Review Article

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Epilepsy: Is there hope?

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Epilepsy is a highly prevalent chronic neurologic disorder and leads to social, behavioural, health and economic consequences. 'Treatment gap' varies from 10 per cent in developed countries to 75 per cent in low-income countries. Stigma and discrimination related to epilepsy are prevalent worldwide. Electroencephalography (EEG) is considered the most important tool for evaluating the patient with epilepsy. Video-EEG monitoring is an important tool for confirming the seizure type and estimating the epileptogenic zone in the brain. Neuroimaging evaluation is important to determine the aetiology of the epilepsies. Genetic testing has increased the probability of identifying the causes of some types of epilepsies. Epilepsy can be treated in an affordable way with low-cost medications. Refractory epilepsies occur in approximately one-third of recently diagnosed patients with epilepsy. For this group of patients, there are options of surgical treatment, diets and neurostimulation to improve seizure control and quality of life. In poorly organized societies, there is a lack of prioritization of epilepsy in national health policies, limited resources for trained personnel and a shortage of basic antiepileptic medications. There is evidence of improvement in the understanding of epilepsy and a clear progress in the management of epileptic seizures in recent times.

Key words Epilepsy - epileptic seizure - epilepsy treatment

Epilepsy is a chronic neurological disorder characterized by repeated seizures (> 24 h apart); by one seizure with a strong potential for recurrence (at least 60%) or diagnosis of an epilepsy syndrome[1]. It affects people of all ages and results in social, behavioural, health and economic consequences to the patients and their families. It is estimated that more than 50 million people worldwide are affected[2]. Eighty per cent of people with epilepsy live in low- to medium-income countries.

The vast majority of the patients with epilepsy, with adequate treatment, are able to live a normal life. However, some patients have serious comorbidities such as psychiatric disorders and mental retardation. Epilepsy is responsible for 0.3 per cent of all deaths worldwide according to the Global Burden of Disease Study, by the World Health Organization, the World Bank and the Harvard School of Public Health supported by the Bill and Melinda Gates Foundation[3].

The 'treatment gap' (the proportion of people with epilepsy who require treatment, but either do not receive or receive inadequate treatment) varies from 10 per cent in developed countries to 75 per cent in low-income countries[4]. To illustrate the prevalence of epilepsy, data from Latin America (Brazil) and Asia (India) show a prevalence of 9.2 (lifetime), 5.4 (active) and 4.19 (lifetime) and 3.91

(active) per 1000 population respectively[5,6]. Stigma and discrimination related to epilepsy are extremely prevalent worldwide[7].

Electroencephalography (EEG) is considered the most important tool for evaluating the patient with epilepsy. When abnormal, it may contribute to the seizure classification, either focal or generalized and it also may characterize the epilepsy syndrome presented by the patient. This possibility allows a prognostic view in most cases in relation to seizure control and also may lead to better treatment choices. Video-EEG monitoring is an important tool for confirming the seizure type and estimating the epileptogenic zone in the brain, particularly when neuroimaging is normal, and surgery is being considered[8].

Computerized tomography (CT) scans are useful in emergent conditions, but focal lesions are detected in only 30 per cent of patients[9].

The use of magnetic resonance imaging (MRI) in the investigation of focal epilepsies requires specific protocols based on the region of onset in clinical and EEG findings. The first reason to investigate with MRI is to find the aetiology of epilepsy, and second, to allow a presurgical evaluation when possible. There are MRI epilepsy protocols to be considered as well as post-processing reconstructions. An MRI adds an extraordinary contribution to diagnosis and management of the main focal epilepsies: mesial temporal lobe epilepsy, low-grade tumours such as gangliogliomas, oligodendrogliomas and dysembryoplastic neuroepithelial tumours, malformations of cortical development such as focal cortical dysplasias, tuberous sclerosis, inflammations such as Rasmussen encephalitis and other lesions[10].

Functional imaging studies such as positron emission tomography (PET) and single photon emission CT (SPECT) can help to identify and confirm the ictal focus to facilitate surgical intervention for refractory focal epilepsies[11].

Genetic testing has increased the probability of identifying the causes of some types of epilepsies. This is a complex task and requires some expertise in its clinical application. Genetic testing modalities are chromosomal microarray analysis, karyotyping, single-gene testing, gene panel testing, whole exome sequencing and whole genome sequencing. If used with wisdom, it can contribute to the clinical diagnosis and management with practical interventions[12]. Advances in molecular genetics have led to the identification of several genes for childhood epileptic encephalopathies with phenotype-genotype correlations[13]. Limitations of genetic testing are the lack of availability and relatively high cost. Clinicians should always be aware of the ethical, legal and social consequences of genetic testing[14].

Epilepsy can be treated in an affordable way with low-cost medication such as the traditional antiepileptic drugs: carbamazepine, phenobarbital, phenytoin, valproic acid and benzodiazepines. Most new drugs add more tolerability than efficacy to the medical treatment of these patients. As such, these can sometimes decisively influence the outcome with better compliance, leading to a seizure-free condition[15]. Refractory epilepsies occur in approximately one-third of recently diagnosed patients with epilepsy[16]. The International League Against Epilepsy (ILAE) defines a refractory epilepsy patient as one who does not respond to two adequate medical treatments[17]. For this group of patients, there are options of surgical treatment, diets and neurostimulation to improve seizure control and quality of life[18]. Currently, the best surgical indications are well defined for the treatment of focal epilepsies, with the best outcome for mesial temporal lobe epilepsy, focal lesions such as tumours, arteriovenous malformations and malformation of cortical development, amongst others[18,19].

The ketogenic diet has been used for refractory epilepsy for many years. Recently, there have been new versions of diets with better compliance and tolerability[20]. These have been used in children with severe epileptic syndromes with relatively good results[21,].

Another palliative procedure that can be used is electrical stimulation for the treatment of refractory epilepsy. There is evidence of the usefulness of vagus nerve stimulation for this population[22]. Recent studies using different technologies suggest that intracerebral stimulation of the anterior thalamic nucleus and the NeuroPace Responsive Neurostimulator can also reduce seizure frequency and improve the quality of life in patients with refractory epilepsies[23,24].

Despite the advances in the evaluation and treatment of refractory epilepsy in developed societies, basic steps in social, economic and political issues can eventually improve the epilepsy perspective for less privileged societies. We are optimistic as there are many modifiable factors that can be implemented. For example, in low income societies, general preventive measures can help decrease the incidence of epilepsy due to: (*i*) improvement of sanitary conditions, which

may decrease infectious endemic diseases such as neurocysticercosis; (*ii*) decrease in the occurrence of brain trauma due to motor vehicle accidents; and (*iii*) improvement in maternal and perinatal assistance. These basic actions may decrease the incidence of epilepsy in the general population.

Political issues also need to be considered. In poorly organized societies, there is a lack of prioritization of epilepsy in national health policies, limited resources for trained personnel and a shortage of basic antiepileptic medications.

In middle-income countries, the creation of comprehensive centres for surgical programmes is increasing, to improve referral for surgical treatment. In 1994, the Brazilian government started an epilepsy programme for surgery, and this is still serving the population. This has had an important impact on the scientific development in epilepsy, training of experts and assistance for patients[25].

To answer the initial question: is there hope? Yes, taking into account the socio-economic perspective of the considered society, there is evidence of improvement in the understanding of epilepsy and a clear improvement in the management of epileptic seizures.

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