Nonpharmacological treatment of epilepsy

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Abstract

Nonpharmacological treatment of epilepsy includes surgery, vagal nerve stimulation, ketogenic diet, and other alternative/complementary therapies, e.g., yoga, Ayurveda, electroencephalography (EEG) biofeedback technique, aerobic exercise, music therapy, transcranial magnetic stimulation, acupuncture, and herbal remedies (traditional Chinese medicine). Alternative therapies, despite the term, should not be considered as an alternative to antiepileptic medication; they complement accepted drug treatment. Alternative therapies like yoga, through techniques that relax the body and mind, reduce stress, improve seizure control, and also improve quality of life. Ketogenic diet is a safe and effective treatment for intractable epilepsies; it has been recommended since 1921. The diet induces ketosis, which may control seizures. The most successful treatment of epilepsy is with modern antiepileptic drugs, which can achieve control of seizures in 70–80% cases. Patients opt for alternative therapies because they may be dissatisfied with antiepileptic drugs due to their unpleasant side effects, the long duration of treatment, failure to achieve control of seizures, cultural beliefs and, in the case of women, because they wish to get pregnant Surgical treatment may lead to physical and psychological sequelae and is an option only for a minority of patients. This article presents supportive evidence from randomized controlled trials done to assess the benefit of non-pharmacological treatment.

Key Words

Ayurveda, epilepsy, non-pharmacological treatment, ketogenic diet, yoga

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Ann Indian Acad Neurol 2011;14:148-52

Introduction

Non-pharmacological treatment of epilepsy includes surgery, vagal nerve stimulation, ketogenic diet, and other alternative/complementary therapies. Alternative therapies include techniques such as yoga, acupuncture, chiropractic, massage therapy, EEG biofeedback, aromatherapy, homeopathy, herbal remedies (traditional Chinese medicine), etc. Most people with epilepsy need to take antiepileptic medication to control their seizures and alternative therapies are more often complementary.

Alternative therapies, including stress-reduction techniques, can help some people to better control their seizures. The epilepsy patient who finds that he/she has more seizures when under stress may benefit from learning stress management and relaxation techniques such as progressive muscle relaxation and deep diaphragmatic breathing. Some people have found that yoga or meditation helps them prevent stress-induced seizures and also to improve their quality of life.

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.85870

Acupuncture uses needles to stimulate nerve endings, the goal being to bring the person's health into a better mental, physical, and emotional balance. Biofeedback techniques in epilepsy use EEG machines to help people identify and alter their own seizure-related brain activity. The person with epilepsy is trained over time to use relaxation or other biofeedback techniques to generate a more normalized brain wave pattern, which may help reduce their seizures. A ketogenic diet is often used as the last resort in the treatment of catastrophic epilepsies in children and is said to be safe and effective.

Ketogenic Diet

The ketogenic diet[1] remains a valuable option for patients with intractable childhood epilepsy and, particularly, epileptic encephalopathies. The success of ketogenic diet on seizure outcome provides some insight into epileptogenesis and anticonvulsant action. Estimates indicate that, overall, complete cessation of all seizures occurs in 16% of patients, a greater than 90% reduction in seizures occurs in 32%, and a greater than 50% reduction in seizures occurs in 56%. It is said that 40–50% of those starting the diet will have a greater than 50% reduction in seizures after 12 months. Parents also report improvements in their child's behavior and attention. A concomitant reduction in antiepileptic drugs is often possible. The ketogenic diet is the

first-line therapy in patients with deficiencies in the GLUT-1 glucose transport, where glucose cannot be transported into the cerebrospinal fluid for use by the brain; the ketogenic diet is also useful in those with pyruvate dehydrogenase (E1) deficiency for the treatment of seizures due to glucose transporter protein deficiency.[2]

Classic ketogenic diet (Johns Hopkins Hospital protocol): The ketogenic diet used at the Johns Hopkins Hospital's pediatric epilepsy center is commonly considered the standard or classic form of this diet. The usual protocol for children between the ages of 3 and 12 years provides a ratio of four parts of fat to one part of protein and carbohydrates combined. The protocol followed in different countries is shown in Table 1.[3]

The largest single-institution intention-to-treat prospective study[4] conducted on 150 patients at the Johns Hopkins Hospital demonstrated that at 3 months (with 125 patients remaining on the protocol) 3% of patients were free from seizure, 31% had a greater than 90% reduction in seizure frequency, and 26% had a 50–90% reduction in seizure.[5] After 12 months (with 83 patients remaining on the protocol), 7% were free of seizures, 20% had greater than 90% reduction in seizures, and 23% had of 50–90% reduction in seizure.

