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Current Scenario and recent advances of Neurological Disorder

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Abstract

Neurological disorders are medically defined as disorders that affect the brain as well as the nerves found throughout the human body and the spinal cord. Structural, biochemical or electrical abnormalities in the brain, spinal cord or other nerves can result in a range of symptoms. Examples of symptoms include paralysis, muscle weakness, poor coordination, loss of sensation, seizures, confusion, pain and altered levels of consciousness. The specific causes of neurological problems vary, but can include genetic disorders, congenital abnormalities or disorders, infections, lifestyle or environmental health problems including malnutrition, and brain injury, spinal cord injury or nerve injury. There are many recognized neurological disorders, some relatively common, but many rare. Mental disorders, on the other hand, are "psychiatric illnesses" or diseases which appear primarily as abnormalities of thought, feeling or behavior, producing either distress or impairment of function. According to the U.S. National Library of Medicine there are more than 600 neurologic diseases.

Neurological disabilities include a wide range of disorders, such as epilepsy, learning disabilities, neuromuscular disorders, autism, ADD, brain tumors, and cerebral palsy, just to name a few. Some neurological conditions are congenital, emerging before birth. Other conditions may be caused by tumors, degeneration, trauma, infections or structural defects. Regardless of the cause, all neurological disabilities result from damage to the nervous system. Depending on where the damage takes place, determines to what extent communication, vision, hearing, movement and cognition are impacted.

Introduction

Neurological illnesses have a significant impact on global health. According to the most recent estimates, neurological disorders such as Alzheimer's and other dementias, Parkinson's disease, multiple sclerosis, epilepsy, and headache disorders (migraine, tension-type headache [TTH], and medication-overuse headache [MOH]) account for 3% of the global disease burden. Despite what appears to be a modest overall percentage, dementia, epilepsy, migraine, and stroke are among the top 50 causes of disability-adjusted life years (DALYs) (Murray and others 2012). Migraine and epilepsy account for one-third and one-fourth of this neurological burden, respectively (Murray and others 2012), while dementia and Parkinson's disease are among the top 15 disorders with the greatest burden growth over the last decade. In 2010, neurological illnesses accounted for 5.5 percent of YLDs, or 42.9 million YLDs; migraine, epilepsy, and dementia were among the top 25 causes of YLDs. Migraine tops the list of neurological illnesses, accounting for more than half of neurological YLDs or 2.9 percent of worldwide YLDs; epilepsy accounts for 1.1 percent of global YLDs (Vos and colleagues 2012). The neurological illness burden in low- and middle-income countries (LMICs) is anticipated to rise exponentially during the next decade (Murray and others 2012). Despite the considerable effect of neurological illnesses on individuals and society, knowledge of their epidemiology, including variation in disease incidence across location and time, as well as comprehension of related risk factors and outcomes, remains poor, particularly in low- and middle-income countries. Because of physical, cognitive, and interpersonal impairments, patients with neurological illnesses frequently require extensive social and economic support (WHO 2006). Despite the high incidence of disability, there is growing understanding that services and resources are disproportionately inadequate, particularly in low- and middle-income countries (WHO 2004).

