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A Comparative Review on Epilepsy and its Treatment Options

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ABSTRACT

In today's fast-paced society, individuals are subjected to numerous forms of stress, and the majority of the world's population suffers from various neurological disorders. The imbalance of excitatory and inhibitory neurotransmitters is one of the mechanisms driving epilepsy. Epileptic seizures can cause loss of awareness, tremors, disorientation, difficulties reacting, and visual or other sensory symptoms, depending on which parts of the brain are implicated. The usage of benzodiazepines, barbiturates, and ion channel modulators in the treatment of epilepsy was categorised depending on the place of origin and symptoms. Allopathic treatment should typically begin with a single antiepileptic medication. Ayurvedic treatment approaches include purifying measures such as therapeutic purgatives and pacifying therapies such as single herb and polyherbal formulations. The review's goal is to look at pathogenesis, epilepsy categorization, signs and symptoms, allopathic and Ayurvedic medicine therapy, and future trends in epilepsy.

Key words: Epilepsy, Seizures, Allopathic treatment, Ayurvedic.

1. INTRODUCTION

Epilepsy comes from the Greek word epilambanein, which means "to assault" or "to seize." Epileptics were supposed to be visited by demons or gods in the past. Hippocrates, a Greek physician who lived around 400 B.C., believed that epilepsy was a brain ailment, and he was correct. [1] Epilepsy is a persistent neurological condition that can cause long-term alterations in the brain circuitry, even if it occurs only occasionally. Comorbidities, such as mental and cognitive deficits, are common in this disease.[2] Epilepsy affects up to 1% of the population, making it the most frequent neurological disorder after stroke.[3] Epilepsy affects around 50 million individuals globally, with 90% of them living in underdeveloped nations.[4] In recent years, the public's opinion of epilepsy has improved in various ways. It is a common chronic neurological illness characterized by recurring unprovoked epileptic seizures as the balance between brain excitability and inhibition shifts toward uncontrolled excitability. [5, 6, 7]

Seizures come in a variety of forms, each with distinct behavioural and electrophysiological manifestations that can generally be identified in scalp electroencephalographic (EEG) recordings.[8] A seizure is a brief epileptic episode that occurs when brain activity is disrupted. A single seizure may not always indicate that someone has epilepsy.[8, 9] 10% of individuals will have a seizure at some point in their lives.

The duration of a seizure might range from a few seconds to many minutes. Convulsions, loss of consciousness, blank gazing, lip smacking, and jerking motions of the arms and legs are only some of the signs and symptoms that patients and health care workers may not identify.[10] The onset, middle, and end of a seizure are all distinct.

2. PHASES OF SEIZURES

Four phases of a seizure can be distinguished.

a) Prodromal phase: This phase begins a few hours or even days before the seizure itself and should not be confused with the aura. Headache, sleeplessness, irritability, sadness, poor temper, or increased activity are all signs of the prodromal phase.

b) Aura: By seconds or minutes, this period precedes the seizure. The seizure episode is just getting started. Extreme terror, odd epigastric sensations, hallucinatory experiences, foul odours, and other sensations are all examples of aura emotions. The aura phase is vivid in the patient's mind.

c) Seizure (ictus phase): There is a loss of consciousness in practically all seizures, and the patient may be unable to provide any information regarding the ictus.

d) Post-ictal phase: This phase may or may not exist, or it may extend for several hours, or even days. Deep sleep and waking up with weariness, headaches, muscle pains, bewilderment, irritability, or ataxia are some of the symptoms. Transient paralysis can last anywhere from a few hours to days. [11]

2.1 Classification

There are three main types of seizures: partial, generalized, and unclassified. [9]

2.1.1 Partial Seizures (seizures begin locally)

A. Simple (without impairment of consciousness) with motor symptoms

- with psychic symptoms
- with psychic symptoms.

B. Complex (with impairment of consciousness)

• Impaired consciousness at onset with or without automatisms

• Simple partial onset followed by impairment of consciousness with or without

C. Secondarily Generalized (partial onset evolving to generalized tonic clonic seizures)

2.1.2 Generalized seizures (bilaterally symmetrical and without local onset)

2.1.3 Unclassified Seizures

2.1.4 Status epileptics

3. PATHOPHYSIOLOGY

The cerebral cortex manifests itself in paroxysmal seizures. When the excitatory and inhibitory forces within the population of cortical neurons become suddenly imbalanced, a seizure results. A volatile cell membrane or its surrounding/adjacent supporting cells are used to identify the fundamental physiology of a seizure event. The seizure starts in any cortical or subcortical location with a grey count. To begin with, certain neurons fire improperly in a tiny number of cases. Normal membrane conductance, inhibitory synaptic contemporary breakdown, and excess excitability might manifest locally, resulting in a focal seizure, or more widely, resulting in a generalised seizure. This onset spreads via physiologic pathways to encompass places in close proximity to far-flung locations.

