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RESEARCH ARTICLE

A CRITICAL REVIEW OF KUSHMANDAGHRITAIN THE MANAGEMENT OF GENERALIZED TONIC-CLONIC SEIZURES

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Abstract

Epilepsy is a chronic disorder characterized by the appearance of frequent seizure episodes associated with a diverse group of symptoms. Generalized tonic-clonic seizure is the most common type of motor seizure usually associated with impaired awareness or complete loss of consciousness. Despite all the available medications one third of the people with epilepsy still seems to be severely affected. Management of Epilepsy still remains a challenge to the medical community. Therapeutic add-ons to the mainline antiepileptic drugs might help in overcoming this challenge.Kushmanda ghrita[1]is one of the simple formulations described in Ashtanga Hridaya for the management of apasmara (epilepsy).This review focuses on the comprehensive management of generalized tonic-clonic seizure with a unique formulation Kushmandaghritapracticed sinceageoldd.

Introduction:-

Epilepsy is a highly prevalent heterogeneous neurological disorder characterized by recurrent seizures.Generalized tonic-clonic seizures (GTCS)are the most common type of motor seizures that presents with bilateral symmetrical tonic contraction, followed by bilateral clonic contractions of somatic muscles, often accompanied by autonomic phenomena.[2]Nearly 50 million people are affected worldwide with a prevalence rate of 5–10 per 1000 people[3]. Developing countries contribute up to 90% of the overall 70 million diagnosed cases of epilepsy worldwide. Out of which one-sixth of the global burden i.e., 12 million cases are seen in India.The rate of social stigma and discrimination pertaining to this disease is still prevalent worldwide.[4]

Pharmacotherapy of epilepsy includes the use of antiepileptic medications like sodium valproate, carbamazepine, levetiracetam, topiramate, etc. Although the seizure control activity of antiepileptic drugs (AED) is evident, about one-third of patients are showing an inadequate response to these medications[5] and still continue to have attacks of seizures.[6]Long-term use of AEDs is frequently associated with cognitive, neurological, and electrolyte disturbances therefore it is necessary to develop safe and effective alternative therapies for the management of epilepsy. Management of Epilepsy still remains a challenge to the medical community due to various factors like non-adherence to current medication, adverse drug reactions, decreased quality of life, and decreased efficacy of monotherapy associated with various comorbidities.[7]More numbers of people with epilepsy believe in

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Complementary and Alternative Medicine (CAM) and its usage is becoming highly prevalent. Therapeutic add-ons to the mainline antiepileptic drugs may be an option to overcome this challenge.[8]

According to Ayurveda, the symptoms of generalized tonic-clonic seizures can be correlated to that of Apasmara lakshana. Apasmara is defined as Apagama (derangement) of Smrti associated with Tamah Pravesha (transient loss of consciousness) and Bibhatsa Chesta (loathsome expressions) due to affliction of Dhi and Satva. Apasmara is a disease that is explained in ancient history with a mythological and mysterious background. Kushmanda ghrita[9] is one of the simple formulations described in Ashtanga Hridayafor the management of apasmara(epilepsy). It is explained as the best medicine for curing epilepsy in Yogaratnakara. Kushmanda (Benincasa hispida) is also mentioned as one of the medhya drugs in the Ayurvedic literature.[10]

Understanding of GTCS in Ayurveda

Seizure is derived from a Latin word that means 'to take possession of'.An epileptic seizure is a transient occurrence of signs and symptoms due to abnormal excessive or synchronous neuronal activity in the brain.[11]This central nervous system (CNS) dysfunction results in various manifestations, ranging from dramatic convulsive activity to experiential phenomena which are not readily discernible by an observer.

Generalized tonic-clonic seizure is a type of generalized onset motor seizure where equal involvement of both the hemispheres is present. This seizure represents a classic picture of epilepsy among the public. The main specialty of GTCS is its onset with loss of consciousness, a cry, generalized tonic muscle contraction, and falls often associated with some autonomic signs including tachycardia, hypertension, cyanosis,salivation,sweating, and incontinence. A single generalized grand mal seizure does not warrant the diagnosis of epilepsy.

Apasmara is a disease in which the faculty of past cognitions is hampered temporarily. It is explained as antakrit according to Sushruta.Dalhana describes it as the disease during the attack in which smrti (memory) is lost.[12]According to CharakaApasmara implies loss of memory, characterized by loss of consciousness, Tamah Pravesha(entering into darkness), and distorted movement of limbs caused by derangement of intellect and mind. Smriti, buddhi, and satva samplavana (vibhrama or perversion) occur during apasmara.[13]GTCS is a vata pradhana tridoshaja apasmaracondition with vata and raja predominant stage in the ictal phase whereas kapha and tama predominant in the initial preictal stage and a kapha pitta involvement in the post-ictal phase.