Neal *et al*.[6] conducted a randomized controlled trial to study the efficacy of ketogenic diet in controlling seizures. They enrolled 145 children aged between 2 and 16 years who had daily seizures (or more than seven seizures per week), had failed to respond to at least two antiepileptic drugs, and had not been treated previously with the ketogenic diet. Seventy-three children were assigned to the ketogenic diet group and 72 children to the control group. Data from 103 children (54 from the ketogenic diet group and 49 from the control group) were available for analysis.

After 3 months, the seizure frequency was significantly lower in the diet group than in the controls (75 % decrease; $P<0.0001$), 28 children (38%) in the diet group had greater then 50 % seizure reduction compared with four(6%) controls ($P<0001$). Twenty-eight children (38%) in the ketogenic diet group had greater than 50% reduction in seizure frequency as compared to four (6%) children in the control group who achieved similar reduction ($P < 0.0001$). Five children (7%) in the diet group had greater than 90% reduction in seizure frequency, whereas none among the controls achieved similar reduction ($P = 0.0582$).

There was no significant difference in the efficacy of the treatment between symptomatic generalized or symptomatic focal syndromes. The ketogenic diet has been used in patients in variety of types of seizure and epilepsy syndromes, including Lennox-Gastaut syndrome[8] and Dravet syndrome.[8] Earlier intervention with a ketogenic diet leads to better outcome in patients with Dravet syndrome.

A multicenter study of ketogenic diet found no relationship between outcome and age, sex, seizure type, and EEG findings.[9]

Ketogenic diet has less side effects and side effects such as dehydration and hypoglycemia have been reported. Nephrolithiasis is seen in 6% of patients on a ketogenic diet. In addition, children may have stunted growth, fractures, and hyperlipidemia.

The mechanism underlying the beneficial effect of ketogenic diet remains a mystery. Recently, a hormone called leptin,[10] which is generated by the ketogenic diet, has been shown to suppress seizures in a rodent model of seizures.

To summarize, the ketogenic diet is useful therapy for patients with intractable epilepsy. A modified Atkins diet[11] has also been tried in a study and was better tolerated.

Yoga and epilepsy

The ancient Indian practice and philosophy of yoga is increasingly becoming a focal point of therapy and research in epilepsy. Yoga offers an ancient yet amazingly modern approach to the treatment of seizures. In Ayurveda, epilepsy is called *apasmara*, meaning loss of consciousness of the body. The ancient Indian texts, the Vedas, describe four types of epilepsy and nine disorders causing convulsions in children. For the treatment of epilepsy, the physical discipline of yoga seeks to re-establish a balance (union) between those aspects of a person's health that cause seizures. Yoga is one of the oldest formal practices known whose purpose is to restore this balance.

Table 1: Sample ketogenic diet recipes[3]

Switzerland (Four-to-one ratio)	India (Two-to-one ratio)	Brazil (Four-to-one ratio)	Singapore (Four-to-one ratio)
6 g 35% Fat cream	34 g Chicken	25 g Skinless chicken breast	8 g Bacon
20 g Carrots	40 g Onion	20 g Okra	17 g Boiled lean pork
11 g Potato	93 g Tomato	5 g Green olives	20 g Cabbage
20 g Vegetable oil	1 g Ginger	14 ml Oil	green, boiled
13 g Ricotta	1 g Garlic	1 Teaspoon of	33 g Sesame oil
(cheese)	34 g Ghee/Oil	Chopped	
	1 or 2 Cloves	coriander	
	Bay leaf	Garlic salt	
	Green chili		
	Salt to taste		
	Red chili powder		
	(Dr Nathan's chart)		

[Courtesy of Maria Joaquina Marques-Dias (Brazil), Dr Gabriela Wohlrab (Switzerland), Dr Janak Nathan (India), and Dr Ong Hian Tat (Singapore)]

Pranayama or deep diaphragmatic breathing

In this method, as a person slips into a seizure state, s/he is trained to reflexively catch and hold their breath as if startled or frightened. This causes changes in metabolism, blood flow, and oxygen levels in the blood. The practice of *pranayama*, i.e., controlled deep diaphragmatic breathing, helps restore normal respiration; this can reduce the chances of going into a seizure or stop the seizure before it becomes full blown.