A change in potassium conductance, a disease of the voltage-gated ion channels, or a lack of membrane ATPases involved in ion transport can all cause neuronal membrane to become volatile and cause a seizure. Certain neurotransmitters (e.g., histamine, peptides, acetyl choline, glutamate aspartate, cytokines, corticotropin freeing factor, norepinephrine, purines, and steroid hormones) increase neuronal excitability and propagation, whereas GABA and dopamine decrease neuronal excitation and propagation.

The need for blood float to the mind increases during a seizure to take off CO and to provide substrate for metabolic interest of the two neurons. As the seizure progresses, the mind experiences more ischemia, which can lead to neuronal loss and mental damage. [12]

Some types of epilepsy are linked to mutations in a number of genes. The generalised epilepsy and infantile seizures disorders have been linked to genes that code for protein subunits of ligand-activated ion channels and voltage sensitive.[13] Seizure awareness is located inside the temporal lobe in psychomotor epilepsy. [14]

3.1 Signs and Symptoms of Epilepsy [15]

3.1.1 Generalised

- All parts of brain affected
- Tonic: clonic Motor, consciousness Tonic and clonic convulsions, loss of consciousness

- Myoclonic: Motor Jerking limbs

3.1.2 Partial

- Frontal lobe Motor Twitching, jerking
- Temporal lobe Sensory Smells, epigastric sensation & any other sensations.
- Behaviour Psychiatric
- Parietal lobe Sensory Tingling etc.

3.2 Management and Treatment

3.2.1 Management of Epilepsy by Allopathic medicine:

The phrases anticonvulsant and antiepileptic are interchangeable. Anticonvulsants inhibit artificially caused seizures in laboratory animals, whereas anti-epileptic drugs are used to treat epilepsies in humans.[16]

3.2.1.1 Principles of management:

- Patients should be informed about the condition, the length of therapy, and the need of adherence.
- Any factor that causes epilepsy, such as a brain tumour, should be addressed.
- Expect natural variation; for example, attacks may occur more frequently or solely around menstruation in women.
- Avoid inciting conditions like alcohol and sleep deprivation while precipitating. stress on the mind
- Only use the antiepileptic if the kind of seizure and frequency warrant it, which means more than one modification every 6-12 months.[17]

3.2.2 Allopathic treatment of epilepsy

A single anti-epileptic drug should be used to begin treatment (AED). Until seizure control is obtained, the dosage should be progressively raised. If the first therapy is unsuccessful, a second AED can be used. The second drug's dose is gradually raised until the maximum tolerable dose is reached. If the first medicine is unsuccessful, the second drug is progressively withdrawn, and then combination therapy is tried. "Conventional" or "first-line" medicines include phenytoin, phenobarbitone, carbamazepine, oxcarbazepine, and valproate. Other AEDs, such as vigabatrin, topiramate, and zonisamide, are referred to as "second-line" or "new" medicines. It is advisable to start with a traditional AED because they are less costly and have less adverse effects. When the first line medicines are contraindicated, newer AEDs can be administered instead.[15]

3.2.3 Management of epilepsy by Ayurvedic drug

Apasmara is a type of disease that affects both the mind and the body. The aetiology of Apasmara is described as eating unwholesome and unclean food, engaging in harmful behaviours, suppressing mental attributes reflecting purity, and disrupted Dosha (humour) balance all have a part in the manifestation of the disease.[21] It is categorised as Vattaja, Pittaja, Kaphaja, and Sannipataja based on the prominent Dosha (humour) involved in its pathophysiology and clinical presentation of epilepsy. These techniques might be regarded palliative and curative in nature, bringing the body back to a physiological state from a diseased one.