Table 1:- Comparison of stage-wise sign symptoms of apasmara and Generalized Tonic-Clonic Seizure.

Seizure phase	Clinical features	Apasmara stage and Dosha involvement
Pre ictal phase	Abrupt loss of consciousness Without aura	Tama pravesha(Kaphaja)
Ictal phase	**Tonic phase:** Ictal cry, stiffness, cyanosis, Fall **Clonic phase**: Convulsions, Jerking movements,Bladder or bowel incontinence,tongue bites,drooling	Bibhatsa cheshta: VishamaVinanatanguli HastaPadaVikshepana Dantha dashana, Phenodvamana Udgamantam Phenam (vataja)
Post ictal phase	Somnolence, Headache, Confusion, Agitation,lethargy, disorientation, and myalgia	Dhisatvasamplava,Nidrartha Cittanasha (Kapha pittaja)

Pathophysiology of GTCS[14]

There occur mainly two phases in seizure pathology i.e., seizure initiation and propagation. The initiation phase is characterized by high-frequency surges of action potentials and hyper synchronization. The former is caused by a comparatively enduring depolarization of the neuronal membrane due to the influx of extracellular calcium (Ca2+), which leads to the opening of voltage-dependent sodium (Na+) channels, the influx of Na+, and the generation of repetitive action potentials. This is followed by a hyperpolarizing after potential mediated by GABA receptors or potassium (K+) channels, depending on the cell type.

Other neuronal mechanisms involved in the pathology are:

1. Increase in extracellular K+, which blunts hyperpolarisation and depolarizes neighboring neurons

2. Accumulation of Ca2+ in presynaptic terminals, leading to enhanced neurotransmitter release
3. Depolarization-induced activation of the N-methyl-D-aspartate (NMDA) subtype of the excitatory amino acid receptor, which causes additional Ca2+ influx and neuronal activation
4. Emphatic interactions related to changes in tissue osmolality and cell swelling.

Samprapti of apasmara can be categorized into two stages apasmara vega kaleenasampraptii.e., the process taking place during the time of seizure episode, and apasmara roga samprapti (chronic disease pathology).Due to Ahita and ashuchi bhojana shareerika dosha dushti will occur and chinta kamadi nidanas causes manasika dosha dushti leading to vitiation of raja and tamas, as well as manoabhighata. This leads to apasmara vega where the satva guna is hampered by raja and tamas afflicting the chetana sthana hridaya. When the mind gets deranged by obstructions of the sanjnavaha srotas lakshana of apasmara are shown.

Gjnanotpatti according to Ayurveda is a sum total of roles played by atma, mana, indriya, indriyartha along with the balanced state of shareerika doshas. Considering the etiopathogenesis of apasmara the mechanism of neurotransmission has a close resemblance with the process of jnana grahana i.e., vata is the prime controller of mind, all the neuronal activities can be correlated as an interplay of vata. Neuronal excitation is controlled by vata as well as rajas whereas inhibition is regulated by kapha as well as tamo dosha.Smriti is also an integral component that overlaps with many higher intellectual faculties including memory, cognition, perception, etc. Apasmara mainly affects the process of indriyarthasannikarsha where smriti is hampered for a short period of time. There occurs a transient detachment from the original sense of awareness due to the involvement of tamas.

Role of Kushmanda Ghrita in GTCS Management

Kushmanda ghrita mentioned as the best apasamarahara yogaconsists of mainly three drugs such as Kushmanda(Benincasa hispida (Thunb.) Cogn), Yashtimadhu(Glycyrrhiza glabra L.), and goghrita (cow ghee).KushmandaGhrita[15]has wide therapeutic activities like Deepana, Pachana, Akshepakahara, Sanjnasthapaka, Sroto Shodhaka, Smrti Vardhaka, Balya, Rasayana, Medhya, etc. Kushmanda ghritais one of the simple formulations described in Ashtanga Hridaya, apasmarapratishedha, and is widely practiced by Ayurveda physicians as an alternative or complementary therapy with AED in clinical settings.According to Acharya, Bhava Mishra, Kushmanda is having vatapittahara and raktashamaka property.Kushmanda and yashti madhu on samskara with ghrita act on mastishka majja thereby improvedhee, dhriti smriti, also promotes the strength of nerves (nadi balya).Yashti madhu is one among the medhya rasayana explained by AcharyaCharaka,exhibits neuroprotective action which helpsin improving components of cognition,emotional wellbeing, and overall quality of life in patients with seizures. Overall properties of Kushmandaghritaaremadhurarasa,guru,snigdhaguna, sheetaveerya, and madhuravipaka. It mainly acts on prana udana vata, sadhaka pitta as well it nourishes the tarpakakapha which in turn, augments memory and intelligence.