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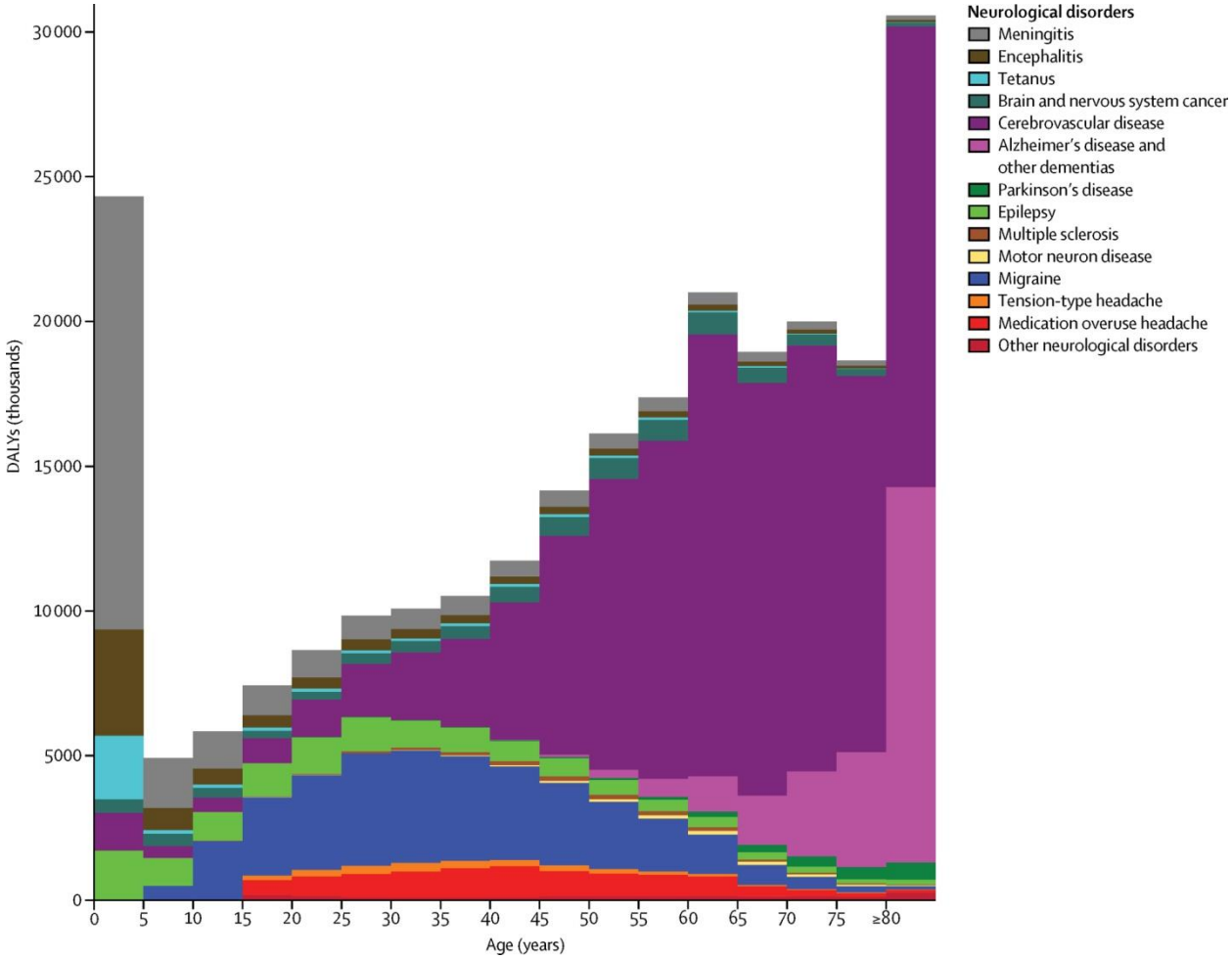
Furthermore, understanding of the cost-effectiveness of measures to enhance neurological care in these settings is inadequate. This chapter focuses on three neurological conditions: epilepsy, dementia, and headache problems. The chapter discusses current epidemiology, risk factors, and cost-effective therapies for various disorders. The emphasis is on solutions that produce a real decrease in the burden on the global population, with a special emphasis on LMIC application.

Prevalence

Neurological illnesses are an expanding concern for global health care systems, necessitating further research, government and societal participation, and infrastructural upgrades.

This chapter describes the worldwide burden of the highlighted neurological illnesses using the World Health Organisation (WHO) areas of Africa, the Americas, the Eastern Mediterranean, Europe, South-East Asia, and the Western Pacific.



