Abstract

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

This article revolves around the strategies to prevent any potential epileptogenic lesion in the brain. 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 possible adverse effects.

The objective of the author is to convey the general knowledge about different prevention measures and therapeutics in epilepsy, get the attention of more healthcare providers in these topics and join forces in the medical guild to detect, refer, treat and follow-up the epileptic patients.

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 [5]. Thus, epilepsy is relevant due to its enormous impact around the world, being one of the most common neurological diseases globally.

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.

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Prevention

Head trauma is the most common cause of secondary epilepsy. Therefore, the use of helmets for sports and transportation is the main strategy. There is special case in elderly, who with a minor head trauma can develop epilepsy. They should be equipped with nonslip carpeting and handholds in appropriate places [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. Moreover, teenage pregnancies should be prevented in order to diminish the risk for premature and low weight infants. Finally, during the delivery, healthcare providers should conduct a secure procedure, which ensure adequate oxygenation for the newborn and avoid any head trauma [6,7].

Nervous systems infections also cause disturbances in the cytoarchitecture and the normal function of the brain. Having a 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 are 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 has a remission of the seizures with a single or a combination of antiepileptic drugs (AEDs) [8]. Several drugs can ameliorate specific cases of epilepsy. We should dedicate an entire chapter to talk about them, however, it will be tackle in future. Meanwhile, table 1 illustrates the AEDs with high level of evidence as the most recommended medications for each type of seizures and epileptogenic syndrome [9].

<table>
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<th>Seizure type or epilepsy syndrome</th>
<th>AEDs</th>
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| 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) |

*Table 1: AEDs level of evidence for each seizure type and epilepsy syndrome (Adapted from Glauser T, et al. Epilepsia, 2013).*
The choice of the AEDs should be tailored to the patients according to the health status, but following the scientific evidence of the safety and effectiveness for each drug.

Healthcare providers should have a special focus on certain social groups, such as children, elderly and pregnant women, because medication can harm the neurodevelopment in newborns and children, and the elderly may present more often adverse effect or drug inefficiency due to liver and/or renal disfunction [9].

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

**Epilepsy surgery and stimulation techniques**

Unfortunately, 30% of the patients falls on a drug resistant epilepsy, which is defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules to achieve sustained seizure freedom [12]. There are two approaches that control the seizures for the 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 responsible of the TLE is the hippocampal formation. The cytoarchitecture features of this structure and the disruption on the regulation and activation exert by other brain areas over the hippocampus generate excitotoxicity. In addition, there is a liability of the hippocampus to be damaged for small changes in the oxygenation, or it also suffers big structural abnormalities described as neural sclerosis and gliosis, both scenarios 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 quadrantanopia 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 [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 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 transection consists 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

Novelty stimulation techniques are implemented in patients with several types of intractable seizures. Vagus Nerve Stimulation (VNS), responsive direct brain stimulation (or response neurostimulation device; RNS) and Deep brain Stimulation (DBS) belong to the palliative approaches too. Nonetheless, they offer a modulated and adjustable stimulation control by the patient and the healthcare providers. Furthermore, the adverse effects are minimal and can be diminished as the parameters of the stimulations also change. Interestingly, this technology allows to give an extra burst of stimulation when the patient is aware of when a seizure happens, swiping a magnet over the generator of these devices.

The 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. VNS modulates 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 to have antiepileptic effects [26].

The 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. Additional to the patient control of the device, the electrodes detect electrocorticographic epileptogenic patterns and send an extra 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 [27].

The 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 due to its big size, its distance from vascular structures and its 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 [28].

A novelty incursion of the Transcranial Direct Current stimulation (TDCs) among the stimulation techniques was established recently. 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 [29]. 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 [30].

Conclusion

Along this work, a variety of preventive strategies and treatments were tackled. The main reasons for the author to briefly describe them is (i) to show to readers the existence of these strategies and approaches, (ii) generate interest in the topic and (iii) encourage people to search and learn more about epilepsy.

The creation and transmission of the knowledge should be on benefit of the patient. Prevention is the cheapest, easiest and the most accurate way to avoid the possible causes of epilepsy. For this action, we must make an effort to implement straightforward schemes that the general population can follow, having an excellent attach to them.

The main goal of the treatment in epilepsy is centered in the reintegration of the epileptic patients in society, enhancing their quality of life. Let’s fight side by side to achieve it!

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