Seminar in Epileptology

Epileptic Disord 2015; 17 (1): 13-18

Management of epilepsy in resource-limited settings

Roberto Caraballo, Natalio Fejerman

Neurology Department, Hospital de Pediatría JP Garrahan, Buenos Aires, Argentina

Received April 22, 2014; Accepted October 08, 2014

ABSTRACT – Epilepsy is one of the most common and widespread neurological disorders affecting over 65 million people worldwide. Although estimates vary considerably, the annual incidence is considered to be almost 50 per 100,000 and prevalence around 700 per 100,000. It is thought, however, that more people are affected in low- and middle-income countries where resources to improve the care for people with epilepsy are limited. Of all people with epilepsy, around 80% live in resource-limited countries and up to 90% of these patients receive no treatment at all. National epilepsy programs to organize comprehensive care and cover educational, economic, and research aspects are necessary. A referral network will enable local healthcare workers to consult patients with more complex diseases and may ensure routine availability of inexpensive AEDs. Adequately identifying people with epilepsy and delivering cost-effective care in resource-limited countries is an important challenge for epileptologists and healthcare policy makers alike. Here we give an overview of the present situation and review the needs and the efforts currently being made in the field.

Key words: education programs, epilepsy, resource-limited countries, treatment gap

Epilepsy is one of the most common and widespread neurological disorders affecting over 65 million people worldwide (Thurman *et al.,* 2011). Although estimates vary considerably (Yemadje *et al.,* 2011), the annual incidence is considered to be almost 50 per 100,000 and prevalence around 700 per 100,000 (Thurman *et al.,* 2011). It is thought, however, that more people are affected in low- and middle income countries where resources to improve the care for people with epilepsy are limited. The World Health Organization (WHO) estimates that 80% of people with epilepsy live in resource-limited countries (WHO, 2005). Up to 90% of patients in the poorest countries receive no treatment at all (Scott *et al.,* 2001; WHO, 2011). In a study on epilepsy in developing countries, it was found that the prevalence of epilepsy is similar to that in developed countries, while incidence is much higher, ranging from 92.7 to 190 per 100,000, probably related to increased risk factors, such as poor perinatal care, a higher frequency of head injury, and a high prevalence of infectious and parasitic diseases in poor countries (Carpio and Hauser, 2009).

Correspondence:
Roberto Caraballo
Neurología. Hospital de Pediatría JP Garrahan,
Combate de los Pozos 1881. CP 1245,
Buenos Aires, Argentina
<rhcaraballo@arnet.com.ar>

doi:10.1684/epd.2014.0721

The management of people with epilepsy in resource-limited countries is an important challenge for epileptologists and healthcare policy makers alike.

Background

In resource-limited countries, mainly located within Latin America, sub-Saharan Africa, and South-East Asia, epidemiological and clinical characteristics of epilepsy and the treatment gap, *i.e.* the difference between the number of people with active epilepsy and the number of patients whose seizures are being appropriately treated (Meinardi *et al.,* 2001), differ greatly by region. Whereas in certain areas, especially in the large cities, epilepsy care may be comparable to that of major North-American and European cities, people living in remote rural areas often do not receive any medical care as referral services are scarce (de Bittencourt *et al.,* 1996). In spite of this heterogeneity, however, resource-limited countries share many features that make them unprepared to deal with the medical, social, and economic burden of epilepsy (Radhakrishnan, 2009).

A wide variation of the treatment gap has been reported. This is probably due to a high degree of heterogeneity and inconsistency in definitions between studies. In a systematic review of the literature, the overall estimate of the treatment gap was 56% (Mbuba *et al.,* 2008). The treatment gap is reported to be influenced by shortage of trained professionals, cost of treatment and lack of access to antiepileptic drugs (AEDs), cultural beliefs and stigma, traditional treatment, and distance to health facilities (Meinardi *et al.*, 2001; Mbuba *et al.,* 2008).

The most common causes of epilepsy in resource-limited countries, especially in the tropical regions, are infectious and parasitic diseases (neurocysticercosis, HIV infection, meningitis, cerebral malaria, and toxocariasis), perinatal brain damage, vascular diseases, and head trauma, which are all preventable (de Bittencourt *et al.*, 1996; WHO, 2005; Yemadje *et al.,* 2011). In addition, toxic agents, mainly lead and pesticides, as well as genetic factors (consanguineous marriages being relatively common) are frequent causes of epilepsy (WHO, 2004; Mac *et al.,* 2007). Malnutrition, to which many children in very low-income countries are exposed, may also be associated with increased risk of epilepsy (WHO, 2004; Birbeck, 2010).