Rank
1–2 5–6 9–10 13–14
3–4 7–8 11–12

	Global	East Asia	Southeast Asia	Oceania	Central Asia	Central Europe	Eastern Europe	High-income Asia Pacific	Australasia	Western Europe	Southern Latin America	High-income North America	Caribbean	Andean Latin America	Central Latin America	Tropical Latin America	North Africa and Middle East	South Asia	Central sub-Saharan Africa	Eastern sub-Saharan Africa	Southern sub-Saharan Africa	Western sub-Saharan Africa
Stroke	1	1	1	1	1	1	1	1	2	2	1	2	1	1	1	1	1	1	1	1	1	1
Migraine	2	3	2	4	2	2	2	2	1	1	2	3	2	2	3	2	3	2	4	4	3	3
Alzheimer's disease and other dementias	3	2	3	3	3	3	3	3	3	3	3	1	3	3	2	3	2	4	3	5	5	4
Meningitis	4	7	4	2	7	11	7	11	12	12	7	12	4	7	7	7	5	3	2	2	4	2
Epilepsy	5	5	5	5	4	6	6	5	6	6	5	6	5	5	4	6	4	6	5	3	2	5
Medication overuse headache	6	6	8	7	6	5	4	4	5	4	4	4	6	4	5	5	6	7	6	7	6	6
Encephalitis	7	8	6	6	8	12	8	12	13	13	11	13	10	8	9	12	8	5	9	8	9	8
Brain and nervous system cancer	8	4	7	8	5	4	5	6	4	5	6	5	7	6	6	4	7	9	8	9	7	7
Tetanus	9	14	10	14	14	14	14	14	14	14	14	14	12	14	14	14	12	8	7	6	14	9
Other neurological disorders	10	10	11	9	9	7	9	7	9	8	9	9	9	11	8	8	10	11	10	10	8	10
Parkinson's disease	11	11	12	10	11	9	12	8	7	7	8	8	8	10	11	9	11	12	11	12	10	11
Tension-type headache	12	9	9	11	10	10	10	9	11	11	10	11	11	9	10	10	9	10	12	11	11	12
Multiple sclerosis	13	13	14	13	12	8	11	13	10	9	13	7	13	13	12	13	13	13	13	13	12	13
Motor neuron disease	14	12	13	12	13	13	13	10	8	10	12	10	14	12	13	11	14	14	14	14	13	14

