

**AN OPEN CLINICAL TRIAL TO ASSESS THE EFFICACY OF
NIRGUNDYADI GRITHA AS AN ADD-ON THERAPY ALONG WITH
AED IN THE MANAGEMENT OF APASMARA WSR TO PARTIAL
SEIZURE WITH SECONDARY GENERALIZATION**

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ABSTRACT

Epilepsy is the most common presentation in a neurological setting and stands next to stroke and dementia in its prevalence. One third of the people with epilepsy seems to be severely affected and continues to have seizure despite all the available medications. The disease and its management have high impact on the quality of life of the affected person and also discrimination in education, employment and social acceptance. In Ayurveda, the disease named ‘Apasmara’ has been explained with its aetiology, symptoms, diagnosis and management. A psycho neurological approach has been explained for managing the condition of Apasmara and it is explained in a medical as well as psychological setting. The approach includes a systematic one, depending on the severity and enormity of the associated doshas. Many

a drugs are also mentioned in this regard, but has not been assessed statistically and the available data is based on the clinical finding only. **Aim:** To assess the efficacy of Nirgundyadi gritha in the management of Apasmara WSR to partial seizure with secondary generalisation Setting: Kayachikitsa and Manasroga OPD, VPSV Ayurveda College, Kottakkal, India. **Method:** An open label uncontrolled clinical trial with sample size 20. Add on usage of Nirgundyadi gritha was done without withdrawing the ongoing AED and those with seizure. Assessment was done after one month, 2 months and after 1 month of followup. **Result-** It was observed that the selected drug has significant efficacy in the management of

apasmara wsr to partial seizure with secondary generalisation. The drug Nirgundyadi gritha is effective in the management of Apasmara and to improve the quality of life of the affected ones.

KEY WORDS: Apasmara, Epilepsy, Nirgundyadi gritha, AED, EEG.

INTRODUCTION

Many a disorders in the human may not be considered as ultimate, but may lead to much ill health and mental agony in the due course. Apasmara is one among them, which undoubtedly makes a man, unhappy and diseased. The individual undergoes a lot of distress, agony and grief leading to lack of performance at the personal as well as the social level. Hence a divine contribution was been suspected in the pathogenesis of such diseases in the olden days.

Crude prevalence of epilepsy in India is 5.5/1000.¹Prevalence rate is more in urban area and is higher in the younger age groups. Onset of epilepsy is higher in 1st decades of life.² In more than 50% of the cases, the cause is yet to be known and the thing to be made sure is that there is no organic cause. The disease and its continuing management can make an impact on the person's quality of life, with untoward effects such as depression, anxiety, reduced vitality and insecurity. The leading nonmedical problem confronting people with epilepsy is discrimination in education, employment and social acceptance. The mortality rate among people with epilepsy is two to three times higher and the risk of sudden death is 24 times greater than that of general population³.

In epilepsy, the normal pattern of neuronal activity becomes disturbed, causing strange sensations, emotions, and behaviour or sometimes convulsions, muscle spasms, and loss of consciousness. Anything that disturbs the normal pattern of neuron activity—from illness or brain damage to abnormal brain development can lead to seizures. A measurement of electrical activity in the brain with EEG as well as MRI or CT scan is the common diagnostic test for epilepsy⁴.

About 3/4th of those diagnosed with epilepsy can control their seizure with the available AED's. However, about 25 to 30 percent will continue to experience seizures even with which is called intractable epilepsy⁵. Most seizures do not cause brain damage, but ongoing uncontrolled seizures may cause damage to the brain. This is the area, where we have to

study the clinically persuasive Ayurvedic medicines, so as to help them lead a normal life. This is the real inspiration behind such a study.

Apasmara

In the Ayurvedic literature, epilepsy is described as 'Apasmara' which means loss of smriti ie. Consciousness, which seems as a temporary one.⁶ The term 'Apa' means 'parivarjana' ie. loss and Dalhana gives its meaning as gamana⁷. The term Smara means smarana, ie. smriti. Smriti is defined as bhootartha vijnaana⁸; ability to remember the past experiences. The term tama: pravesha has been used by Dalhana, which leads to jnaana abhaava or lack of awareness during the episode of Apasmara.