Poverty and lack of education are important problems. In resource-limited countries, a large part of the population lives in rural areas or the suburbs of large cities in poor conditions, characterized by overcrowding, poor water supply, and bad sanitation, contributing to a higher risk of brain infections (WHO, 2004; De Boer *et al.,* 2008; PAHO, 2011). Not only the general public, but even physicians are sometimes unaware of epilepsy. Morbidity and mortality are increased because of the failure to identify cases, difficulties with infrastructure, and the unavailability of adequate AEDs. In resource-limited countries, people with epilepsy who were diagnosed and put on AED treatment often discontinue the treatment because they cannot afford the drugs or are unaware of the consequences of non-compliance with the drug regimen (Radhakrishnan, 2009). The median cost of first-line AEDs is variable across regions and is generally higher in resource-limited countries than in the developed world (WHO, 2005; Mac *et al.,* 2007; Radhakrishnan, 2009).

The stigma associated with having epilepsy severely affects the life of people with epilepsy living in developing countries. In many countries, the disease is traditionally considered to be caused by ancestral spirits or attributed to possession by evil spirits (WHO, 2004). Cultural beliefs about the contagious nature of epilepsy are widespread. The breath, blood, sperm, and genital secretion of people with epilepsy are often believed to transmit the disease leading to social exclusion of people with epilepsy and hesitation to help or touch the person who is having a seizure (Scott *et al.*, 2001; WHO, 2004, 2005). The stigma associated with epilepsy also greatly affects the education of children and young people, and the possibility to find work for adults. People with epilepsy often have problems finding a partner (De Boer *et al.*, 2008) and in some South-East Asian countries, there were even laws preventing marriage for people with epilepsy (Meinardi *et al.*, 2001). Patients and their families frequently prefer not to reveal their condition, leading to further isolation and less possibilities of access to adequate treatment (WHO, 2005). In some cultures, women with epilepsy may be particularly vulnerable to accidental and intentional injury, social rejection by the family and community, and abandonment (Birbeck *et al.*, 2008, Birbeck, 2010).

Due to the limited access to conventional health systems and low levels of literacy and knowledge, people with epilepsy living in remote rural areas or in indigenous communities often first consult faith or traditional healers and follow their recommendations for long periods of time (WHO, 2004). There is a great lack of even primary healthcare centres and qualified medical doctors, and available healthcare personnel often have little knowledge of how to diagnose and treat epilepsy.

Resources

In resource-limited countries, epilepsy is not recognized as a public health priority. Budgets for healthcare

are low and resources are generally directed toward infectious diseases, such as HIV/AIDS, malaria, and tuberculosis (Meinardi *et al.,* 2001; Scott *et al.,* 2001). There are great differences between public healthcare and the private sector.

As the number of neurologists is very low in many resource-limited countries, especially in South-East Asia and sub-Saharan Africa, epilepsy care is often managed by primary-care physicians. There is great difficulty in diagnosing people with severe and refractory epilepsy. Diagnostic studies are important for the appropriate management of people with epilepsy, however, whereas electroencephalography (EEG) and computerized axial tomography (CT) are generally available, equipment for electroencephalographic video monitoring and magnetic resonance imaging (MRI) is scarce and usually concentrated in the private sector and only in major cities, and therefore unaffordable and/or inaccessible to the majority of the population (WHO, 2004, 2005; PAHO, 2011). An additional problem in very-low-income countries is that this equipment is very often badly maintained or out of order (WHO, 2004; Mac *et al.,* 2007). When available in the public sector, waiting times for all these studies may be extremely long. Thus, physicians frequently have to make the diagnosis of epilepsy based solely on clinical data.

In the majority of resource-limited countries, the four most commonly used AEDs (phenobarbital, phenytoin, carbamazepine, and valproic acid) are available, but mostly at the secondary and tertiary levels of care, and the supply of these drugs is not always steady (WHO, 2004; Kwan and Brodie, 2004). Newer AEDs, including lamotrigine, gabapentin, oxcarbazepine, levetiracetam, and topiramate, are currently being used in both the public and the private sector in some countries, but are typically neither affordable nor available for the majority of patients (WHO, 2005). Phenobarbital is the least expensive and most widely used AED. In 1990, the WHO determined that the average cost of phenobarbital could be as low as US$ 5 per patient per year (PAHO, 2011).

Surgery for refractory epilepsy can be cost beneficial, however, because of the high level of expertise and sophisticated technology required, epilepsy surgery is largely out of reach for most people in resource-limited countries. Nevertheless, epilepsy surgery is increasingly being performed in some Latin American and South-East Asian countries (WHO, 2004, 2005; PAHO, 2011).

