs were seen in 43% of cases receiving the standard dosage regiment. Forty five patients died over the 2-year follow up period of the study, but this is not excessive, given that this was an elderly population. Of the 2-year survivors in our study, 34% had had recurrent seizure, which is a little higher than other studies which have reported recurrent seizures ranging from 11% to 28% in 2 years follow up.[6,8] Of those patients with a previous history of stroke in our study, recurrent seizures recurred in more than 72%, similar to the rate as reported by Lühdorf et al.[7].

Data on the risk of recurrence in elderly patients following their first seizure are largely inconclusive. However, in the presence of a recognized structural brain lesion to which the seizure can be attributed, the risk of recurrence is roughly double that of a cryptogenic first seizure.[8] Our results agree with a report from Lühdorf et al.[7] in which there was seizure recurrence in more than 80% of elderly patients with a history of stroke. Status epilepticus de novo frequently occurs in the elderly with no prior history of epilepsy and represents a considerable risk for the subsequent development of epilepsy.[9] Our study found that status epilepticus presented as a first seizure in elderly patients in 21.6% of cases, and among those 61.7% had recurrent seizure. Our study found, as have other studies, that epileptiform activity on an EEG was a risk factor for