Epilepsy

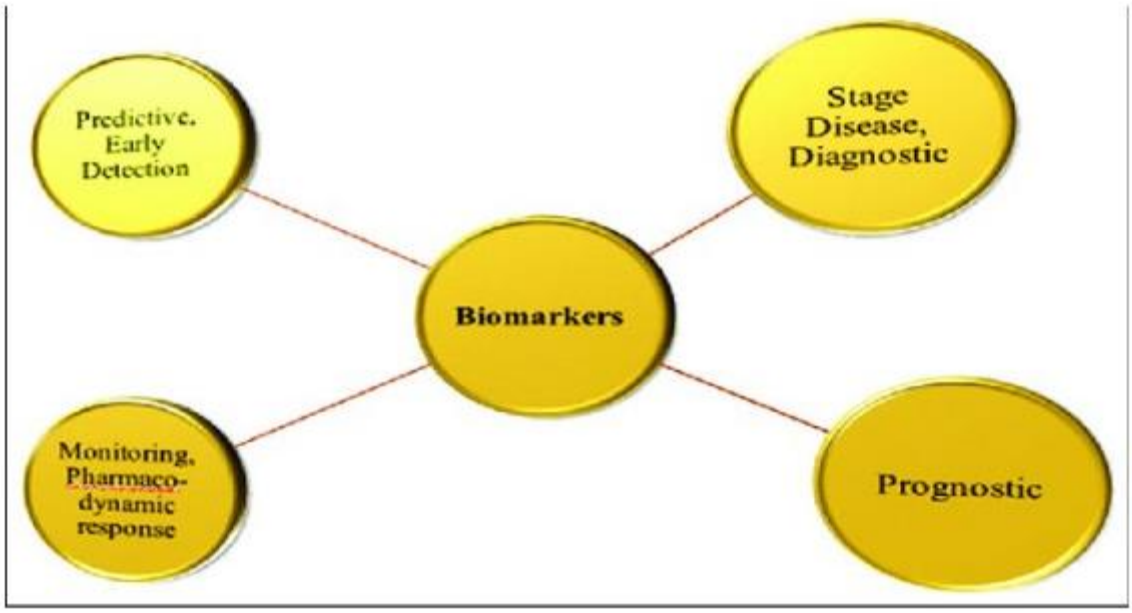
Definitions

Epilepsy is a neurological illness that is generally described as two unprovoked seizures occurring more than 24 hours apart with a persistent proclivity to induce subsequent seizures (Fisher and others 2014). The International League Against Epilepsy published an updated definition of epilepsy in 2014. If a person has an age-dependent condition and is now older than the predicted age for this syndrome, or if the individual has been seizure free for at least 10 years and off anti-epileptic medicines for at least five years, epilepsy is deemed resolved (Fisher and others 2014). Those who continue to suffer seizures despite a sufficient trial of two well-tolerated and adequately selected anti-epileptic medicines (AEDs), whether in monotherapy or polytherapy, are deemed drug resistant. Epilepsy is split into three types.

Biomarks - Classification of biomarkers

- Epilepsy triggered by a distant stroke, for example, might be structural or metabolic in nature.
- Epilepsies of known or suspected genetic origin, such as juvenile myoclonic epilepsy
- Unknown cause epilepsies (Berg and others 2010).

Brain tumours, viral infections, brain damage, stroke, and hippocampal sclerosis are some of the more prevalent causes of epilepsy. Less common reasons include genetic causes, autoimmune causes, and cortical development abnormalities (Bhalla and others 2011). In LMICs, perinatal and infection-related aetiologies frequently prevail.



Epidemiology and Burden of Disease

A worldwide systematic review of prevalence has not yet been published; however, in door-to-door studies, the prevalence has been reported to range from 2.2 per 1,000 to 41.0 per 1,000 people, with higher estimates in LMICs (Banerjee, Filippi, and Allen Hauser 2009; Benamer and Grosset 2009; Burneo, Tellez-Zenteno, and Wiebe 2005; Forsgren and others 2005; Mac and others 2007). The median incidence per 100,000 people in LMICs is 81.7 (interquartile range (IQR) 28.0-239.5) compared to 45.0 (IQR 30.3-66.7) in HICs (Ngugi and others 2011). The higher prevalence or incidence rates reported in many LMICs are thought to be due to the occurrence of endemic conditions such as malaria or neurocysticercosis; the higher incidence of road traffic injuries; birth-related injuries; and variations in medical infrastructure, availability of preventative health programmes, and accessible care. In HICs, the prevalence of epilepsy is stable until after age 50, when it rises; in LMICs, the prevalence is stable in the third and fourth decades, drops in the fifth decade, and rises again after age 60 in some studies (Banerjee, Filippi, and Allen Hauser 2009). Epilepsy is linked to early death, with the largest standardised mortality ratio occurring during the first year or two of diagnosis (Neligan and colleagues 2010). In general, the standardised mortality ratio for epilepsy is around 3 (Hitiris and colleagues 2007). Premature mortality epidemiology is especially important in LMICs, where 85 percent of persons with epilepsy live and the risk of premature mortality is highest (Diop and others 2005; Jette and Trevathan 2014; Newton and Garcia 2012). The fact that a higher proportion of deaths in LMICs are theoretically avoidable, such as falls, drowning, burns, and status epilepticus, is particularly troubling (Diop and others 2005; Jette and Trevathan 2014). Status epilepticus, for example, was responsible for 38% of all epilepsy-related fatalities in a large cohort of adults with convulsive seizures in rural Kenya (Ngugi and colleagues 2014). Status epilepticus is defined as five minutes or more of continuous seizure activity, or two or more seizures with no return of consciousness in between (Lowenstein and colleagues 2001). This is an essential criteria since research indicates that seizures lasting longer than five minutes are unlikely to self-terminate. Acute symptomatic diseases (for example, brain tumour or stroke), abrupt unexpected death in epilepsy, suicide, and accidents are other major causes of early mortality in persons with epilepsy (Hitiris and others 2007). According to the GBD 2010 report, epilepsy is the 36th biggest cause of DALYs worldwide. In western Sub-Saharan Africa, epilepsy is the 14th biggest cause of DALYs. Epilepsy is the 20th biggest cause of YLDs worldwide, trailing only migraine in terms of brain illnesses (Vos and others 2012). Importantly, models in the GBD 2010 report that calculate the global burden of epilepsy consider only idiopathic/cryptogenic epilepsy and not epilepsy secondary to infections, stroke, or genetic syndromes, which may account for more than half of deaths in these regions (Murray and others 2012). As a result, the results likely understate the real burden of epilepsy, particularly in LMICs.