Vagus nerve stimulation, because of its high cost, and the ketogenic diet, because of the need for strict adherence to a diet, are not widely available or feasible in most resource-limited countries. Vagus nerve stimulation is currently being used in some Latin American countries. The ketogenic diet, however, is starting to be used in neurology departments all over the world, adapted to local diets (Caraballo and Fejerman, 2009; Cersósimo *et al.,* 2011; Kossoff *et al.,* 2012).

Approach to a solution

Policies to improve care for people with epilepsy should be tailored to the situation in each country based on epidemiological data, local resources, local beliefs, behaviours, and cultural practices. Already, several studies have assessed the treatment gap and possible interventions to bridge it (Noronha *et al.,* 2004; Mbuba *et al.,* 2008; Hu *et al.,* 2014). Before intervention strategies may be planned in each country, well-designed epidemiological studies should be conducted which are necessary to identify health priorities and other education and service needs. Recently, the ILAE Commission on Epidemiology has published standards for epidemiological studies and surveillance of epilepsy in an important effort to provide consistency in definitions and methods, in order to enhance future population-based epidemiological studies (Thurman *et al.,* 2011).

Epilepsy legislation, based on internationally-accepted human rights standards, is important to protect the people with epilepsy from discrimination and enhance their autonomy. Laws promote equal access to healthcare services and community integration. Legislation is also a useful framework to support the implementation of policies and programs related to epilepsy (De Boer *et al.,* 2008).

National epilepsy programs that could organize comprehensive care throughout a country and cover educational, economic, and research aspects are needed. However, countries either lack intervention protocols or have protocols that are not up-to-date (WHO, 2005). National epilepsy programs should develop local epilepsy care at a primary care level, but closely integrated with specialist epilepsy departments, to identify people with epilepsy and guarantee access to AEDs and other basic needs. However, neurologists specialized in epilepsy are few in the majority of resource-limited countries (Diop *et al.,* 2003; WHO, 2005; Mac *et al.,* 2007; PAHO, 2013). Specialist training in epileptology is currently possible only in very few countries (WHO, 2005) and young neurologists should be sent to specialized centres in the developed world for further training. In such a setting, the most effective role for a neurologist to assume is the role of educator, advisor, and advocate (Birbeck, 2010). By training primary care physicians and health workers to diagnose and treat patients with epilepsy, it becomes feasible to reach as many patients as possible and sustain the process in time. Local communities should also be involved in the planning and implementation of this process (Scott *et al.*, 2001; Radhakrishnan, 2009). On the other hand, a well-organized referral network will enable local healthcare workers to consult patients with more complex diseases and may ensure routine availability of inexpensive AEDs (Radhakrishnan, 2009; Birbeck, 2010).

Epilepsy often has preventable causes, such as infections and perinatal brain damage, and in resource-limited countries, epilepsy programs should be linked to national primary-healthcare programs, such as those concerned with sanitation, safe water, nutrition, and mother-and-child health for a more efficient use of the health budget (WHO, 2004; Scott *et al.*, 2001).

A first step towards better drug availability would be to include the basic four AEDs (phenobarbital, phenytoin, carbamazepine, and valproic acid) in the list of essential drugs in these countries. Even though the use of phenobarbital is controversial because of possible deleterious cognitive and behavioural side effects, it remains the drug of choice in resource-limited countries because of its low cost. An additional advantage of the drug is its long half-life that may protect against the occurrence of withdrawal seizures if intake is abruptly stopped because of interrupted supply, something that is not uncommon in many regions (Kwan and Brodie, 2004). In a large study conducted in China, Wang *et al.* found that phenobarbital seems to be efficacious and well tolerated when used in resource-poor areas. The study confirmed that in this setting, the phenobarbital treatment protocol is feasible, that phenobarbital has good efficacy and tolerability, and that it can help to reduce the large treatment gap. Additionally, they found that adverse effects became less severe or disappeared as time went on (Wang *et al.*, 2006).

For the management of ictal events and status epilepticus, the basic therapeutic protocol, including intravenous benzodiazepam, lorazepam, phenytoin, and phenobarbital, should be made available. The use of rectal diazepam by the parent or caregiver is an option to manage acute situations, and the use of IV valproic acid should be gradually incorporated into the protocol for status epilepticus. However, new IV antiepileptic drugs, such as levetiracetam and lacosamide, are not readily available in poor countries. It should be included in the protocol that pyridoxine be administered to all patients less than 2 years of age with refractory seizures with unknown aetiology. In non-responders, pyridoxal phosphate and folinic acid should also be considered, however, these latter drugs may not be easy to obtain in these settings.