Ghrita having samskarasaya anuvartana property inculcates all the effects of both Kushmanda as well as yashti and gives a synergistic effect. Ghrita is considered the best remedy for Pittaja diseases. Dhee, Dhriti, Smriti,and Buddhi are one of the properties of Pitta; which is vitiated in Apasmara. Pittadharakala is directly or indirectly related to the majja dhatu. Hence this Ghrita kalpana acts on majja dhatuwith a curative effect on GTCS.

Comparison of Kushmandaghrita with the action of conventional AED

Antiepileptic drugs appear to act primarily by blocking the initiation or spread of seizures. This occurs through a variety of mechanisms that modify the activity of ion channels or neurotransmitters.The major mechanisms include inhibition of Na+ -dependent action potentials and voltage-gated Ca2+ channels, Potentiation of GABA receptor function, increase in the availability of GABA, or modulation of release of synaptic vesicles.

Experimental studies have proven that Kushmandaswarasa (fruit extract)has antioxidant activity on the human brain.[16]Vitamin –B present in Kushmanda has a direct impact on energy levels, brain functioning, and cell metabolism. It also reduces fatigue and boosts mood. The seeds of Benincasa hispida (Thunb.)Cogn is enriched with GABA and helps in seizure control action.

Yashti madhu is one of the medhyarasayanadravyasthat contains the active ingredient glycyrrhizin, a triterpenoid compound,which accounts for the sweet taste. It has the capacity to alter the activity of ion transport processes including ion channels and inhibition of Na+ -K + -ATPase.[17]This will block the voltage-gated Na+ channels that remain open due to repetitive neuronal firing.

The antioxidant and neuroprotective effect root of Yashtimadhu protects susceptible brain cells from oxidative stress resulting in reduced brain damage and improved neuronal function with improvement in memory.

Ghrita as a medium induces the process of ketosis. The ketone bodies, β- hydroxybutyrate, aceto-acetate, and acetone are synthesized and are able to cross the blood-brain barrier to provide an alternative source of energy for the brain.[18]As compared to the conventional AEDs a similar action can be obtained through this synergism present in Kushmanda ghrita. Kushmanda ghrita is a unique combination that can be practiced in conditions of chronic cases of GTCS and it also acts as a rasayana.

Action of ghrita kalpana in seizure inhibition

Snehapana is the treatment modality followed in the management of neurological disorders including neurodegenerative disorders. The type of fatsused in clinical practice is oil and ghee. Ghee preparations are consideredthe foremost medium for delivering the active principles in neurologicalconditions affecting the brain because of their ability to cross the blood-brainbarrier. Ghee is considered yogavahi since it will carry the active principles of the processed drugs to the target tissue, also it will act as medicine by itself with itsinnate property. Ghee obtained from cow's milk consists of short-chain andmedium-chain fatty acids. Ketone bodies produced as a secondary metabolitefrom fat metabolism are proved to be having anticonvulsant activity.[19]The neuroprotective effect of ketone bodies is explained using the antioxidantactivity, an alternate source of energy, especially during a low carbohydrate diet.This potential of the ketone body is used in the keto diet by the conventionalsystem of medicine for the treatment of epilepsy.

Conclusion:-

Kushmanda and yashtimadhu have properties like Madhura,Guru,snigdha,Sheetaveerya,and Madhura vipaka on samskara with ghrita act on mastishka majjahelps in improving dhee dhriti smriti and alsosubside thevata affected in the mahamarma.This reduces the episodes of apasmara.Mano abhitapa caused by nidanas such as chinta, shoka, bhaya,etc is one of the major reasons for acute onset seizures. As all the three drugs present in Kushmanda ghrita are medhya and Kushmandaactaschetovikaranashaka.The GABAergic property of kushmanda, Na+ K+ channel inhibition property of yashtimadhu, and the ketogenic effect of ghritaact as a perfect trio in generalized tonic-clonic seizure management and thereby highlighting its uniqueness.

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