



Brief Communication

Utilization of antiepileptic drugs in Israel

Erez Berman^a, Eli Marom^a, Dana Ekstein^b, Ilan Blatt^c, Sara Eyal^{d,*}^a Department of Pharmacology, Israel Ministry of Health, Jerusalem, Israel^b Department of Neurology, The Agnes Ginges Center of Neurogenetics, Hadassah-Hebrew University Medical Center, Jerusalem, Israel^c Department of Neurology, Sheba Medical Center, Tel Hashomer and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel^d Institute for Drug Research, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

ARTICLE INFO

Article history:

Received 28 March 2016

Revised 2 May 2016

Accepted 4 May 2016

Available online 23 June 2016

Keywords:

Antiepileptic drugs

Drug utilization

Drug preparations

ABSTRACT

Purpose: The aim of the study was to identify trends in utilization of antiepileptic drugs (AEDs) over time in a nation-wide population in Israel.

Methods: Data on AED utilization (for all indications) for the period 2010–2014 were obtained from pharmaceutical companies that distribute AEDs in Israel. Prevalence of AED utilization was reported as defined daily doses (DDD)/1000 inhabitants/day.

Results: The utilization of most AEDs included in our analysis remained stable over the study period. The greatest increases in utilization of drugs established in Israel were observed for lamotrigine (33%), oxcarbazepine (31%), and primidone (18%). Decreases in use were recorded for carbamazepine (18%) and phenobarbital (15%). Use of older AEDs appeared to be relatively high, compared with the use of newer AEDs.

Conclusions: During the study period of 2010–2014, conventional AEDs remained a main treatment choice in Israel, in certain cases in contrast to current recommendations and guidelines, for reasons yet to be revealed in further research.

© 2016 Elsevier Inc. All rights reserved.

1. Introduction

Antiepileptic drugs (AEDs) are a heterogeneous group of medications with regard to chemical structure, putative mechanism of action, and indications. The rapid expansion in the number and types of AEDs over the past decades has been accompanied by shifts in their utilization worldwide [1–8]. Although the settings, type of information collected, and time period varied among studies, they largely demonstrated increased use of AEDs over time. Multiple factors accounted for these changes, among which the most consistent was availability of new AEDs and their use for the treatment of conditions other than epilepsy [1,2,6–8]. Indeed, most AEDs were developed to treat epilepsy, and their therapeutic activity in other disorders was discovered later [9,10]. Yet, in recent years, more people seem to use some AEDs for other indications besides to epilepsy, including migraine headache, chronic neuropathic pain, and mood disorders. For example, in 2003, neurologists in the United States reported that almost half of their AED prescriptions were for conditions other than epilepsy. This percent was even higher (63%) among primary care physicians [10]. In a

nationwide population-based study in Germany, only 36% of AED users had epilepsy [2].

Studies on AED utilization are important for yielding markers for crude estimates of disease prevalence and providing the basis for risk estimates and pharmacovigilance. This can be exemplified by the use of AED sales data as the denominator for comparing risk for adverse reactions related to individual AEDs [5]. In Israel, data on prescription of medications are seldom available on a population level, with few exceptions [11–13]. Information on nationwide AED consumption can be mostly obtained through analysis of sales data. Although this kind of information is not linked to diagnoses and cannot be used to study medication use by subpopulations, it reflects nationwide drug utilization across all sections. In this study, we used sales data, provided for older and newer AEDs, to evaluate trends of AED consumption in Israel.

2. Methods

We examined temporal changes in AED use from 2010 to 2014. The data were collected with collaboration of the pharmaceutical companies by receiving the numbers of milligrams per active ingredient dispensed each year to the community. The data were divided by the defined daily dose (DDD), which is the average maintenance dosage as defined by the World Health Organization Collaborating Center for Drug Statistics for the drug's main indication in adults [14]. Defined daily doses are based on the Anatomical Therapeutic Chemical (ATC) classification index [15]. The collected data were plotted into graphs of DDDs per

* Corresponding author at: Institute for Drug Research, Room 613, School of Pharmacy, The Hebrew University, Ein Kerem, Jerusalem 91120, Israel. Tel.: +972 2 675 8667; fax: +972 2 675 7246.

E-mail addresses: erezberm@post.bgu.ac.il (E. Berman), ELI.MAROM@MOH.GOV.IL (E. Marom), dekstein@hadassah.org.il (D. Ekstein), Ilan.Blatt@sheba.health.gov.il (I. Blatt), sarae@ekmd.huji.ac.il (S. Eyal).

1000 inhabitants per day. Total population figures for each year were obtained from the Israeli Central Bureau of Statistics [16]. Upon distributors' request, no data on the sales of certain specific products could be presented. Therefore, the data of each active compound were presented as combined sales of all preparations and those of brand versus generic preparations as combined sales of several AEDs.

We considered all drugs listed under the ATC code N03 (antiepileptics) that were licensed for the treatment of epilepsy in Israel in 2010–2014. Antiepileptic drugs were classified into two groups: older AEDs (introduced before 1992), including carbamazepine, clonazepam, phenobarbital, phenytoin, primidone, and valproic acid; and newer AEDs, including gabapentin, lamotrigine, levetiracetam, oxcarbazepine, perampanel, retigabine (ezogabine), rufinamide, topiramate, and vigabatrin. Pregabalin and clobazam (not registered in Israel for the treatment of epilepsy), zonisamide, felbamate, and stiripentol (not registered in Israel) were excluded. We also excluded diazepam and midazolam because they are mostly used for the treatment of status epilepticus or prolonged seizures. Sales data were not available from all distributors of valproic acid, topiramate, and levetiracetam. No sales information was obtained for lacosamide. Descriptive statistics were tabulated.

