

## CONCEPT OF MEDICATED GHEE (*GHRITA KALPANA*) IN THE MANAGEMENT OF CHILDHOOD EPILEPSY (*APASMARA*)

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### ABSTRACT

Epilepsy is defined as a disorder of the brain characterised by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological and social consequences of this condition. *Apasmar* (seizure disorder/ Epilepsy) is the disease in which the recalling power (*Smaranshakti*) gets vitiated / affected. Most of the clinical presentation of *Apasmar* resembles with Epilepsy/Seizure disorder. Ancient *Ayurvedic* scholars have described many drug preparations to combat with *Apasmar* in the form of Ghee/Oil (*Snehakalpana*); the *Ghrítikalpána* (Ghee boiled with various medicinal plants) is one of these. Various *Ghrítikalpána* are used to combat with seizure along with the adverse effects of synthetic antiepileptic drugs (AEDs); which showed positive results as well as maintenance of good general health. Intractable or refractory epilepsy is defined by inadequate control of seizure despite optimal treatment with conventional medications. The ketogenic diet had shown dramatic seizure control effects in such patients. Ayurveda's basic principles of disease management includes the dietary measures along with the medication; fasting (*Langhan*) and *Ghrítikalpanas* (medicated Ghee preparations) are one of them. Dramatic improvements in seizure frequency after a period of fasting (*Langhan*) & *Ghrítikalpanas* (medicated Ghee preparations) induced ketone bodies had been noted. Various Ancient scholars advised various *Ghrítikalpanas* for the management of *Apasmara* (Epilepsy) in different *samhitas*. Management of Seizure disorder with AEDs along with *Apasmaraghna Ghrítikalpána* (ketogenic diet) as adjuvant seems to be more beneficial. Hence the therapeutic as well as the biochemical, patho-physical changes by *Apasmaraghna Ghrít* are highlighted in this manuscript.

**KEYWORDS:** Seizure disorder, *Apasmaraghna Ghríta kalpána*, *Apasmara*, *Ghríta*, Ketogenic diet, Epilepsy.

### INTRODUCTION

Seizures are the commonest paediatric neurological problem, by themselves or as manifestation of many underlying problems. The disease in which the recalling power (*Smaranshakti*) get vitiated/affected that is called *Apasmara* (seizure disorder/ Epilepsy).<sup>1</sup> Most of the clinical presentation of *Apasmar* resembles

with Epilepsy/Seizure disorder. There are number of synthetic drugs available for treatment of Epilepsy/Seizure disorder; but having major disadvantage of their chronic side effects. There are many drug preparations are described in *Ayurvedic* literature by *Acharyas* in the form of Ghee/Oil (*Snehakalpána*); the *Ghrítikalpána*

(Ghee boiled with various medicinal plants) is one of these.<sup>3,5</sup> *Ghritkalpana* is used to control of seizures or adverse effects of antiepileptic drugs (AEDs) as well as for the maintenance of general health. Intractable or refractory epilepsy is defined by inadequate control of seizure despite optimal treatment with conventional medications. Over the last decades, the ketogenic diet has gained popularity as another treatment option for this group of patient.<sup>4</sup> Dietary measures have been described for the treatment of seizures/epilepsy since ancient times. There are dramatic improvements in seizure frequency after a period of fasting induced ketone bodies. *Langhan* (fasting) & many *Ghritkalpanas* (Ghee preparations) are indicated by Acharya's for the management of *Apasmar* (Seizure disorder/epilepsy) in different *samhitas*.<sup>1,2,3,5,9</sup> Management of Seizure disorder with AEDs along with *Apasmaraghna Ghrita kalpana* (ketogenic diet) as adjuvant seems to be more beneficial.

**Seizure:** a seizure is the clinical manifestation (i.e. signs & symptoms) of an abnormal excessive paroxysmal synchronous neuronal activity in the brain. This abnormal neuronal activity is conducted to the body and produces seizure. Seizures may be easy to manage, but often present a diagnostic or therapeutic dilemma. The types of seizures are depends on: area of the brain producing the discharge, type of discharge, age of the patient.<sup>4</sup>

Practically, epilepsy is a disease of the brain defined by any of the following:

1. At least two unprovoked seizures occurring more than 24 hours apart

2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (approximately 75% or more)

3. At least two seizures in a setting of reflex epilepsy.

**Pathophysiology<sup>4</sup>:** the pathophysiology of seizure is still not well understood. However recent researches showed that seizures are produced when there is an abnormality in the:

1. Neurotransmitter levels

2. Ion channels

3. Receptors

In many of the genetic epilepsies, there is abnormality of the ion channels or the receptors due to mutations, resulting in epilepsies. These abnormalities can result in hyper-excitability of neurons, which thus have a tendency to seizures. The other epilepsies result from neuronal damage because of various insults like infections, trauma and vascular events.