The ketogenic diet may be an excellent option for the treatment of some kinds of epilepsy, especially because it can be adapted and modified to fit the local gastronomy, making it cheaper and more comfortable to use (Caraballo *et al.*, 2011).

In resource-limited countries, traditional healers are often more numerous and more affordable than physicians and they play an important role in the management of epilepsy. Although they may sometimes use practices that are harmful to the patient, they generally are important and respected members of the community. Training them to provide basic epilepsy care, correcting harmful practices, and developing productive collaborative working relationships that encourage the referral of people with active epilepsy may be useful for people living in remote areas that are difficult to reach with conventional health care (Diop *et al.*, 2003; WHO, 2004; Birbeck, 2010).

The stigma associated with epilepsy could be diminished through a national epilepsy awareness campaign for the general public. Nurses, community health workers, and community leaders, such as teachers and priests, can help identify people with epilepsy. They are reached through community-based epilepsy education programs.

People with poorly controlled seizures often have severe social problems, such as fewer social contacts, friends, and leisure activities. Special social rehabilitation programs are useful to help patients lead a more independent life and to reduce psychosocial disabilities. In resource-limited countries, few of such social rehabilitation services are available (WHO, 2005). Lay associations and patient groups also play a significant role in dealing with the non-medical aspects of the disease. They can help patients integrate into society and the work environment, and are important for education of self-management, *i.e.* the measures and behaviours that people with epilepsy can adopt to improve the control of their illness. There is an urgent need to establish more of such patient groups, but finding the required resources is difficult.

Within the framework of the Global Campaign Against Epilepsy established by the International League Against Epilepsy (ILAE), the International Bureau for Epilepsy (IBE), and the WHO, to bring epilepsy "out of the shadows" and raise awareness of the disease among healthcare workers and the general public, demonstration projects were conducted in China, Senegal, Zimbabwe, and Brazil, among others (ILAE/IBE/WHO, 2001). They were designed to identify people with epilepsy and to reduce the treatment gap through the education of health personnel, to dispel stigma, to eradicate preventable causes of epilepsy, and to integrate epilepsy care in national health systems (Sander, 2002; Diop *et al.*, 2003). The phenobarbital project, carried out in rural China, with the enrolment of 2,455 patients, showed that primary care physicians with basic training could effectively treat people with epilepsy by prescribing phenobarbital to be taken once daily at night (Wang, 2006).

A small pilot project carried out in Argentina to evaluate the knowledge of epilepsy and attitudes towards people with epilepsy before and after an education campaign, aimed at the general public, priests, and schoolteachers, clearly showed the benefits of different education programs. Most importantly, this type of intervention program may improve the negative social attitude of the population toward people with epilepsy. The outcome of the project also supported the hypothesis that priests and school teachers are key members in a community education program (own unpublished data).

Overall, the results of these projects have been encouraging and should lead to larger scale models upon which National Epilepsy Programs may be developed. Further efforts should now be directed at encouraging national governments to adopt these programs in their health policies.

In 2011, the Pan American Health Organization adopted a Strategy and Plan of Action on Epilepsy. The Resolution explicitly recognized the burden that epilepsy represents and the existing treatment gap (PAHO, 2011). In 2013, with the support of the ILAE and the IBE, a report was submitted, the principal data of which were made available to countries in Latin America and the Caribbean, concerning resources, programs, and services for the care of people with epilepsy, allowing countries to identify their strengths and weaknesses and to set priorities in order to improve the health sector response (PAHO, 2013). Similar reports already existed for Africa (WHO, 2004) and the South-East Asia Region (WHO, 2011).

Conclusion

The greatest challenge for epilepsy specialists and government health policy makers in resource-limited countries lies in adequately identifying people with epilepsy and delivering cost-effective epilepsy care. Well-conducted epidemiological studies are necessary to set public healthcare priorities and to identify other education and service needs. National epilepsy programs providing integrated care for people with epilepsy and coordinating education programs for the community and primary healthcare workers may help to reduce the enormous treatment gap that currently exists. □

Disclosures.

None of the authors have any conflicts of interest to disclose.

References

Birbeck GL. Epilepsy care in developing countries: Part I of II. *Epilepsy Curr* 2010; 10(4): 75-9.

Birbeck GL, Chomba E, Atadzhanov M, *et al*. Women's experiences living with epilepsy in Zambia. *Am J Trop Med Hyg* 2008; 79(2): 168-72.

Caraballo R, Fejerman N. *Tratamiento de las epilepsias*. Buenos Aires: Editorial Médica Panamericana, 2009.

