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Epilepsy: Prevention and Overview of the Treatments

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Abstract

Epilepsy is one of the most common neurological disorders worldwide. It affects people from different ages and conferred a huge handicap, halting patients with epilepsy to develop themselves in different life aspects and worsening their quality of life. Therefore, the knowledge about the prevention and treatment of this disease is essential in the medical practice of each healthcare provider.

This article revolves around the strategies to prevent any injury that trigger epileptic seizure. Moreover, different treatments are tackled along this work in order to understand the aim of the approaches, the candidates who benefit from each procedure and the adverse effects.

The aim of this work is to convey the general knowledge about different prevention strategies and approved therapeutics in epilepsy, get the attention of more healthcare providers on these topics in order to join forces to detect, refer, treat and follow-up patients based on the latest scientific evidence.

Keywords: *Epilepsy; Prevention Measures; Therapeutics*

Introduction

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures with neurobiologic, cognitive, psychological, and social repercussions [1]. Clinically, the definition is fulfill when a person have (i) at least two unprovoked seizures occurring > 24h apart, or (ii) one unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures occurring over the next 10 years or (iii) have a diagnosis of an epilepsy syndrome [2].

An epileptic seizure is generated by an abnormal excessive or synchronous neuronal activity in the brain [1]. The signs and symptoms are varied; tonic and clonic muscles contractions, brief lost of consciousness, sudden lost of muscle tone, complex movements in the face, myoclonus, illusions, dejávùs, epigastric sensations, fear, aphasia, apraxia and others [3].

Around 45.9 million people worldwide have epilepsy [4]. The prevalence of active epilepsy is 6.38 per 1000 persons, meanwhile, the annual cumulative incidence of epilepsy is 67.77 per 100,000 persons globally [5]. Thus, epilepsy is relevant due to its enormous impact around the world, being one of the most common neurological diseases worldwide.

Aim of the Study

The main aim of this work is to illustrate the main strategies to prevent and treat patients with this neurological illness.

Prevention

Head trauma is the most common cause of secondary epilepsy and the use of the helmets for sports and transportation is a protective strategy in the daily life. For elderly, minor head traumas should be avoided with the installation of nonslip carpeting and handholds at home [6].

Stroke represents a potential insult that generates a potential epileptogenic foci. Thus, eating well, exercising, and not smoking helps to avoid any post-stroke epilepsy [7].

Maternal care is essential for a good development of the newborn. Therefore, antenatal and perinatal care should be assured for each woman. Furthermore, teenage pregnancies should be closely monitored in order to diminish the risk for premature and low weight infants. Finally, during the delivery, healthcare providers should ensure adequate oxygenation for the newborn and avoid any head trauma [6,7].

Infections of the nervous system also cause disturbances in the microarchitecture and the normal function of the brain. Good hygiene and preparing food safety are strategies that eliminate parasites like *Taenia solium*, reducing the risk to get Neurocysticercosis. Immunization against *Haemophilus influenzae*, measles, rubella and other microorganisms is employed to avoid any sequelae include continuing epileptic seizures [7].

Overview of the treatments

The pharmacological treatment is the cornerstone in the treatment of epilepsy. Seventy percent of the patients have a remission of the seizures with a single antiseizure medication [8]. Several drugs can ameliorate specific types of epilepsy. Table 1 illustrates the antiseizure medication with high level of evidence as the most recommended drugs for each type of seizures and epileptogenic syndrome [9].

Seizure type or epilepsy syndrome	AEDs
Adults with partial-onset seizures	Carbamazepine (CBZ) Levetiracetam (LEV) Phenytoin (PHT)
Children with partial-onset seizures	Oxcarbazepine (OXC)
Elderly adults with partial-onset seizures	Gabapentine (GBP) Lamotrigine (LTG)
Adults with generalized onset tonic-clonic seizures	Carbamazepine (CBZ) Lamotrigine (LTG) Oxcarbazepine (OXC)
Children with generalized onset tonic-clonic seizures	Carbamazepine (CBZ) Phenobarbital (PB) Phenytoin (PHT)
Children with absence seizures	Ethosuxamide (ESM) Valproic Acid (VPA)
Benign epilepsy with centrotemporal spikes (BECTS)	Carbamazepine (CBZ) Valproic Acid (VPA)
Juvenile myoclonic epilepsy (JME)	Topiramate (TPM) Valproic Acid (VPA)
Seizure type or epilepsy syndrome	Antiseizure medication

Table 1: *Antiseizure medication for each seizure type and epilepsy syndrome (Adapted from Glauser T., et al. Epilepsia, 2013).*

The choice of the antiseizure medication should be tailored to the patients according to the health status, but following the scientific evidence of the safety and effectiveness for each drug.