Interventions

Population-Based Interventions

Targeting Epilepsy Risk Factors

Although hereditary causes of epilepsy cannot be avoided, the more prevalent structural or metabolic

reasons can be addressed by public health policy. Motorcyclists wearing helmets, for example, and regulations prohibiting drinking and driving can minimise the chance of traumatic brain injury, a common risk factor. Improved prenatal care, especially in rural areas, has the potential to lower the incidence and future prevalence of epilepsy. In one Tanzanian community-based case-control research, adverse perinatal events were found in 14% of children with epilepsy but not in any of the controls (Burton et colleagues 2012). An relationship between aberrant prenatal period and active convulsive epilepsy was found in a population-based cross-sectional and case-control study conducted in Ghana, Kenya, South Africa, Tanzania, and Uganda (Ngugi and others 2013). Although abnormal delivery and home delivery did not approach statistical significance, they were related with active convulsive seizures.

Controlling neurocysticercosis, a prevalent risk factor in LMICs, would be an efficient strategy to minimise epilepsy globally. In rural Salama, Honduras, an eight-year public health and educational intervention programme targeted at lowering symptomatic epilepsies (especially those induced by prenatal traumas and neurocysticercosis) began in 1997 (Medina and colleagues 2011). The programme comprised education and media campaigns, pig farmer animal husbandry training, water project building and correct sewage disposal, school student deworming, continued taeniasis surveillance, and other measures (Medina and others 2011). Neurocysticercosis-related epilepsy was decreased from 36.9 percent in 1997 to 13.9 percent in 2005 (Medina and others 2011). The whole cost of this study was $1.33 million, but no economic analysis was performed to assess if it was cost-effective. A smaller-scale research in western Kenya looked at the effectiveness of training approaches for preventing seizures caused by neurocysticercosis (Wohlgemut and colleagues 2010). The authors discovered that utilising this teaching strategy considerably enhanced knowledge. It was not determined if this programme reduced the incidence of epilepsy induced by taenia solium, but the findings are a step in the right direction. The expert consultation study on foodborne illnesses, such as taeniasis/cysticercosis, suggests several techniques for long-term prevention and control of this often endemic agent. These options are given in box 5.2, however the study does not specify the costs of adopting them (WHO 2011).

Anti-Stigma Interventions

Civil rights abuses are prevalent, such as uneven access to health and life insurance or the unfair weighing of health insurance provisions. Discrimination in the workplace and limited access to education are common occurrences. School instructors frequently lack understanding about seizure diseases and have unfavourable attitudes towards children with seizure disorders (Akpan, Ikpeme, and Utuk 2013). Stigma has both social and economic implications. People with epilepsy may not seek treatment or communicate relevant health problems to their care providers, expanding the treatment gap even more. Improved understanding of epilepsy is connected with more positive views and less stigma, although the long-term durability and influence are unknown (Fiest and colleagues 2014). To tackle stigma at the population level through legislation and campaigning, a comprehensive approach is required. Furthermore, education and information providing among employers and instructors to debunk myths and improve seizure control could empower persons with epilepsy to seek treatment and encourage them to be more actively engaged in their communities. The cost-effectiveness of initiatives for stigma reduction has not been properly evaluated.

Legislation

One of the most significant contributions to the epilepsy treatment gap in LMICs is the scarcity of anti-epileptic medications. The majority of nations do not have access to second-generation pharmaceuticals, and even older anti-epileptic therapies are only available on an irregular basis. Researchers in Zambia evaluated 111 pharmacies and discovered that 49.1 percent did not have anti-epileptic medications. Paediatric syrups, which are widely used in HICs, were completely unavailable (Chomba and colleagues 2010). Personal conversations with epilepsy care professionals in other LMICs, however, indicated that this issue may be prevalent (Chomba and others 2010). Clearly, measures are required to ensure that patients worldwide continue to have access to inexpensive and effective anti-epileptic medications. Few nations have a distinct budget for epileptic services, and more public financing for epilepsy care is required. In 73 percent of low-income countries, including those in Africa, the Eastern Mediterranean, and South-East Asia, out-of-pocket payments are the predominant source of funding for epilepsy care (WHO 2011). Many areas lack disability benefits, and sufferers are unable to acquire financial assistance.