The Caraka Samhita contains abundant references regarding all the aspects of epilepsy including symptomatology, etiology, diagnosis and management. The samhitas also described the factors like diet, life style, injuries; psychological factors etc. leading to its causation. Detailed description of the pre-ictal and ictal phases are also available. The components which gets altered is smriti (recollection), budhi (awareness) and satwa (mental strength)⁹.

Ayurveda has given equal importance to psychological factors just like as to the somatic factors. Even though, the disease is included among the Kayachikitsa or general medical conditions; it is explained along with the psychiatric disorders. This explains the dual as well as the most practical approach of Ayurveda, in the management of Apasmara, which is now very well appreciated by the modern medical world.

There is also a limitation in the diagnostic aspect, due to the transitory loss of consciousness of the subject during a seizure. The drug selected for the study was Nirgundyaadi ghrita which is widely used in Apasmaara cikitsa. It contains many drugs like nirgundi which have antiepileptic effect. It also contains rasayana drugs like Lasuna, Citraka, Vaca, Yashti, Aswagandha etc which acts as a booster to the functioning of nerves, which seems to have altered in Apasmara.

Caraka has classified cikitsa into three types ie. Daiva Vyapaasraya, Yukti Vyapaasraya and Satvaavajaya.¹⁰ All these three are used as a combination accordingly to effectively manage the conditions like Apasmara. The management protocol differs during and in between the seizure in the case of a disease like Apasmara, which are having vegas or is episodic. The Cikitsa of Apasmaara can be sodhana or samana, depending on the severity of affection of the

doshas as well as the bala of the patient. The protocol includes snehana, sodhana, vasthi, Nasya, Anjana, Dhoopana and Lepa, as per the condition ¹¹.

Siva aaraadhana, Sree panchaakshari mantra seva, and wearing ratna are explained in the treatment of Apasmaara as a part of the daivya vyapasraya aspect.¹² Satvavachaya aims at improving the mental strength or satwabala of the individuals, by adopting the different methods of psychotherapy ¹³. The improvement in satwabala is very much helpful in avoiding the relapse in conditions like apasmara.

Clinical study

Aim And Objective

- To study the types of epilepsy in detail from the Ayurvedic point of view
- To evaluate the efficacy of Nirgundyadi gritha as an add on therapy along with AED in management of Apasmara WSR to partial seizure with secondary generalisation

Research Question

Does Nirgundyadi ghrita, has any significant add on effect along with AED in the management of Apasmara WSR to partial seizure with secondary generalisation at a dose of 30 ml, administered for 2 months, at 9 PM, in those in the age group of 16 – 50 years, attending the OPD of VPSV Ayurveda college Kottakkal?

Materials

1. Concerned Modern and Ayurvedic literature
2. Participants 20 in number
3. Nirgundyadi gritha
4. Patient Consent Form
5. Case Record Form

Clinical Study

Study Design

Open label Uncontrolled Clinical Trial.

Settings

- Kayachikitsa OPD & IPD - VPSV Ayurveda College Hospital, Kottakkal
- OPD of Govt. Ayurveda research institute for mental diseases, Kottakkal

Duration of Treatment:

- 2 month's intervention and 1 month follow up

Intervention

Nirgundyadi gritha 30 ml was administered at 9PM for 60 days with anupana of sufficient quantity of warm water.

Sample size: 20

Ethical committee clearance: Synopsis submitted and approved by The Research Committee and Institutional Ethics Committee on 11. 04. 2011 (Approval No: IEC/ CL/ 002/ 11 dated 18.04.2011).

Informed consent: obtained from all the included subjects.

Diagnostic criteria

- ICD 10 criteria for partial seizure with secondary generalization ^[14].

Patient selection

- Those satisfying the inclusion and exclusion criteria

Inclusion criteria

- Age group 15 – 60 years
- Those with an established diagnosis of epilepsy
- At least 1 seizure within a month in spite of ideal AED
- Continuing appropriate AED at least 6 months prior to treatment
- No sex, age, religion and financial discrimination
- Those willing to give a written consent

Exclusion Criteria

- Pseudo seizures
- Recent history of alcoholism and drug abuse
- Pregnancy and lactating mothers
- Chronicity greater than 10 years
- Other organic brain disorders
- A known hepatic, renal, cardiac or endocrine disease

Assessment Criteria

- Based on the four parameters¹⁵
- Severity of attack, Frequency of attack, Duration of attack, Post ictal features

The assessments were done before treatment, at the end of 1st month, at the end of 2nd month and after the follow up of one month.