Physicians should focus on certain social groups, such as children, elderly and pregnant women, because drugs can jeopardize the neurodevelopment in newborns and children, and the elderly may present more often adverse effect due to liver and/or renal impairment, mainly drug intoxication [9].

The follow-up of the patients submitted to a pharmacological regimen is based on the blood levels monitoring of the antiseizure medication, the detection of side effects [10], the registration of the number of seizures, guided by EEG recording periodically [11].

Epilepsy surgery and stimulation techniques

Unfortunately, 30% of the patients suffer from drug resistant epilepsy, which is defined as a failure of adequate trials of two tolerated and appropriately chosen and used antiseizure medication schedules to achieve sustained seizure freedom [12]. There are two approaches that control the seizures for these group of patients; curative and palliative procedures.

Curative procedures

The curative procedures have a high probability to remove the epileptogenic zone because the abnormal structure is localizable and well-delimitate and does not overlap with eloquent brain areas. The patients submitted to these surgeries have an excellent control of the seizures with a complete remission of the seizures in a long-term [13]. Some of these interventions are temporal lobectomy, cortical excision and hemispherectomy.

The most frequent surgery is the temporal lobectomy due to the high prevalence of the Temporal Lobe Epilepsy (TLE) in several epileptic centers [14]. The main cause of the TLE is the hippocampal formation damage. The hippocampus is prone to present excitotoxicity due to its architecture and the disturbances in the regulation and activation exert by other brain areas over it. In addition, there is a liability of the hippocampus to be damaged for small decrements in the oxygen levels, as well as the occurrence of neural sclerosis and gliosis, causing a great disruption in its normal circuitry and a potential epileptogenic foci [15]. In the surgery, the anterior temporal lobe is removed along the amygdala and the hippocampal formation, leading a reduction of seizures around 70% to 80% of the cases [16]. Nonetheless, memory and language can be affected if the approach is performed on the dominant hemisphere [17], as well as quadratanopsy can occur [18].

Cortical excision is another type of epilepsy surgery and could be applied for temporal and extratemporal epilepsy, which not imply eloquent areas. Brain cortex is removed at the seizure focus area. About 30% of patients have a total seizure control [19].

Hemispherectomy refers to the complete removal or functional disconnection of a cerebral hemisphere. It is usually performed in children who suffer intractable seizures and have a long cortical damage due to neurodevelopmental malformation, extended inflammation and vascular abnormalities. According to many patient series, this surgery have a remission of seizures around 54% to 90%. Patients often improve in cognitive functioning, attention span, and behavior. Nonetheless, patients may present hemiparesia after surgery [20].

Palliative procedures

Surgical techniques

On the other hand, the palliative epilepsy surgeries offer the reduction of disabling seizures in cases when there are multiple epileptogenic foci, or the epilepsy onset is located in eloquent areas, or when the epileptogenic focus is not identifiable [21]. Corpus callosotomy and subpial transection belong to this group.

The corpus callosotomy is based on the hypothesis that the corpus callosum is the major pathway for the interhemispheric spread of ictal discharges, and its disconnection leads to a disruption of rapid seizure spread. The anterior 2/3 portions of the corpus callosum

or the whole structure can be cut. The candidates for this surgery are patients with atonic, tonic and myoclonic seizures leading to debilitating falls [22]. However, there is are some transient adverse effects, such as memory deficits, language impairments and the disconnection syndrome [23], expressed as impairments on motor control, spatial orientation, vision, hearing, and language [24].

Multiple subpial transections consist of shallow cuts into the cerebral cortex damaging the horizontal intracortical fibres at intervals of 5 mm, while preserving both vertical fibres and penetrating blood vessels. This results in reduction of synchronised discharge from the epileptic focus and limitation of its spread, without jeopardised function of the cerebral cortex. This approach is useful in patients for whom the epileptogenic lesion cannot be resected because it lies in an eloquent cortical area, or in regions where excision may produce major deficits. The adverse effects are minimal but the trails have reported aphasia, dysphasia and limb paralysis as the most common after surgery [25].