Self-Management

Self-management allows patients to take a more active role in their care. Patients are more likely to comprehend, adopt better lifestyles, and stick to therapy (Fitzsimons and others 2012). Self-management can assist people with epilepsy better identify and control seizure triggers, which can lower seizure frequency as well as health-care utilisation and expenditures (Fitzsimons and colleagues 2012). A few studies have looked at the efficacy of self-management education programmes in adults and children and found some evidence of benefits; further study is needed to look at the cost-efficiency of such programmes in low-income countries (LMICs) (Bradley and Lindsay 2008; Lindsay and Bradley 2010).

Pharmacological Interventions

The decision to begin anti-epileptic medication treatment might be difficult. The Multicentre study

for Early Epilepsy and Single Seizures found minimal advantage in starting therapy for people who had a single seizure, no known neurological condition, and normal electroencephalograms (EEGs) (Kim and colleagues 2006). Medical care, on the other hand, should be addressed in those at moderate to high risk, defined as more than two to three seizures at presentation, underlying neurological diseases, and abnormal EEGs (Kim and colleagues 2006). More than 60 randomised control trials (RCTs), mostly in HICs, have looked at the efficacy of anti-epileptic drugs, but there is still a scarcity of well-designed RCTs looking at the efficacy of these medications in patients with generalised epilepsy syndromes and children (Glauser and others 2013). Newer AEDs are better tolerated and have fewer long-term negative effects, although their superiority has not been demonstrated.

There have been no studies comparing the cost-effectiveness of anti-epileptic medicines in patients with new-onset epilepsy. A new systematic review summarises the evidence for their effectiveness as first-line treatment in epileptic patients. Children and adults with convulsive epilepsy should be given monotherapy with any of the conventional anti-epileptic medications (carbamazepine, phenobarbital, phenytoin, and valproic acid). Several lower-quality trials have shown that phenobarbital is effective in adults and children with partial onset and generalised onset tonic-clonic seizures (Glauser and others 2013). Given the high acquisition costs, phenobarbital should be provided as a first option if it is available. Children and adults with partial-onset seizures should be given carbamazepine if it is available (WHO 2009b). Using the smallest amount feasible should reduce side effects, improve seizure outcomes, and close the treatment gap. Although valproic acid is suggested since it is on the list of necessary drugs, ethosuximide and valproic acid have been demonstrated to be the most beneficial in the management of absence seizures, particularly in youngsters. Ethosuximide is a supplementary drug that is accessible. However, because of its increased link with significant congenital abnormalities and lower neurodevelopmental outcomes, the medicine should be avoided in women of reproductive potential whenever feasible. Although novel treatment drugs that are not metabolised by the liver, such as levetiracetam, are available, their cost-effectiveness in LMICs has not been explored. Unfortunately, typical drugs are not widely available or affordable in LMICs, creating hurdles to therapy. According to one survey, the average availability of generic pharmaceuticals in the public sector for all medicines, excluding diazepam injectable, is less than 50%. The availability of generic oral drugs in the private sector ranged from 42 percent for phenytoin to 70 percent for phenobarbital. Generic carbamazepine and phenytoin patient costs in the public sector were 5 and 18 times higher than international reference prices, respectively; private sector patient prices were 11 and 25 times higher, respectively. Original brand pricing were almost 30 times higher for both medications. Approximately 60% of patients in Sub-Saharan Africa do not have access to AEDs, increasing the risk of seizures, seizure-related accidents, and status epilepticus, a substantial cause of morbidity and death in epilepsy patients (Ba-Diop and colleagues 2014). Adherence to medication and avoidance of alternative seizure triggers are two of the most effective patient-related measures for avoiding status epilepticus. On a population level, the greatest method to reduce the morbidity and mortality associated with status epilepticus is through health policy that increases the availability and accessibility of AEDs, as well as through health professional education that ensures health practitioners understand that time is crucial.