4. CONCLUSION

Epilepsy is a neurological disorder that mostly affects the central nervous system. It has an impact on one's physical, psychological, family, and professional lives. As a result, anticonvulsant medication is chosen largely for its efficacy in treating certain types of epileptic seizures and epilepsy. Despite early and appropriate daily therapy with a sufficient anticonvulsant medication, a significant number of individuals with epilepsy suffer from intractable or drug-resistant epilepsy. Excessive firing of excitatory neurotransmitters and a reduction in inhibitory neurotransmitter activity characterize epilepsy. Epilepsy is best treated with benzodiazepines, barbiturates, and ion channel modulators. If seizures are not controlled with monotherapy, polytherapy is a recommended treatment for epilepsy in Ayurveda, which includes pharmacological and non-pharmacological measures with many herbal, herbo-mineral formulations in different dosage forms with a variety of techniques to provide good control of seizures for most people with epilepsy.

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Table 1: Mechanism of Anti-epileptic drugs [18, 19, 20]

S. No.	Drug	Mechanism of action
1	Carbamazepine	Suppress seizure spread. Inhibit voltage gated sodium channel.
2	Clobazam	Binds and activates GABAA receptor which increase the frequency of Cl-channel opening.
3	Diazepam	Binds and activates GABAA receptor, which increase the frequency of Cl-channel opening.
4	Ethosuximide	Inhibition of T-type calcium channels.
5	Felbamate	Increases intracellular Ca2+and blocks excitatory postsynaptic potentials.
6	Gabapentin	Enhances GABA release.
	Lamotrigine	Blocks sodium channels. Presynaptically, it inhibits the release of excitatory amino acids. Postsynoptically, it diminishes the excitability of neurons.
7	Levetiracetam	Enhances the release of inhibitory neurotransmitter.
8	Oxcarbazepine	Inhibits voltage-dependent fast sodium channels. Hyponatremia, sedation, dizziness.
9	Phenytoin	Enhances the release of inhibitory neurotransmitter.
10	phenobarbital	Binds and activates GABAA receptor which increase the frequency of Cl-channel opening.
11	Sodium valproate	Prolongation of Na+ channel inactivation and augments release of GABA.
12	Tiagabine	Inhibits GABA uptake.
13	Topiramate	Potentiation of GABAA receptor-mediated currents.
14	Vigabatrin	Inhibits GABA-transaminase and increase synaptic GABA concentration.
15	Zonisamide	Blockade of sodium channels, reduction of voltage dependent calcium currents and glutamate induced synaptic excitation.

Table 2: Herbs having anticonvulsant activity for the management of Epilepsy described in Ayurveda [22, 23]

Common Name	Plant Name	Active Principle	Mechanism of Action and activity
Clove	*Eugenia caryophyllus* Myrtaceae	Eugenol, acetyleugenol, β-caryophyllene, vanillin, crategolicaci, tannins, gallotanic acid methylsalycylate, flavonoids, eugenin, kaempferol, rhamnetil, eugenitin & triterpenoidslike oleanolic acid.	Increases onset of convulsions. Reduce duration of convulsions. Delay onset on seizures. Increase GABAergic and glycinergic activity.
Coconut	*Cocos nucifera* Arecaceae	Monounsaturated fatty acids, Saponins.	Inhibit PTZ induced convulsions. Increase GABA level, serotonin level.
Karkandu	*Zizphus jujube* Rhamnaceae	Flavonoids, saponins, tannins, vitamin A, vitamin B, sugars, mucilage, calcium, phosphate & iron.	Anticonvulsant action
Lotus	*Nelumbo nucifera* Nelumbonaceae	N-nornuciferine, O-nornuciferine, nuciferine, and roemerine, protein, amino acids, unsaturated fatty acids, minerals, starch, and tannins.	Decrease tonic extensor convulsions. Anticonvulsant action
Mango	*Mangifera indica* Anacardiaceae	Polyphenolics, triterpenoids, mangierin, catechin, iso-mangiferin, alanine, glycine, γ-aminobutyric acid, kinic acid	Inhibit PTZ and MES induced convulsions, increases GABA levels, Anticonvulsant action.