**Intractable or refractory epilepsy:** Intractable or refractory epilepsy is defined by inadequate control of seizure despite optimal treatment with conventional medications.

**Ketogenic diet<sup>31, 33</sup>:** the diet induces ketosis by high fat and low carbohydrate diet. Ketosis has an anticonvulsant effect in certain types of epilepsies. As many of the *Ayurvedic* management plans described by many Acharyas includes the preparations of *Ghritas* i.e. *Ghrita kalpanas*; which indicates the high ketogenic diet (*Ghrita*) is used as vehicle for various antiseizure *Ayurvedic* formulations. The ketogenic diet should be considered for patients whose seizures are refractory to anticonvulsants.

### GLUT-1 Deficiency:

Infants with GLUT-1 deficiency having seizure disorder were found to have low cerebrospinal fluid (CSF) glucose concentrations despite normal plasma glucose. Lactate concentrations in CSF were also low, suggesting decreased glycolysis rather than bacterial infection, which causes low CSF glucose with high lactate. The erythrocyte glucose transporter was defective, suggesting a similar defect in the brain glucose transporter responsible for the clinical features. A ketogenic diet reduced the severity of seizures by supplying an alternate source of brain fuel that bypassed the defect in glucose transport.<sup>6</sup>

### Vagal nerve stimulation<sup>4</sup>:

A device (the impulse generator) is implanted under the skin in the chest with a coil around the vagal nerve. It is activated in case of an impending seizure by passing magnet across it. The impulses generated stimulate the vagus nerve and control the seizure. Various anti-seizure Ayurvedic management plans include *Tikshnadravya / Apasmaraghna dravya siddha Ghrita Nasya* (medicated Ghee by nasal route), *Tadana chikitsa*<sup>17</sup> which can be considered as vagal nerve stimulation.

### AYURVEDA AND EPILEPSY/SEIZURE DISORDER<sup>28, 29, 30, 34</sup>:

The disease in which the recalling power (*Smaranshakti*) gets vitiated/affected that is called *Apasmara* (seizure disorder/ Epilepsy). *Acharya Charaka* and *Madhava Nidana* has described various causes and clinical features of *Apasmara*.<sup>5</sup> The management of *Apasmara* requires *Yuktivyapashraya chikitsa* (*Tikshna dravya Nasya, Ghrita kalpana Nasya, tikshna samshodhana* with various

*Ghritkalpana / Tailkalpana* and *Upashaman*) along with *Daiv-vyapashraya chikitsa*.<sup>5</sup> Out of which the *Ghrita kalpana* is one of major part of *Apasmara* management and *Aushadhi chikitsa*.

Ayurvedic Management focuses on the individual rather than just on their condition. According to Ayurveda, the same type of disturbance can result in different disorders, whereas the same disorder can result from different forms of disturbances/ imbalances. Ayurvedic medicine seeks to treat *Apasmara* (seizure/epilepsy) by unblocking the channels (*srotasas*) of the heart and the mind that may be clogged by the excess of *dushita-doshas / kleda / Aama* or humors. This opening of the channels is practiced using various concoctions and purgatives. The drugs to be taken orally are cooked with oils and ghee (purified butter) and, in addition, external oil applications, massages, and baths are also part of the treatment. There are several Ayurvedic treatments that have been used in the past to treat epilepsy and some that are still being used today. However, as mentioned before, the treatment selected for one patient with epilepsy may not be appropriate for another. Treatment modalities that include strong elimination purgatives are used to alleviate the symptoms, depending upon specific requirements, are mentioned as being useful for epilepsy patients. When epilepsy is associated with extrinsic factors, then mantras (hymns) and *Dhoopana* (fumigation) have been recommended. Using drastic emesis (*vatika apasmara*) and enema (*paittika apasmara*), the physician first takes steps for opening the channels of the heart and the mind that have been

blocked by *dushita-doshas* (humors). Drug formulations are recommended only after the patient has been cleansed by all means. A wide variety of ghratas (purified butter/ghee) have been recommended for internal use. One of the most important among these is *Maha-panchagavya ghrita*<sup>18</sup>. The use of mixtures of ghrita and taila (oil) cooked with drugs has also been mentioned. Oil cooked with different herbal medicines and animal products have been recommended for anointing the body of the patient. Even *Nasyas* (nasal applications) have been recommended. The use of a wide variety of *Anjanas* (eye applications) to bring the unconscious patient to his/her senses has also been mentioned. A variety of Ayurvedic medicines for epilepsy is available for example, *Asvagandha dyarishta*, *Bala taila*, *Brahmighrita*, *Chandanadi*, *Kalyanaka ghrita*, *Mahamrutyunjaya rasa*, etc.<sup>13</sup> In Ayurveda, the modes of administration of drugs for epilepsy include external application, internal use, and application in the eyes and nose. The only first-aid measure recommended in epilepsy is blood-letting (*siravyadha*) from the veins in adults<sup>19</sup> while it is rarely performed in pediatric age group. Cauterization of both parietal bones with needles (*soochivedha*) has also been mentioned.<sup>19</sup>