Asanas or postures

The *asanas* or *yogasanas* aid in restoring balance to the body and its metabolic systems. Practicing *asanas* increases physical stamina and calms the nervous system. *Asanas*, used as a physical exercise alone, improve circulation, respiration, and concentration, while decreasing the chances of having a seizure. These exercises also help to improve the health-related quality of life (HRQOL).[12]

Dhyana or meditation

Stress is a well-recognized trigger of seizure activity. *Dhyana* or meditation soothes the mind even as it heals the body. Meditation improves blood flow to the brain and slows the production of stress hormones. Meditation also increases the levels of neurotransmitters, like serotonin, which keep the body's nervous system calm. Practicing relaxation techniques such as Yoga meditation is well known as a definitive aid in seizure control.

In 1996, The Indian Journal of Medical Research published the results of a study on the effects of *Sahaja Yoga* practice on seizure control.[13] The study was not large enough to be considered conclusive. However, its results were so promising that the study caught the attention of researchers in Europe and North America. In this study, a group of patients with epilepsy who practiced *Sahaja Yoga* for 6 months experienced 86% decrease in their seizure frequency.

Effect of yoga meditation on electroencephalography

The effect of yoga meditation on electroencephalography (EEG) was first recorded by Anand *et al*.[14] In 1961 in a controlled study conducted at the AIIMS, the EEG of four yogis was recorded both during rest and during meditation. All subjects displayed considerable alpha activity during the resting state and this activity became more prominent, with increased amplitude, during meditation. During rest, visual and auditory stimuli block the alpha activity, whereas during meditation these stimuli fail to block the alpha activity, indicating the absence of external influence on the EEG in the meditation state. Arambula[15] studied the effects of Kundalini Yoga meditation on EEG. The study subjects were physicians who practiced Kundalini Yoga meditation. Respirarition, heart rate, EEG, skin conductance, and blood pressure were monitored at baseline, during meditation, and post meditation. There was more alpha amplitude during meditation (M = 1.7/μV) than at baseline (M = 0.47 μV) or post meditation (M = 0.78 μV). Increased theta amplitude was seen during meditation (M = 0.62 μV) and before meditation (M = 0.26 μV). Bagchi and Wenger[16] also studied the effects of breathing exercises and found that some of their subjects, especially the experienced ones, could produce bi-directional changes in every autonomic variable that the experimenters measured. Further evidence that contemplative practice produces different physiological profiles was provided by Anand[17] who studied four yogis and found that they exhibited persistent alpha activity with increased amplitude during the state of trance. Prominent alpha band activity and cardiac rhythm modulation were observed after adjuant Yoga therapy in patients with refractory epilepsy.[18]

The practice of Yoga regulates body physiology through control of posture, breathing, and meditation. The effects of Yoga on the autonomic functions of patients with refractory epilepsy, as quantified by standardized autonomic function tests, were determined. The Yoga group showed significant improvement in parasympathetic parameters and a decrease in seizure frequency scores.

RCT in Refractory Epilepsy

Deepak[19] conducted a study on 11 adult patients of refractory epilepsy who were taught meditation. They practiced for 1 year. The control group was matched for age and duration of epilepsy. The results of the trial showed the following:

1. The meditation group showed decrease in frequency and duration of seizures (as compared to the baseline) after 6 months of Yoga practice.
2. There was normalization of the EEG after prolonged practice of meditation.
3. The slow wave spectrum (<7Hz) decreased and the 8 - 12 Hz spectrum increased.

No changes were seen in the control group.[17] The practitioner of Yoga combines physical posture, breathing exercises, relaxation, and meditation to attain optimal physical fitness. Some schools of Yoga place emphasis on *yogasanas*, others on breathing control and *Sahaja Yoga*. In a study of 32 patients with epilepsy, randomized to group 1 (n=10 receiving yoga therapy), group 2 (n=10, receiving sham yoga) and group 3 (n=12, control group), 40% of group 1 became seizure free after six months.[20] Experimental and clinical studies on Yoga and epilepsy from 1961 till 2007 show that different types of Yoga – *Hatha Yoga, Sahaja Yoga* mediation, and *yogasana* practice – not only reduces the stress associated with epilepsy but also modifies brain rhythm and thereby helps in controlling seizure frequency.

