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The long-term prognosis of newly diagnosed epilepsy in Egypt: A retrospective cohort study from an epilepsy center in Greater Cairo

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ABSTRACT

Purpose: To investigate the long-term prognosis and prognostic patterns of epilepsy in a single practice study from a developing country.
Methods: Consecutive patients first seen in an epilepsy clinic in Cairo, Egypt between January 1994 and December 2009 with at least 4 years of follow-up were included. Demographic, clinical, EEG and imaging findings at diagnosis were recorded. At follow-up, treatment was adjusted as clinically indicated. The response to the first drug was defined as 6-month seizure remission. Outcome measures included 2-year remission (R) and 2-year sustained remission (SR). Prognostic patterns were early (ER) and late remission (LR), relapsing-remitting (RR) course, worsening course (WC) and no remission.
Results: Included were 287 patients aged 1–66 years and followed for 2237.0 person-years (mean 7.8 years). 244 (85%) attained 2-year R. The cumulative time dependent probability of R was 86.7% at 10 years. Only the response to the first drug predicted R. 82 (28.6%) attained 2-year SR. The probability of SR was 40.9% at 10 years. Poor treatment response and nocturnal seizures predicted lowered SR. R and SR were inversely correlated to the number of drugs. 208 patients (72.5%) entered ER, 36 (12.5%) entered LR, 138 (48.1%) had RR course. A WC was present in 24 (8.4%), 43 (15.0%) never entered remission. Prognostic patterns varied with neurological examination, MRI findings, pre-treatment seizure frequency, seizure type, number of seizure types, etiology, syndrome and response to first drug.
Conclusions: The long-term prognosis of newly diagnosed epilepsy patients from a developing country is in keeping with published reports.

1. Introduction

Epilepsy is a chronic neurological condition representing a significant burden for the patient and the society [1]. Although epilepsy is treatable, little is known on the long-term prognosis of the disease. Epidemiologic studies from Europe and North America indicate that up to 95% of patients with newly diagnosed epilepsy achieve at least 1-year seizure remission at some time after the onset of the disease [2–9] and up to 71% are in remission at last observation with or without drugs [2–4,9–11]. However, studies in European and US populations have investigated the timing and outcome of prolonged periods of seizure freedom (the so called prognostic patterns) [2–4,10–14]. These studies have shown that early remission predicts long-term remission. However, some patients enter remission during the course of the disease while others experiencing early remission may relapse and eventually fail to achieve further remission or may again become seizure-free. These different outcomes show that the long-term prognosis of epilepsy is variable and not always predicted by the response to the first treatment. To our knowledge, these findings have been confirmed by only one study done outside of Europe and North America [15] and there are no reports on the long-term prognosis of epilepsy in newly diagnosed patients from developing countries.

As the efficacy and tolerability of antiepileptic drugs is genetically determined [16–18], the prognosis of epilepsy may vary according to the genetic and ethnic profile of the affected individuals.

On this background, the main purposes of the present study were to investigate the long-term prognosis of epilepsy and define the temporal patterns of seizure outcome in a cohort of newly diagnosed patients seen in a single center in Greater Cairo in Egypt, a developing country, from the time of the diagnosis and followed for a prolonged period of time.

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2. Materials and methods

2.1. Setting and patients

This is a retrospective cohort study of patients with epilepsy firstly seen by a single senior epileptologist (HH) in the Epiclue epilepsy clinic, a tertiary health facility serving mostly Greater Cairo, which includes the capital and its province in Egypt, The city is the largest urban area in Africa and ranks number 17 among the largest cities in the world as regard population, with 15.6 million people in 2016.

In Egypt, in the absence of a strong primary physician system, there are two parallel heath care systems, governmental and private. Private clinics are easier to access than waiting for referral to a neurologist. Patients are aware that seizures fall in the domain of the neurologists and for this reason they seek medical advice directly from the neurologists both in the pediatric and adult population. Our institution has been a specialized private epilepsy clinic since 1994, gaining reputation all over Egypt and in neighboring countries. The clinic receives both newly diagnosed and referred patients.

Enrolled were consecutive patients who had their first visit in the clinic between January 1994 and December 2009 and were followed up until date of last observation or January 2014, whichever came first. To be included in the study, a patient must have had recurrent unprovoked seizures, an epilepsy syndrome or a single unprovoked seizure with high probability of recurrence (generally, a structural lesion and/or EEG epileptiform abnormalities)" [19], be untreated at the time of diagnosis, and have at least 4 years of follow up. A patient was excluded if (s)he had only acute symptomatic seizures "clinical seizure occurring at the time of a documented systemic insult or in close temporal association with a documented brain insult" [20].