Stimulation techniques

Approved stimulation techniques are implemented in patients with several types of intractable seizures. Those interventions are the vagus nerve stimulation (VNS), the responsive direct brain stimulation (or response neurostimulation device; RNS) and the deep brain stimulation (DBS), which belong to palliative approaches too. These devices offer a modulated and adjustable stimulation control by the healthcare providers, and also patients but only with VNS devices. In blinded studies, they have achieved an efficacy of 12.7% for VNS, 20.6% for DBS and 25.9% for RNS. Furthermore, the adverse effects are minimal and can be diminished as the parameters of stimulation also change. [26]

VNS is a peripheral intervention in which a neurocybernetic prosthesis is implanted subcutaneously in the upper chest that generates an intermittent stimulation given periodically. Additionally, helical electrodes are placed on the left cervical vagus nerve to stimulate the aforementioned structure. Tachycardia during the seizure triggers VNS automatically, and interestingly, the device also allows the user to give an extra burst of stimulation when he or she is aware of when a seizure happens, swiping a magnet over the VNS generator. The main effect of VNS is the modulation of the hyperexcitable brain regions by increasing activity in the nucleus tractus solitarius, and its downstream projections to the limbic system and thalamus, increasing the production of norepinephrine and serotonin, which have been shown antiseizure effects [27].

RNS contains a neurostimulator with 1 or 2 strip leads. The neurostimulator is seated in the skull, and is connected to depth or cortical strip leads that are surgically placed in the brain at 1 or 2 seizure foci. Each lead contains 4 electrodes that can be used for both sensing and stimulating. The neurostimulator delivers biphasic pulses through any or all of the 8 electrodes in different situations. When the electrodes detect electrocorticographic epileptogenic patterns, the device sends stimulation to halt the seizure progression. The continuous electrocorticographic recording system and the parameters of the whole device is stored in the device itself and lately in a remote monitor and a patient data management system over the internet. The information is used to adjust the stimulation to achieve the best parameters to mitigate the seizures [28].

DBS is a neurointerventional technique that involves the implantation of electrodes and a pacemaker-like device to deliver pulses of electricity to specific areas of the brain. The anterior thalamic nucleus stimulation is the main target to approach because of the existence of scientific data about the intervention of this structure with DBS extracted from randomized control trials, Moreover, the anterior thalamic nucleus has extensive connections with the limbic system, having a crucial role in the maintenance and propagation of seizures. Other targets are the hippocampal formation, centromedian thalamic nucleus, caudate nucleus, subthalamic nucleus and cerebellum. The basic mechanism of DBS revolves around an inhibition effect by either the blockade of depolarization and inactivation of voltage-gated currents or by activation of GABAergic afferents in the stimulated nucleus [29].

An experimental device called transcranial direct current stimulation (TDCs) has a novelty incursion among the stimulation techniques. This non-invasive neuromodulation method has a current generator that elicits a low voltage current, and anodal and cathodal electrodes that are set in the scalp and where the current pass through them. TDCs uses anodal or cathodal stimulation to modulates cortical excitability. In epilepsy, the cathodal stimulation is used because it generates a hyperpolarization of the neurons, suppressing the epileptiform discharges and clinical seizures [30]. This device was made to be controlled by patients and caregivers. In a long-term, the stimulation could be conducted at home.

Miscellaneous

The Classic Ketogenic Diet (CKD) consists of a high-fat and low-protein and carbohydrate diet, with restricted calories and fluids, mimicking the fasting state. The anticonvulsant mechanism lies on the shifting the energy metabolism from glycolytic energy production to energy generation through oxidative phosphorylation by means of fatty acid ß-oxidation and ketone-body production. Patients with specific metabolic diseases, epileptogenic encephalopathies and genetic illnesses are the candidates for this treatment. There should be a close vigilance of the patients to see if the diet cover the energy requirements. This screening is composed by liver and kidney tests, serum electrolytes and amino acids, fats and vitamins profile and a complete blood count with platelets [31].

Conclusion

It is important to clarify that these preventive measures and drugs are used to reduce the occurrence of seizures. Nonetheless, these strategies do not influence in the epileptogenic process of the brain, meaning that both do not cure epilepsy or treat the reason why epilepsy has started. In some cases epilepsy can only be cured through surgery.

However prevention is the simplest, fastest and most effective way of preventing potential seizure causes. Also, medical treatment is relevant not only for decreasing the number of seizures but also for reducing the risk of head trauma and sudden unexpected death.

The main goals of the treatment in epilepsy is centered in the wellbeing of the patients and their reintegration in society, enhancing their quality of life. Let's fight side by side to achieve it!

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