Management of Infectious Etiologies of Epilepsy

In LMICs, neurocysticercosis is a prevalent cause of epilepsy. Recent evidence-based guidelines for the treatment of parenchymal neurocysticercosis are available (Baird and others 2013). These guidelines indicate that albendazole treatment, with or without corticosteroids, in combination with AEDs is likely to be successful in improving outcomes (Baird and others 2013).

Because simultaneous AED-antiretroviral medication may be suggested in up to 55% of persons, evidence-based guidelines were produced to assist the selection of anti-epileptic medicines for people with HIV/AIDS (Birbeck and others 2012). According to the recommendations, patients on antiretroviral regimens that contain protease inhibitors or nonnucleoside reverse transcriptase inhibitors should avoid enzyme-inducing AEDs because pharmacokinetic interactions may result in virologic failure. Patients may be evaluated using pharmacokinetic studies to guarantee the success of the antiretroviral regimen if such regimens are necessary for seizure management (Birbeck and others 2012).

Surgical Management

The majority of patients (70 percent in those presenting with new onset epilepsy) achieve one-year seizure independence after using up to three anti-epileptic medicines. Drug resistance, however, occurs in up to 40% of all patients, particularly those with focal epilepsy (Berg and others 2009; Kwan and Brodie 2000; Schiller and Najjar 2008; Semah and others 1998). Attempting to treat with further anti-epileptic medications after three unsuccessful anti-epileptic treatments is unlikely to result in persistent seizure independence (Jette, Reid, and Wiebe 2014). Drug-resistant patients who have failed two adequate AED treatments should be evaluated for surgical examination, according to experts (Jette, Reid, and Wiebe 2014; Kwan and others 2010; Wiebe and Jette 2012). Children with complex syndromes, patients with stereotyped or lateralized seizures or focal findings, and children with a magnetic resonance imaging lesion amenable to surgical resection regardless of seizure frequency

should all be referred to a comprehensive epilepsy programme for a surgical evaluation (Jette, Reid, and Wiebe 2014; Wiebe and Jette 2012). Strategies for surgical epilepsy management in resource-limited settings have been presented, and epilepsy surgery is increasingly being performed in LMICs with outstanding results (Asadi-Pooya and Sperling 2008).

Alternative Therapies

food therapy, medicinal marijuana, and acupuncture are among the proposed alternative therapies for epilepsy; nevertheless, only food therapies have been exposed to randomised studies. The ketogenic diet can improve seizure outcomes in people with drug-resistant epilepsy, but it can be difficult to stick to, especially in adults (Levy, Cooper, and Giri 2012). In one observational study, the Atkins diet was linked to better seizure management, but further research is needed to compare it to the benefits of other dietary interventions, such as the modified Atkins diet and the low glycemic index diet (Levy, Cooper, and Giri 2012). Despite their expanding usage, nutritional interventions are resource demanding, expensive, and primarily restricted to HICs (Cross 2013). In LMICs, more cost-effective and easier methods of applying these medicines are required.

Interventions to Optimize Health Care Delivery

The treatment gap is defined as the number of persons with active epilepsy who require anti-epileptic treatment but do not receive it. Unfortunately, people living in LMICs, where the prevalence of epilepsy is high, are disproportionately affected by the epileptic treatment gap (Jette and Trevathan 2014). The treatment gap is greater than 75% in low-income countries, greater than 50% in many LMICs and upper-middle-income countries, and less than 10% in the majority of HICs (Meyer and others 2010).

Conclusions

Seizures and accompanying injuries cause severe morbidity and death in those who have untreated epilepsy. The persistent stigma associated with seizures, as well as the lack of effective drugs that may adequately treat this group, continue to be important challenges to clinical care in many places. Finally, legal reforms and anti-stigma measures are likely to be the most effective means of closing the global epilepsy treatment gap. Among the necessary legislative initiatives are those advocating for improved benefits for functionally impaired people with epilepsy, particularly in resource-poor nations where they are most needed.

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