**GOGHRITA:**<sup>20,21,22,23,24</sup>

**Gana :** Madhura Skandha (Charaka)

**Properties:****Guna:** Snigdha, Guru; **Rasa:** Madhur; **Virya:** Sheeta; **Vipaka:** Madhura; **Dosha:** Tridoshaghna **Karma:** Rasayana, Vajikara, Rasavardhaka, Varnya, Ojavrudhi, Smrutivardhak, Agni and Indriya balya, Vataghna, Sanskaranuvartana, Sarva

SnehaUttama, Rasa Shukra Ojaheetakari, Varna Prasadankara, Rasayana, Kshaya, Raktavikarahara, emollient, Vrishya, Medhya and Vayasthapana.

**Chemical composition of Ghrita<sup>20</sup>:** Diglycerides, Monoglycerides, free fatty acid, phospholipids sterols, and vitamins A, D, E and K.

**Pharmacological Action of Ghee<sup>20, 21</sup>:**

It contains approximately 8% lower saturated fatty acids which makes it easily digestible. These are the most edible fat and which are not found in any other edible fat or oil. It contains vitamins, in which Vitamin A and E are antioxidants. Ghee resists spoilage by microorganisms or chemical action. The melting point of ghee is 350C which is less than the normal temperature of the human body. Its digestibility coefficient or rate of absorption is 96% which is highest of all oils and fats. Most Ayurvedic preparations are made with Ghee. Digestion, absorption and delivery to target organ system are crucial in obtaining the maximum benefit from any formulation. Since active ingredients are mixed with Ghee, they are easily digested and absorbed. Lipophilic nature of Ghee facilitates entry of formulation into the cell and its delivery to mitochondrion, microsome and nuclear membrane.<sup>22, 23</sup>

The colour of Ghee is yellow to white depending upon the carotene content. Ghee contains approximately 8% lower saturated fatty acid which makes it easily digestible. These lower saturated fatty acids are the most edible fat and which are not found in any other edible oil or fat.

Ghee also contains Vitamin A, D, E and K. Vitamins A and E are anti-oxidant and are

helpful in preventing oxidative injury to the body & brain. Vitamin A keeps epithelial tissue of the body intact; keeps the outer lining of the eyeball moist and prevents blindness. Ghee also contains 4-5% linoleic acid, an essential fatty acid, which promotes proper growth of human body.<sup>20</sup>

Lipophilic action of Ghee, they easily facilitate transportation to a target organ and final delivery, inside the cell, because cell membrane also contains lipid. This lipophilic nature of ghee facilitates entry of the various medicated Ghee formulations into the cell and its delivery to the mitochondria, microsome and nuclear membrane.<sup>22, 23</sup>

In the process of evaluating the activities of natural compounds, it has been found by means of sophisticated research that when herbs are mixed with ghee; their activity and utility is potentiated, many times.

## DISCUSSION

### Hypothesis behind action of Ghrita kalpana (various Apasmarghna Ghrita) on Apasmara (seizure/epilepsy):

Nose is the best route for administration of drugs for the diseases of brain and head (*Nasa hi shirasodwaram*<sup>25</sup>). There are some CNS disorders which require a constant concentration of medicine for curative and prophylactic measures. For direct delivery of medicine to brain it requires to pass blood brain barrier, nano form, volatile/vapour form; which can easily take up through mucus membrane of nose. The olfactory neural pathway provides both intra-neural (via axonal transport, a high time consuming process) and extra neural (via bulk flow transport, through peri-neural channels taking only few minutes) access to the brain.<sup>7</sup> Also an odour enriched environment

increases neurogenesis in adult mouse brain.<sup>8</sup> Ayurveda's basic principles state that the drug/diet is composition of *Panchabhautika* and their *matras* (*Shabda, Sparsha, Rupa, Rasa* and *Gandha*) which nourishes the body accordingly. Ghee also nourishes in the same way to *Panch-gyanendriyas* (five senses) accordingly.

