**BRIEF COMMUNICATION OF ASSESSMENT OF CLINICAL PRACTICE
REGARDING PHARMACOLOGICAL TREATMENT OF EPILEPSY: A SURVEY
OF NEUROLOGISTS IN REPUBLIC OF MACEDONIA****Emilija Cvetkovska¹, Igor Kuzmanovski¹, Bojan Boshkovski²**¹ University Neurology Clinic, Medical Faculty, Ss Cyril and Methodius University, 1000 Skopje, R. Macedonia² 8th September City General Hospital, Skopje, R. Macedonia

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Abstract

A questionnaire of 15 items was developed in order to evaluate clinical practice regarding pharmacological treatment of epilepsy among adult neurologists in R. Macedonia. It was mailed to 30 practising neurologists, 24 answered (80%). Half of them administer AED after a first unprovoked seizure considering EEG and MRI, while others usually wait for a second one before introducing treatment. Discontinuation of treatment should be individualized. Carbamazepine and lamotrigine are the most frequently prescribed first-line drugs for partial seizures; second choices include a number of older and new generation AEDs. For generalized tonic-clonic seizures, absences, myoclonic, mixed or undetermined seizures, valproate is by far the most commonly used AED. The survey showed that prescription patterns are in accordance with current evidence about the spectrum of efficacy of individual AEDs in different types of seizures. Yet some results are a cause of concern and continuous education of the neurological community on AED treatment of epilepsy is needed.

Key words: neurologist, survey, epilepsy, pharmacological treatment, antiepileptic drugs.

Introduction

The ILAE/IBE/WHO report on epilepsy in Europe, launched 2010, identifies a series of problems and challenges in appropriate care for people with epilepsy, one of the most important being that professionals involved in the treatment of patients with epilepsy sometimes do not have sufficient specialized knowledge of the condition [1]. A survey initiated from the Commission on European Affairs assessing the provision of epilepsy care in Europe identified insufficient professional education and knowledge about epilepsy as crucial all across Europe [2]. Specialization of a medical doctor as a neurologist in a field as specific as epileptology and the expertise that is required to deal with

other than the most straightforward cases is very often lacking [1].

The aim of the study was to evaluate clinical practice toward pharmacological treatment of epilepsy among adult neurologists in R. Macedonia.

Methods

A 15-item questionnaire was developed covering initiation and termination of antiepileptic drug (AED) therapy, preferable drugs used as first-line and alternative choice in different types of seizures (partial seizures in young and older adult, GTCS, myoclonic seizures, absences, multiple types or undetermined type of seizures) as well as minimal and maximal do-

ses for each drug used. For initiation of AED therapy after the first unprovoked seizure several possibilities were offered: 1. No, one seizure is not epilepsy, waiting for a second seizure; 2. Yes, considering EEG, MRI and other investigations; 3. Only if it is GTCS; 4. Yes, every seizure is potentially dangerous for the patient. Discontinuation of AED included: 1. Individualized (considering syndrome, etiology);

2. After 1 to 2 years without seizures; 3. After 3 to 5 years without seizures; 4. After a more than 5 years seizure-free period; 5. Never.

Usually used first-line and alternatives if the first is not effective or not tolerable in the type of seizure; all available AEDs were listed (Table 1). The questionnaire was mailed to 30 adult neurologists in three different hospitals in R. Macedonia.

Table 1

*Available antiepileptic drugs (AED), mode of prescription, range of minimal and maximal daily doses and mean daily minimal and maximal dose**

AED	Mode of prescription**	Minimal daily dose mg/day	Mean minimal daily dose mg/day	Maximal daily dose mg/day	Mean maximal daily dose mg/day
Carbamazepine	EDL	200 - 400	300	1200 - 1600	1400
Valproic acid	EDL	300 - 500	350	950 - 2500	1700
Lamotrigine	EDL	25 - 50	45	150 - 500	350
Topiramate	EDL	25 - 100	55	150 - 400	350
Oxcarbazepine	SP	300 - 600	450	1200 - 2400	1700
Levetiracetam	SP	250 - 1000	750	1250 - 3000	2300
Ethosuximide	EDL	250 - 500	350	750 - 1500	1000
Clonazepam	EDL	0,5 - 1,5	1	6 - 8	6,5
Phenobarbiton	EDL	50 - 100	75	100 - 200	150
Diazepam	EDL				
Gabapentin	not in EDL	300 - 900	500	900 - 3600	1600
Pregabalin	not in EDL				

* Question about doses was not completely answered in half of questionnaires.