Musta	*Cyperus rotundus* Cyperaceae	Cyperone, selinene, cyperene, cyperotundone, patchulenone, sugeonol, kobusone and isokobusone, pinene (monoterpene) derivatives of sesquiterpenes such as cyperol, isocyperol and cyperone.	Anticonvulsant action.
Nagkesara	*Mesua ferra* Calophyllaceae	Sesquiterpene, diterpenes, triterpenes, carboxylic acids and saturated hydrocarbons	Reduce HLTE. Inhibit MES induced convulsions. Increases the onset time of seizures and decreases the duration of seizure.
Nutmeg	*Myristica fragrans* Myristicaceae	Myristicin and Macelignan	Inhibit seizures and uses the severity of seizures.
Saffron	*Crocus sativus* Iridaceae	Crocetin, picrocrocin, safranal, isophorone	Increases seizure threshold, block PTZ induced convulsions, increases GABA-ergic neurotransmission, Inhibit absence seizure, Improve tonic clonic seizures.
Spikenard	*Nardostachys jatamansi* Caprifoliaceae	Valeranone, Calerene, patchouol, α-gurjunene, aristolone, β-maalien, spathulenol	Increases seizure threshold, inhibit the electroshock convulsions Increases GABA, 5-HT, 5-HIAA.
Sesame	*Sesamum indicum* Pedaliaceae	Propanone, ethanone	Decrease ROS, MDA in epileptics
Sway	*Acorus tatarinowii* Schott Acoraceae	Essential oils and asarone	Prevents convulsion related GABA -ergic neuron damage in the brain, Neuro protective aginst N-methyl-D-aspatate or Glu-induced excitotoxic neuronal cell, Receipting-binding assay act as specific binding to striatal dopamine D1 and D2 receptors
Tagara	*Valeriana wallichi* Caprifoliaceae	Valerian, valipotriates GABA sesquiterpene, diterpenes, triterpenes, carboxylic acids and saturated hydrocarbons	Sedative action. Decrease HLTE. Anticonvulsant activity.

Table 3: Ayurvedic Formulations used for the management of Epilepsy [24-31]

S. No.	Formulation	Name of formulation	Mechanism of action and activity
1	Arka	Rasonadi Arka.	As adjuvant drug
2	Aasava-Arista	Aswagandharista	Antipsychotic drug Especially for epilepsy.
		Saraswatarista	Intellect promoting &Antipsychotic drug.
3	Avaleha	Chandravaleha	Epileptic effect
4	Churna	Saraswata	Nootropic and cognition enhancer.
		Jatamansi	Sedative and anxiolytic effect.
		Aswagandha	-

		Sarpagandha	Used in hysterical fits, insomnia
5	Ghrita	Panchagavya	Controls the frequency of convulsions and Duration of convulsions. It can be given for a long duration of time in therapeutic dosage without the fear of any side-effects.
		Kushmanda	Increases memory and reduces stress.
		Brahmi	Reduces the extensor tonus phase of convulsion in their standard doses, as a Shamana Sneha provided significant relief in severity, frequency of attack, salivation, pre and post ictal features in comparison to other groups. Brahmi Ghrita in the form of Brumhana Sneha shown better relief in duration of attack and impaired higher mental functions.
		Mahapancha gavya	Especially for epilepsy and it controls the frequency of convulsions. Mahachaitasa Contents are Jeevaniya Dravyas which plays Rasayana effect on body and also effective for cognitive development of patient. Specially for insanity & epilepsy.
6	Kwatha	Manasyadi	Used in hysterical fits.
		Dasamula Kashaya	Used as anupana in Apasmara along with Kalyanaka Ghrita.
7	Rasausadhi	Chaturbhuja rasa	Anticonvulsant effect.
		Smritisagara rasa	Intellect promoting, reduces the stress.
		Unmada Gajakesari	Antiepileptic activity after prolonged administration and also balances the excitatory and inhibitory neurotransmitters in CNS, the main action being GABAergic action and additional antioxidant activity of herbs.
		Tantupashana	Tantupashana is affective against MES seizures in animals and it may be useful in generalized tonic clonic seizures/grandma epilepsy in human beings.
		Kausheyashma Bhasma	Useful in Epilepsy.
		Apasmarari rasa	Act as an anti-convulsant drug, on MES animal model of convulsion preceded by LD 50 determination. It also has some significant result when compared to other drugs like Phenytoin and Samritisagar rasa.
8	Taila	Bala Taila	For external application, Apasmaram pranashayet
		Shatavari	It predominantly Vata Shamaka, have Anulomana (carminative) property. The drug as a whole is Medhya & Rasayana. Considering all these properties, the drug acts on the mind and exhibits anticonvulsive activities.
		Shirisha	Apasmaramhanyat.

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