3. Results

Utilization of most AEDs, both older and newer, appeared stable over the study period. The incomplete data did not allow us to estimate the total AED utilization in Israel or the proportion of newer versus older drugs. Nevertheless, some trends could be identified. The greatest increases in utilization of drugs which had been established in Israel before 2010 were observed for lamotrigine (33%), oxcarbazepine (31%), and primidone (18% increase). Increases were also observed with regard to valproic acid, an AED for which complete data were not available (Fig. 1). Decreases in use were recorded for carbamazepine (18%) and phenobarbital (15%). Perampanel, retigabine, rufinamide, and vigabatrin had values below 0.05 DDD/1000 inhabitants/day. Retigabine was added to the Israeli pharmaceutical basket only in 2013, and its sales fell from 0.004 DDD/1000 inhabitants/day during that year to 0.002 DDD/1000 inhabitants/day in 2014, after the publication in April 2013 of the FDA alert regarding blue skin discoloration and retinal pigmentation associated with the use of this drug [17].

The proportion of generic substitutions of carbamazepine, lamotrigine, and oxcarbazepine, combined, did not change throughout the study period, consisting two-thirds of total sales of these AEDs (Fig. 2). However, this represents three trends that offset each other:

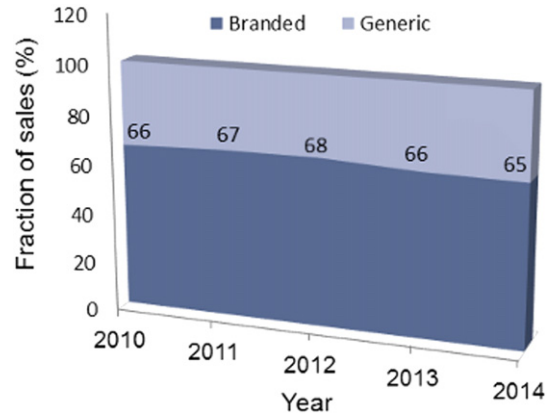


Fig. 2. Contribution of generic products to the total sales of carbamazepine, oxcarbazepine, and lamotrigine. Calculation took into account the proportion of individual AEDs in total sales.

the proportion of generic carbamazepine and oxcarbazepine declined with time, whereas that of lamotrigine increased.

4. Discussion

During the 5-year period under study, the overall consumption of AED preparations included in our analysis remained stable, in contrast to reports from other countries which indicated increases in AED use over time [1,4,6,7]. However, direct comparison is impossible because our data were incomplete, and because of the different methodologies, study periods, population age structure (different proportions of pediatric and geriatric patients for whom certain AEDs are preferred), and reimbursement systems in different countries. Yet, some similarities and differences with regard to trends in other countries could be identified. In previous studies, growth in AED consumption was attributed mostly to increased use of newer AEDs [2,4,6–8]. Indeed, we found increased sales of lamotrigine and oxcarbazepine. Gabapentin sales appeared to increase only marginally, despite its broad use for alleviation of neuro-pathic pain.

The sales of three older AEDs, namely carbamazepine, clonazepam and phenytoin, were comparable with those of lamotrigine, and larger than those of any other new AED for which data were complete (Fig. 1). Previously, Johannessen Landmark et al. demonstrated that the most commonly used AED in epilepsy in Norway was carbamazepine, followed by lamotrigine and valproic acid, and there has been a trend towards decreased use of carbamazepine [6]. Although data

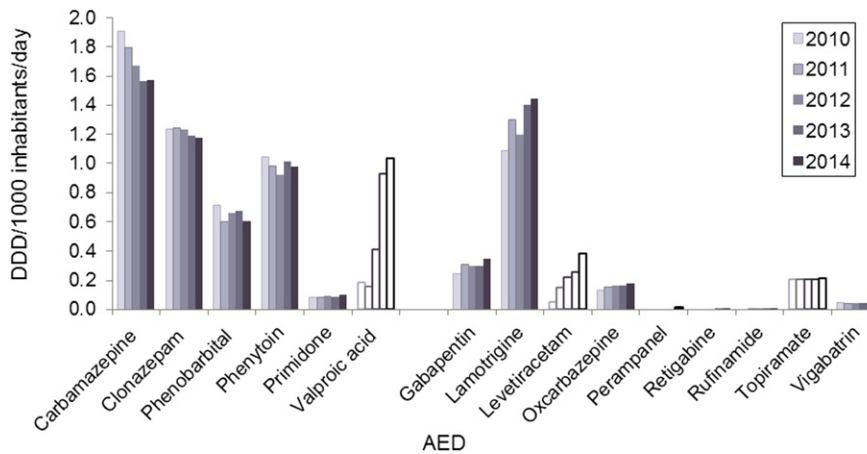


Fig. 1. Sales of individual AEDs over the study period. Old AEDs are located at the left. AEDs for which data were not obtained for all preparations are indicated by open bars. The following DDDs (in grams) were used: carbamazepine, 1.0; clonazepam, 0.008; phenobarbital, 0.1; phenytoin, 0.3; primidone, 1.25; valproic acid, 1.5; gabapentin, 1.8; lamotrigine, 0.3; levetiracetam, 1.5; oxcarbazepine, 1.0; perampanel, 0.008; retigabine, 0.6; rufinamide, 1.4; topiramate, 0.3; and vigabatrin, 2.0.

Download English Version:

<https://daneshyari.com/en/article/6010050>

Download Persian Version:

<https://daneshyari.com/article/6010050>

[Daneshyari.com](https://daneshyari.com)