*Nasya* involves intranasal delivery of dry herbal powder or medicated ghee/oils & is practical, non-invasive, rapid & simple method to deliver the therapeutic agents into the CNS.<sup>9</sup> *Nasya* is advised for various childhood disorders by various *Acharyas*; some of them claim by birth and some claim by 8 years of age for *Pratimarshya Nasya* as management.<sup>26</sup> Most of the components of *Apasmarghna Ghritas* enter into the CNS through intranasal route. These help in preventive & curative effect on seizure disorder (*Apasmara*) by stimulating the biochemical changes in the CNS.

The process of *Ghritakalpana* magnifies the advantage of the desirable medicinal phytochemicals and other healthy nutritional substances. *Ghrita* is also a great *Anupana/Vahak* (mediator) for the delivery of specific herbal medicines in various diseases. Ghee (*sneha*) is good for stimulating the gastric fire. If the gastric fire is stimulated (kindled) by the fuel in the form of *sneha* (ghee), then it cannot be suppressed by too heavy food.<sup>10</sup>

The *dhatu*s get vitiated in *Apasmara* are mainly *Rasa* and *Majja*<sup>29,30</sup>; *panchabhautikatva* is *Aapya* (*Jaliya*) of both of them. *Ghrita* (Ghee) which is also a *Jaliya* (*Aapya*) *dravya*; by *Samanya-Visheshsinddhanta Ghrita* increases the qualitative and quantitative *Rasa* &

*Majjadhatu*. The medicated ghee also works on *Aksivit* (eye secretions) and *Tvaksneha* (sebum) as these both are *malas*(wastes) of *Majjadhatu*.<sup>10, 11, 28</sup> Ghee contains Vit A which nourishes the eye proves that.

The *kala* (layers) that obtain between *amashaya* and *pakvashaya* is known as *pittadharakala* and the part of the *kostha* where it obtains is spoken as the *grahani*. The main function of *Grahani* is to support the *pachaka pitta* which is required for the digestion of food brought to this part of *kostha* on its way to *pakvashaya*. *Ghrita* is considered a best remedy for *Pittaj* diseases. *Dhee, Dhruiti, Smruti, Buddhi* is one of the property of *Pitta*<sup>28</sup>; which is vitiated in *Apasmar*. *Pittadharakala* is directly or indirectly related to the *majjadhatu*. Hence the *Ghritakalpana* acts on *Majjdhatu* with curative effect on *Apasmara* with other CNS disorders.

#### **Scientific evidences for effect of Ghritakalpana on seizure disorder (Apasmar):**

One of the main ingredients of the *dhoopan karma* is Cow's ghee (Clarified butter) which has enormous beneficial properties. The ghee when burnt with medicinal plants; produces natural fumes which heal the respiratory system, clear blood clots, bacterium affecting the nasal mucosa, lungs and veins. The reduction in the level of Nitrous Oxide (NO) may helpful in reduction in the epileptic seizures<sup>27</sup>; which is achieved by antioxidant property of medicated ghee (*Ghrita kalpana*).

Apart from the significant physical & medical applications like cleansing of the environment, curing bodily ailments & augmenting vitality and physical potentials,

*Ghrita kalpana* is also found to be of immense use in treatment of psychosomatic disorders and *Balagrahas*, psychological and psychiatric problems.

Most of the childhood disorders (with multiple system involvement) managements are described in the form of the *Ghrita kalpanas*. In childhood seizures having multiple causative factors various *Acharyas* prescribed *Ghritas* including the *Balagraha* disorders which having seizures as a sequel. The ghee can be considered as a high ketogenic diet which covers the seizures along with the dense energy provider for the brain during seizures (hypoxic conditions) preventing the brain/CNS (*Majjadhatu*) damage.<sup>32</sup>

Nutritional therapy especially ketogenic diet is effective across wide variety of ages, seizure types and severities. Carnitine is a transport molecule that helps the cells to make their energy available; it also helps the cells to remove their waste products. Most of human bodies requirement of carnitine is obtained with meat and dairy products (Ghee).<sup>16</sup> Hence ancient *Ayurvedic* scholars described the *Apasmaraghna* management with broad spectrum of nutritive, curative and balancing the vitiated *doshas/dhatus* through various *Ghritakalpana*.

#### **CONCLUSION**

To summarise the ketogenic diet seems to be efficacious in reducing the frequency of seizures in children with refractory epilepsy. Various *Ghritakalpanas* for the management of *Apasmar* (seizure/epilepsy) described by ancient scholars are nothing but the holistic approach with due consideration of ketogenic diet, energetic nourishment for the brain and CNS parenchyma and various

herbal medicinal combinations to combat with the seizure disorders. Most of the components have been found to be having anticonvulsant activity through one or other mechanism. Therefore, treatment with the various medicated ghee (*Ghrita kalpanas*) along with the standard AED's should be considered a valid therapeutic option for children with seizure disorders/epilepsy (*Apasmara*).

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