During the first visit, the senior epileptologist collected the medical history and seizure details from the patients and any witnesses, by using a structured questionnaire. Neurological examination and mental status assessment (based on patient's interview and history of academic or social achievements) were performed in all patients. A standard awake interictal EEG was performed in all cases, whereas a sleep EEG and/or a video-EEG were performed only when clinically indicated. Magnetic resonance imaging (MRI) was performed in patients diagnosed with focal epilepsy by semiology or EEG. All other patients underwent brain computer tomography (CT).

Patients were compliant with follow up visits, scheduled every 3–6 months or earlier, if clinically indicated.

2.2. Treatment

Monotherapy was the first antiepileptic drug (AED) regimen in all cases. The choice of the drug was made on account of the indication, the patient's personal characteristics (child, woman of childbearing potential, elderly), the tolerability profile, the patient's socio-economic status, and the potential for drug interactions (in patients receiving drugs for other clinical conditions). The first maintenance dose was preferably in the lowest effective dose, except for patients with benign childhood epilepsies (rolandic or occipital epilepsy) in whom just reassurance or, if required, a low dose (approximately half of the recommended dose) was purposefully administrated.

In patients relapsing with the first maintenance dose, further increases were attempted to achieve seizure control or up to the highest tolerated dose, whichever came first. When the first monotherapy failed, a second regimen could be another drug given as alternative monotherapy or an adjunctive therapy based on the presence of single or multiple seizure types and the overall disease severity. Treatment was changed to another drug if the patient had an idiosyncratic reaction or intolerable side effects.

At each follow up visit, seizure frequency, AED daily doses, and compliance were routinely recorded (by history or AED serum levels), with treatment adjustments as dictated by the clinical circumstances.

For each case, a number of variables were searched and noted in ad-hoc case-record forms and the following were collected for the purposes of this study: Epilepsy syndrome, sex, status epilepticus, history of febrile convulsions, family history of epilepsy, age of onset of seizures, disease duration at diagnosis, pre-treatment seizure frequency, number and type of seizures, presence of nocturnal seizures, etiology, first EEG record, MRI/CT findings, neurological and mental examination, first AED used, response to initial monotherapy, and number of AEDs tried until seizure remission (if achieved).

2.3. Definitions

Epilepsy syndromes were defined according to the 1989 recommendations of the International League Against Epilepsy (ILAE) [21] and classified in broad categories. Seizure types were classified according to the 1981 ILAE definitions [22] and grouped as focal or generalized. Epileptiform discharges in the first EEG was a prerequisite for the diagnosis of well known epilepsy syndromes, like idiopathic generalized epilepsies and Rolandic epilepsy. Status epilepticus (a seizure or a flurry of seizures lasting more than 30 minutes), if present, was coded separately. History of febrile convulsions was recorded when present. Family history of seizures was also collected and considered positive when epilepsy was present in first degree relatives (i.e., parents, siblings and offspring). Age at onset of seizures (excluding febrile seizures) was noted and grouped in the following categories: $\leq$5 years, 6–15 years, 16–29 years, 30–59 years and 60 years or older. Disease duration at diagnosis was noted and categorized as $<$1 year; $\geq$1 year. Pre-treatment seizures were counted and indicated in categories ($<$6, $\geq$6). Nocturnal seizures were seizures occurring during sleep. Etiology was classified as idiopathic, cryptogenic or symptomatic. The first EEG record was defined as normal, slow or epileptiform (with or without slow waves). Neurological examination and mental status were coded as normal or abnormal according to clinical judgment. The first AED included carbamazepine, valproate, phenobarbital, phenytoin, vigabatrin, lamotrigine, oxcarbazepine, topiramate and ethosuximide. The AEDs used during the disease course were counted and coded as 1, 2, 3, 4, 5 or more.

A period of remission was defined as two or more years of complete seizure control after the diagnosis of epilepsy.

Early remission was defined as a 2-year remission period started immediately or within the first 2 years after diagnosis of epilepsy with or without relapses.

Late remission was defined as a 2-year remission period achieved at least 2 years after diagnosis of epilepsy with or without relapses.

Sustained remission was defined as a 2-year remission started at any time after diagnosis (early sustained remission or late sustained remission) and persisting until the last follow-up visit (**Remitting course**).

Relapse was the occurrence of seizures after one or more periods of remission (**Relapsing-remitting course** or, if not in remission at last follow-up, **Worsening course**).

Terminal remission was defined as a 2-year remission at the last follow-up visit, with (**Relapsing-remitting course**) or without (**Remitting course**) previous relapses.