Caraballo R, Vacarezza M, Cersósimo R, *et al*. Long-term follow-up of the ketogenic diet for refractory epilepsy: Multicenter Argentinean experience in 216 pediatric patients. *Seizure* 2011; 20(8): 640-5.

Carpio A, Hauser WA. Epilepsy in the developing world. *Curr Neurol Neurosci Rep* 2009; 9(4): 319-26.

Cersósimo R, Bartuluchi M, Fortini S, Soraru A, Pomata H, Caraballo R. Vagus nerve stimulation: Effectiveness and tolerability in 64 paediatric patients with refractory epilepsies. *Epileptic Disord* 2011; 13(4): 382-8.

de Bittencourt PR, Adamolekum B, Bharucha N, *et al*. ILAE commission report epilepsy in the tropics: I. epidemiology, socioeconomic risk factors, and etiology. *Epilepsia* 1996; 37(11): 1121-7.

De Boer H, Mula M, Sander J. The global burden and stigma of epilepsy. *Epilepsy Behav* 2008; 12(4): 540-6.

Diop AG, De Boer HM, Mandlhate C, *et al*. The global campaign against epilepsy in Africa. *Acta Trop* 2003; 87(1): 149-59.

Hu J, Si Y, Zhou D, *et al*. Prevalence and treatment gap of active convulsive epilepsy: A large community-based survey in rural West China. *Seizure* 2014; 23(5): 333-7.

ILAE/IBE/WHO. *Global campaign against epilepsy: Out of the shadows*. International League Against Epilepsy/International Bureau of Education/World Health Organization, 2001.

Kossoff E, Caraballo R, du Toit T, *et al*. Dietary therapies: A worldwide phenomenon. *Epilepsy Res* 2012; 100(3): 205-9.

Kwan P, Brodie MJ. Phenobarbital for the treatment of epilepsy in the 21st century: A critical review. *Epilepsia* 2004; 45: 1141-9.

Mac TL, Tran DS, Quet F, *et al*. Epidemiology, aetiology, and clinical management of epilepsy in Asia: A systematic review. *Lancet Neurol* 2007; 6: 533-43.

Mbuba CK, Ngugi AK, Newton CR, Carter JA. The epilepsy treatment gap in developing countries: A systematic review of the magnitude, causes, and intervention strategies. *Epilepsia* 2008; 49(9): 1491-503.

Meinardi H, Scott RA, Reis R, *et al*. The treatment gap in epilepsy: The current situation and ways forward. *Epilepsia* 2001; 42(1): 136-49.

Noronha AL, Marques LH, Borges MA, Cendes F, Guerreiro CA, Min LL. Assessment of the epilepsy treatment gap in two cities of south-east of Brazil. *Arq Neuropsiquiatr* 2004; 62(3B): 761-3.

PAHO (Pan American Health Organization). *World Health Organization 51st directing council, 63rd session of the regional committee*. Washington DC (USA): 26-30 September 2011.

PAHO (Pan American Health Organization). *Informe sobre la epilepsia en América Latina y el Caribe*. Washington DC (USA): 2013.

Radhakrishnan K. Challenges in the management of epilepsy in resource-poor countries. *Nat Rev Neurol* 2009; 5: 323-30.

Sander JW. Overview of the demonstration projects. *Epilepsia* 2002; 43(6): 34-6.

Scott RA, Lhatoo SD, Sander JW. The treatment of epilepsy in developing countries: Where do we go from here? *Bull World Health Organ* 2001; 79(4): 344-51.

Thurman DJ, Beghi E, Begley CE, *et al*. ILAE commission on epidemiology. Standards for epidemiologic studies and surveillance of epilepsy. *Epilepsia* 2011; 52(87): 2-26.

Wang WZ, Wu JZ, Ma GY, *et al*. Efficacy assessment of phenobarbital in epilepsy: A large community-based intervention trial in rural China. *Lancet Neurol* 2006; 5(1): 46-52.

WHO. *Epilepsy in the African region: Bridging the gap*. Geneva: World Health Organization, 2004.

WHO. *Atlas epilepsy care in the world 2005*. Geneva: World Health Organization, 2005.

WHO. Regional office for South-East Asia. *Epilepsy in the South-East Asia Region. Bridging the gap*. World Health Organization, 2011.

Yemadje LP, Houinato D, Quet F, *et al*. Understanding the differences in prevalence of epilepsy in tropical regions. *Epilepsia* 2011; 52(8): 1376-81.

TEST YOURSELF

(1) Why is the incidence of epilepsy so much higher in resource-limited countries than in the developed world?

(2) Why is phenobarbital still the drug of choice in resource-limited countries?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, *under the section "The EpiCentre".*