Analysis

The outcome was measured and the data was statistically analyzed by paired t test¹⁶.

Drug Study

Nirgundyadi gritha is a classical preparation extensively used by practitioners all over Kerala. The drug reference is in the Yogagrandha, a compilation from several books edited by PS varier published by Arya Vaidya Sala Kottakkal¹⁷. The same combination is available in use in the gritha as well as the gutika form. The gritha is used by traditional vaidyas for application on the body parts, to relieve the attacks. Nirgundyaadi Ghrita is a combination of 36 medicines. It is indicated in Garavisha, Kukshyaamaya, Apasmaara, Bhootonmaada, Sirasoola and in all the Baalarogas. The lipophilic action of ghee facilitates transportation to a target organ and final delivery inside the cell since the cell membrane also contains lipid, also is the case of blood brain barrier. That is the logic behind the mention of maximum ghee preparations in psychiatric conditions.

The drug nirgundyadi gritha was prepared from a GMP certified company, as per the requirement of the study.

Observation and Analysis

A) Demographic data

35% patients in the study were of 21-25 years age group. Many studies from the developing countries point to the highest prevalence of epilepsy in the 2nd and 3rd decades of life¹⁸. Maximum of 55% participants had age of onset between 11-20 years, 10% participants had age of onset between 1-10 years, 15% patients had age of onset between 21-30 years, the prevalence in the age of onset decreases, with the increasing age¹⁹.

In the study 70% participants were male and 30% participants were female. Prevalence rate of epilepsy in male is more compared to female as per modern texts like Cecil Medicine and other studies²⁰. Out of the 20 participants in the study, 70% participants were Muslim and 30% participants were Hindus as the study was conducted in a muslim dominated area. Out of 20 participants, 70% were unmarried and 30% participants were married. According to the study conducted by Agarwal P et.al subjects with epilepsy had lower marriage prevalence rate, delayed marriage, withheld marriage and higher divorce rate compared to general population²¹

Maximum ie. 60% of the patients have only primary class education. A study conducted by Singh et.al states that the educational problems are commoner in children with epilepsy. Maximum (45%) patients of this study were from lower middle class, 35% were economically poor and 20% were from upper middle class. The studies shows that prevalence of epilepsy is higher in people with low socio economic status.²²

B) Data related to clinical picture

65% of the patients in the study were taking mixed food and 35% of the patients were vegetarians. 30% of the participants in the study were anxious about the disease, 25% of participants had depressed mood, 25% were having euthymic mood and 20% of the participants were with other mood like anger. In the present study, 60% patients were with kapha vaata prakrti, 25% patients were of kapha pitta prakrti and 15% patients were with vaata pitta prakrti. 90% participants in the study were not addicted to cigarette, alcohol or any other addiction forming substances. Maximum of 50% of the participants reported sleep deprivation as the precipitating factor in epilepsy. Tension, irregular food intake etc were also reported as the precipitating factors. Studies show that, sleep deprivation is the main precipitating factor in epilepsy²³.

40% of the participants in the present study had frequency of attack of 1-2 times per month, 30% participants had frequency of attack between 2-5 times per month and 30% participants had frequency >5 times per month. 60% of the patients were with duration of the attack of 1-5 minutes, 40% were with duration less than 1 minute. Post ictal features were present but relieved with in 1 hour of attack in 50% cases. 90% patients in the study reported loss of consciousness with falling and mild convulsions.

C) Observations on the effect of therapy

Assessment was done at the end of first month, second month and after the follow up of one month. Laboratory investigations were done before and after study. EEG was also included as the investigative tool²⁴. The data obtained were assessed using self gradation scale. Severity, frequency, duration of attack and post ictal features was assessed.