** Essential drug list (EDL), Special prescription (SP) fully reimbursed only for refractory epilepsy.

Results

Answers were obtained from 24 neurologists, a response rate of 80%. Half of the neurologists would administer AED after a first unprovoked seizure considering EEG, MRI and other investigations, while others usually wait for a second seizure before introducing treatment.

According to most of the neurologists, discontinuation of the treatment should be individualized, taking account of the syndrome and its etiology (58%), some would do this after a seizure-free period of 3–5 years (21%) or a seizure-free period of more than 5 years (21%).

The most commonly prescribed AEDs in partial epilepsy were carbamazepine and lamotrigine, followed by topiramate, valproate, levetiracetam and oxcarbazepine (Figure 1). By contrast, valproic acid was the most frequently prescribed AED in generalized tonic-clonic sei-

zures and in undetermined or mixed types of seizures. The second most prescribed AED and usual second choice if valproate was inadequate was lamotrigine, followed by a wide range of other AEDs: carbamazepine, topiramate, levetiracetam, phenobarbital, even diazepam (Figure 1). The utilization pattern of AEDs in myoclonic seizures was to some extent similar: valproate dominated, lamotrigine followed, and then topiramate and clonazepam in decreasing order (Figure 1). In absences valproate was also prescribed by far the most; other AEDs included ethosuximide, lamotrigine, and surprisingly carbamazepine and oxcarbazepine in some percentage (Figure 1).

The mean of minimal and maximal prescribed daily dosages of individual AEDs are shown in Table 1.

Figure 1 – Pattern of utilization of AED in different type of seizures among adult neurologists in R. Macedonia*

Discussion

Initiation and termination of antiepileptic treatment should be individualized according to the majority of answers, which is in keeping with existing evidence [3, 4, 5, 6, 7]. The results of our survey indicate that patterns of AED utilization follow the current recommendations regarding seizure type [8, 9, 10, 11]. Carbamazepine, lamotrigine and topiramate dominated in the prescription pattern for partial epilepsies, which is consistent with evidence that these agents are particularly useful in the treatment of partial seizures [8, 9, 10]. Among patients with generalized and in mixed and/or undetermined seizures, the ranking of the most frequently prescribed AEDs was comparable with current recommendations, except for a lower utilization of levetiracetam [12, 13, 14]. Valproate dominated, which could be expected in view of its broad spectrum of activity against all seizure types [15] and references it that should remain the drug of first choice for many patients with generalized and unclassified epilepsies [16]. Overall, second generation AEDs were quite widely prescribed, lamotrigine and topiramate were extensively used; lower exploitation of levetiracetam is due to its special prescription (fully reimbursed only for refractory epilepsy).

Surprisingly, carbamazepine and oxcarbazepine were considered to some extent as treatment options for absences; both being narrow-spectrum AEDs which appear to be the major causes of seizure aggravation in absence epilepsies [17, 18, 19]. The explanation might be that adult neurologists relatively rarely deal with absence seizures and are quite unfamiliar with their treatment.

Mean minimal and mean maximal doses for prescribed drugs tend to be lower and a small number would administer maximal tolerated doses.

Although the study has limitations (sex differences in the prescription pattern were not examined), it gives substantial information about the pattern of pharmacotherapy with AEDs.

In conclusion, utilization of individual AEDs was mostly in accordance with international guidelines and recommendations. However, some data indicate that additional education is needed and increasingly important for improvement of the pharmacological therapy of epilepsy.

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