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Drug treatment in patients with newly diagnosed unprovoked seizures/epilepsy

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Summary
Purpose: The objective of this study was to analyze drug treatment in patients with newly diagnosed unprovoked seizures/epilepsy in a population-based cohort in Stockholm, Sweden.
Method: Clinical data from the Stockholm Incidence Registry of Epilepsy was cross-linked with drug dispensing data from the Swedish Prescribed Drug Register to analyze drug treatment in patients diagnosed with unprovoked seizures between 2006 and 2008. Specific questions addressed were the use of other medications at seizures onset, the proportion of patients initiated on different antiepileptic drugs (AEDs) within one year after inclusion, and the extent of switching between different AEDs during the first year.
Results: In total 367 patients were included. More than 50% had other medications prescribed at date of first seizure. All together, 262 patients received an AED within one year and 257 patients (98%) were initiated on monotherapy. One year after first prescription, 147 patients (56%) remained on the initially prescribed AED and 48 patients (18%) had switched to another AED. Among the remaining patients, 29 (11%) had died and 38 patients (15%) had discontinued AED treatment.
Conclusions: A majority of all patients with epilepsy receive treatment within one year. Many patients use other medications and several of them are related to known comorbidities and can also be involved in drug—drug interactions. Nevertheless, most patients remained on the same AED at the end of the first year.

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Introduction

Treatment options for patients with epilepsy have increased dramatically with the introduction of several new antiepileptic drugs (AEDs) to the market during the last 20 years (Bialer et al., 2013; Dichter and Brodie, 1996). Simultaneously randomized management studies have assessed different strategies for the treatment of patients with newly diagnosed epilepsy, in particular regarding the pros and cons of early vs. deferred AED treatment (Leone et al., 2006; Marson et al., 2005). These advancements have created opportunities for more rational and individualized treatment strategies in early epilepsy, but also difficulties in selecting among all available options. These challenges in finding the optimal treatment are augmented by comorbidities, concomitant medication, age- and gender specific issues as well as the diversity of the epilepsies. Several different evidence based guidelines have been developed to assist the physician with recommendations for the management of patients with newly diagnosed seizures (Glauser et al., 2013; NICE, 2004; SIGN, 2003).

However, population based data on how patients with newly diagnosed seizures are treated are scarce. The objective of this study was to examine pharmacological treatment of patients with newly diagnosed unprovoked seizures and epilepsy in a defined part of the northern region of Stockholm, Sweden. Specifically, we sought to analyze current use of other prescribed drugs at the time of onset of the seizure disorder, the proportion of patients initiated on different AEDs, and the course of AED treatment during the first year after seizure onset.

Methods

This study utilized the Stockholm Incidence Registry of Epilepsy (SIRE) to identify a study population of patients with newly diagnosed unprovoked seizures or epilepsy. SIRE is a population based registry aiming at including all incident cases with an unprovoked first seizure or epilepsy in Northern Stockholm. Details of the SIRE methodology have been presented before (Adelow et al., 2009). The registry has been operational since September 2001 and has included nearly 2000 patients up to December 2008 with individual information on the date of the index seizure, defined as the first seizure that prompts the patients to seek medical advice. Potential cases have been identified through multiple methods; medical record screening in specific hospital units (including outpatient clinics), networks of health care professionals, emergency room services, and review of requests for electroencephalography (EEG). All information in SIRE is based on information recorded in relevant medical records during the first six months following the index seizure. Potential cases have been validated and classified by the research team of SIRE based on data obtained from the medical charts. Each case included in the present study population has been classified as definite first unprovoked seizure or definite epilepsy (two or more unprovoked seizures up to the six months' time limit from the index seizure). For the present analysis, the date of the index seizure was considered as date of inclusion in the study. We included all validated cases in SIRE who had an index seizure between 1 January 2006 and 31 December 2008 ($n = 398$). Patients who had been dispensed AEDs before the index date were excluded ($n = 31$) leaving 367 patients, our study population for the analysis.

SIRE includes among other things information on patients' age and gender, date of the index seizure, classification of seizure type, and classification of the epilepsy syndrome. Information about drug treatment was obtained from The Swedish Prescribed Drug Register (SPDR) (Wettermark et al., 2007). Established in 2005, this database contains complete data on all drugs dispensed in Sweden regardless of reimbursement status. Included variables are patient's age, and gender, prescribed and dispensed drugs classified according to ATC codes, date of prescribing and of dispensing, and the prescriber's speciality. Individualized data on dispensed prescription drugs was linked to clinical data in our SIRE study population by using the unique personal identity number assigned to each Swedish resident (Ludvigsson et al., 2009).

To assess the use of medications taken at the time of each patient' index seizure, all prescriptions dispensed to patients during 90 days prior the day of the index seizure were identified. According to Swedish reimbursement regulations, the maximum quantity of drugs allowed to be dispensed each time is for 3 months of supply and therefore this period prior to index date was applied to provide a valid estimate of current use of prescribed medications, for chronic as well as short-term treatment.

The day of the first dispensed prescription of an AED after the index seizure was considered as the day of starting treatment. For each patient, the number of days from index seizure to first dispensed prescription of an AED was calculated. The cumulative proportion of patients with a dispensed prescription of an AED within a year after the index seizure was calculated.

A dispensed prescription of an AED during the period 300—420 days after the first prescription of an AED was considered as current use of AEDs one year after treatment initiation. This period of time covers a current use of a prescription. For each patient, the number of days from first dispensed prescription of an AED was calculated, and the latest dispensed AED at 300—420 days was compared to the first AED. Discontinuation of AED treatment was defined as no dispensed prescription of AED during the time period 300—420 days after the first prescription. Switches of AEDs were also analyzed during the same period of time.

Statistical analysis

Standard descriptive statistics, such as numbers and proportions with 95% confidence intervals (CI) were used to describe the study cohort and the utilization pattern of the drugs of interest. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, North Carolina, USA) and Microsoft Excel.

Ethical considerations

The Ethics Committee at Karolinska Institutet, Stockholm, Sweden, approved this study. No individual informed consent was obtained since this is a registry study in which no