Table 1 Effect of the therapy on symptoms

Symptom	BT	AT	Mean diff	% of relief	SD	t		p
Severity of attack	2.05	1.55	0.5	24.4	0.8272	2.703	<0.02	
Frequency of attack	1.9	1.35	0.55	28.94	1.1356	2.166	< 0.05	
Duration of attack	1.6	1.05	0.55	34.37	0.686	3.584	<0.01	
Post ictal feature	1.30	1.0	0.30	23.07	0.5712	2.349	< 0.05	

(BT – before treatment; AF – after treatment; SD – standard deviation)

Table 2 Overall effect of the therapy

BT	AT	Mean diff	% of relief	SD	t	p
6.85	5.00	1.85	27	1.785	4.635	<0.01

Severity of attack

Nirgundyaadi Ghrita is effective in reducing the severity of attack of the disease. The change occurred in the severity of attack after the first month of the treatment was statistically significant ($p < 0.05$) with 17% relief. After the second month, the percentage of relief was 24.4% which was statistically significant ($p < 0.02$). Severity of attack after the follow up was same as that of after treatment. The percentage of relief was 24.4% and also statistically significant ($p < 0.02$).

Frequency of attack

In frequency of attack, the percentage of relief was 26.31% after the first month of the treatment which was statistically significant ($p < 0.001$). Frequency of attack after second month was also statistically significant ($p < 0.001$) with a percentage of relief of 31.58%. After follow up, the percentage of relief on frequency of attack was 28.94%. The result was statistically significant ($p < 0.05$).

Duration of attack

Duration of attack was reduced after first month of treatment by 15.63% relief which was statistically insignificant ($p > 0.05$) But after second month of treatment patients got 37.5% which was statistically significant ($p < 0.001$). Effect on duration of attack after follow up was 34.37% with a p value < 0.01 which was statistically significant.

Post ictal features

Change in post ictal feature after first month of treatment was 19.23% which was not statistically insignificant ($p > 0.05$). After second month of treatment the percentage of relief

was 26.9% which was statistically significant ($p < 0.01$). After follow up period, the percentage of relief was 23.07% which was statistically significant ($p < 0.05$).

Overall effect of the drug

The drug is effective in reducing the severity, frequency, duration and post ictal features of the disease and the effect is maintained during the follow up period also. The overall effect was 19.7% after first month ($p < 0.01$), after second month the effect was 29.92% ($p < 0.001$). The effect after follow up was 27% ($p < 0.001$).

DISCUSSION

Eventhough medical world claims of the advancements in the management of Apasmara, many a drugs are not working as expected. The present AED medication has so many draw backs like adverse reaction, drug interaction and teratogenicity²⁵. Cognitive impairment to an extent, is also seen in some patients, with epilepsy. This points to the need for the search and development, of newer drugs in this regard.

The Ayurvedic preparations work astonishingly in this area and can do a spectacular job. Ghrita has a main role in the management of diseases with prominent psychological component, like Apasmaara. Puraana ghrita is indicated in Apasmaara due to its property in bringing all the doshas to normalcy²⁶.

Nirgundyaadi ghrita is a combination of 36 drugs. Many of the ingredients in this medicine have established anti convulsive activity. Also they are good anti oxidants. According to recent researches increased level of free radicals are seen during the seizure in an individual²⁷. These free radicals can damage the neurons leading to cognitive impairment.

The drug Nirgundyaadi ghrita is ushna in veerya and katu in vipaaka. Due to the sookshma guna of these, the drug is able to remove the aavarana of srotus. The drugs in the formulation have Deepana and paacana properties, which control the formation of ama in the initial stage, which is very important in preventing the manifestation of the disease. Due to the deepana, paacana and srotosodhaka property, there is an increase in agni of the patient which helps to trim down the remaining doshas after the vegaavastha. Thus there will be a decrease in the post ictal feature of the disease. Nirgund'yaadi Ghrita also contain drugs like Triphala, Vaca, Yashtimadhu, Lasuna, Citraka etc which are well known for its rasaayana property²⁸.

Rasayanās have a crucial role to play in the management of diseases like apasmara, where there is involvement of all the three doshas and also the satwa or the mind²⁹.

CONCLUSION

For many people with epilepsy, the risk of seizures restricts their independence and also recreational activities³⁰. AED's are not answering the problem in a reasonable manner. Some of the drugs tried here like Nirgundyadi gritha, is to be studied scientifically to evaluate the efficacy in such condition. The drug has given statistically significant results in reducing the partial seizure, with secondary generalization. Thus the vast Ayurvedic literature is able to provide effective contribution in improving the quality of life of those, affected with conditions like Apasmara.

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