Seizure (2005) **14**, 198—206

ELSEVIER

SEIZURE

www.elsevier.com/locate/yseiz

Complaints associated with the use of antiepileptic drugs: results from a community-based study

J.A. Carpay [a,*], A.P. Aldenkamp [b], C.A. van Donselaar [c]

[a] *Department of Neurology, Hospital Gooi-Noord, P.O. Box 900, 1250 CA Laren, The Netherlands*
[b] *Departments of Neurology and Behavioural Science, University Hospital of Maastricht, Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands*
[c] *Rudolf Magnus Institute of Neuroscience, Department of Neurology, Section Epilepsy, University Medical Center Utrecht, Utrecht, The Netherlands*

KEYWORDS
Epilepsy;
Treatment;
Antiepileptic drugs;
Side effects;
Tolerability;
Checklist;
Community

Summary

Background: Few data exist with respect to the occurrence of chronic side effects due to antiepileptic drugs (AED) in routine clinical practice.
Objective: To evaluate the prevalence of subjective complaints which patients with epilepsy regard as side effects of their AED treatment in a community-based population.
Methods: Cross-sectional study. Subjects were identified through the database of AED-use in the pharmacies in a suburban area in The Netherlands. Respondents completed a brief questionnaire about their epilepsy, including a checklist with 30 complaints, which are common in AED users.
Results: We present data of 346 responding adults with treated epilepsy from a population of 107,000 adult inhabitants. Eighty percent was using monotherapy, with few patients taking new AEDs. Almost 60% of the patients reported complaints probably due to side effects in at least three domains. General CNS-related side effects were reported most often; memory problems (21.4% of the patients) and fatigue (20.3%) were dominant. Polytherapy was associated with more side effects than monotherapy. We identified differences in profiles of complaints between valproate, carbamazepine and phenytoin monotherapy. Complaints were not substantially associated with ongoing seizures or other treatment factors.
Conclusions: The majority of patients taking AEDs for epilepsy think they have side effects form their drugs, even when seizures were in remission and when monotherapy was used. Our findings suggest a need to improve monitoring of complaints of side effects of AEDs and to explore the feasibility of interventions aimed at reduction of such complaints in everyday clinical practice.

Abbreviations: AED, antiepileptic drug; CBZ, carbamazepine; CNS, central nervous system; PHT, phenytoin; VPA, valproate

* Corresponding author. Tel.: +31 35 539 1111; fax: +31 35 539 1792.
E-mail address: jcarpay@gooi-noord.nl (J.A. Carpay).

1059-1311/$ — see front matter
doi:10.1016/j.seizure.2005.01.008

Introduction

Antiepileptic drug (AED) treatment aims at controlling seizures without inducing side effects. All AEDs have the potential to cause central nervous system (CNS) dysfunction and other side effects.[1–3] Patients consider avoiding side effects a very important issue in epilepsy treatment.[4] Side effects are also a crucial factor determining the willingness of patients to take drugs at long-term.[5] There is no generally accepted method of assessment for many side effects related to the use of AEDs (such as fatigue or dizziness). Gold standards for quantification of occurrence, severity and tolerability of side effects are seldom available.[2,6] Therefore, the clinician often has to rely in medical decision-making on the patient's subjective reporting.

Most information about the impact of side effects has been obtained from clinical trials. This information may have been biased. In- and exclusion criteria are often stringent. The side effects are those reported in a well-structured environment of a trial, which is distinctly different from normal clinical practice. The monitored side effects are the effects at short-term, given the relatively short duration of clinical trials. Furthermore, physicians may be more alert to detect objective, biological side effects (e.g. rash, weight gain) than subjective side effects.

We embarked on a cross-sectional study, to evaluate complaints associated with the use of AEDs with maximum effort to avoid selection bias. We identified adult AED users in one area through local pharmacy databases. We mailed all identified AED users a questionnaire asking them to confirm that they had epilepsy. We report a cross-section of the respondents' subjective complaints that are probably due to their AED treatment. We had no access to clinical records, hence information with respect to diagnosis and treatment was limited.

Methods

Seventeen of the 18 outpatient pharmacies in the Gooi-Noord region, a suburban area South-East of Amsterdam with approximately 107,000 inhabitants >15 years, co-operated. We identified all pharmacy-clients using AEDs in the pharmacy databases. The only pharmacy which did not participate (due to lack of time) has about 5000 clients. Patients with epilepsy living in institutions, such as nursing homes or homes for mentally retarded were excluded. After identification, the pharmacies mailed a questionnaire to all eligible clients (>15 years of age), with an accompanying letter explaining the purpose of the study and enclosing a prepaid return envelope. Patients who responded remained anonymous to the investigators. A number of articles in local newspapers paid attention to the study, encouraging people to respond. For medical ethical reasons, we sought no further contact with non-responders. The Medical Ethics Commission of the Gooi-Noord Hospital approved the study.

In the questionnaire, the subjects were firstly asked to confirm that they used AEDs for epilepsy, and not for another reason. Subjects without epilepsy or those who were not willing or able to complete the questionnaire were asked to return it without further comment in the prepaid envelope. The questionnaire for respondents with epilepsy focused on information about their epilepsy and included a simple checklist to report side effects of the treatment (see addendum). The responses on the checklist were categorised from 'none', via 'mild' and 'moderate/serious' to 'very serious'.

Specific questions addressed the following issues:

Did you have any (major or minor) seizures in the past 2 years, if so, how many seizures (major and minor rated separately) in the past year?
Do you find your ongoing seizures acceptable, meaning that you don't consider it necessary to do something about them when this was possible?
Have you discussed your epilepsy with a physician in the past 2 years, if so when was the last visit and how many times this last year did you discuss epilepsy with your treating physician? Who prescribes the medication, do you have personal contact with your prescribing doctor or do you receive repeat recipes without further personal contact (e.g. from the doctors secretary)?

From the pharmacy database we received data on age, gender, and AEDs the respondent was using at the time of completing the questionnaire. However, these databases did not provide information about a client's diagnosis. Hence, further information with respect to the validity of the diagnosis, the average duration of epilepsy at the time of the questionnaire and the length of time the patients were treated with the actual drugs, co-morbidity, or classification of epilepsy or seizures was not available. Because we expected that most patients taking AEDs for another reason than epilepsy, would in fact suffer from psychiatric disorders for which AEDs can be indicated, we excluded these patients from our study.

Statistical analysis

Because of the exploratory character of this study, when analysing the responses to the side effects