Ayurveda and epilepsy

Ayurvedic treatment 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 epilepsy by unblocking the channels of the heart and the mind that may be clogged by the excess of *doshas* 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. Listed below 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. It is also important to note that most, if not all, of the traditional medicines listed below have not been scientifically or clinically proven to cure or help people with epilepsy and are generally

recommended because of patient's confidence in alternative treatment.

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) 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 *doshas* (humors). Drug formulations are recommended only after the patient has been cleansed by all means. A wide variety of *ghrtas* (purified butters) have been recommended for internal use. One of the most important among these is *maha panca gavya ghrta*. The use of mixtures of *ghrta* and *taila* (oil) cooked with drugs has also been mentioned. Oil cooked with different herbal 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* (*cpllyriu* sticks) to bring the unconscious patient to his/her senses has also been mentioned. A variety of Ayurvedic medicines for epilepsy is available in the Indian market, for example, *asvagandhadyarishta*, *bali tail*, *brahmi ghruta*, *chandanadi*, *kalyanaka ghruta*, *mahamrutyunjaya rasa*, *ajata bhasma*, *vaatakulantaka rasa*, and *ogendra rasa*.[21] 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 (*siravdha*) from the veins. Cauterization of both parietal bones with needles (*soocivedha*) has also been mentioned.

One type of Ayurvedic herbal remedy believed to be effective for epilepsy is called *siddharthaka ghrita*. *Aswagandharistam* is used for epilepsy and insanity; it is thought to increase one's energy, vitality, and strength and to provide physical nourishment.

Saraswata rishta is another herbal medicine that Ayurveda has assigned to epilepsy treatment. It contains 21 different ingredients, some of which can be found in Cerebrex® capsules, a commercially available drug from the European Institute for Scientific Research on Ayurveda. Pandit Shiv Sharma, Asian Director of the World Federation of Life Sciences and a professor of Ayurveda in Bombay, India, recommends a mixture of three preparations for the treatment of epilepsy - *smriti-sagara rasa* – a metallic mixture containing mercury, arsenous sulphide, and red arsenic. Skullcap Ramayana #16 is another Ayurvedic herbal preparation used for epilepsy treatment. It is made from Skullcap (*Scutellaria* spp.) and 18 other rejuvenating, healing, and carminative Ayurvedic ingredients in a base of honey and herbal ghee. Skullcap is given for insomnia, tremors, muscle spasms, neuralgia, neurosis, and nervous headaches.

A RCT of Mentat® (an Ayurvedic medicine) in various types of epilepsy was conducted by Moharana, *et al*.[22] in 31 adult epileptic patients. Mentat® is a remedy containing certain important Ayurvedic ingredients such as *Bacopa monnieri* (*jalbrahmi*), *Centella asiatics* (*mandookaparni, brahmi*), *Withania somnifera* (*ashwagandha*), *Evolvulus alsinoides* (*shankhapushpi*), *Nardostachys jatamansi* (*jatamansi*) etc., and many others. A review of the literature suggests that Ayurvedic medicines cannot be recommended as primary or add-on therapy in epilepsy patients at present but they may form the basis of a future new antiepileptic drug.

EEG Biofeedback and Epilepsy

EEG biofeedback is also known as EEG-operant conditioning or neurotherapy. In this method, the subject learns to voluntarily control his/her EEG rhythm and thereby gains control over seizures. Initial work done demonstrated on sensory motor rhythm (SMR) of somato-sensory cortex for which biofeedback was initiated .It is still debated that specific cortical rhythm is useful for bio feedback in specific seizures types. Sterman and Friar[23] observed protection against drug-induced seizure in cats following operant conditioning of 11–15 Hz SMR.

Sterman enrolled 174 patients with refractory epilepsy for a study on the efficacy of EEG biofeedback. Of the 174 patients, 142 (82%) showed clinical improvement and 30% became seizure free. On average, there was a reduction of seizure frequency of 50% and also a decrease in seizure severity; 5% of these patients achieved complete control of seizures after 1 year. Advocates of biofeedback point to the evidence of positive effects that has accumulated over the last 25 years. Skeptics say that while it may be useful in some patients, much more data is needed before biofeedback is accepted generally as an option for people with refractory epilepsy.

The instruments and the training required for conducting studies on EEG biofeedback is expensive. The NYU Medical School has enrolled many patients for one such study which is ongoing.

Botanicals and Epilepsy

Siegward M.[24] Elsas has stated that there are a multitude of botanicals that are used traditionally for epilepsy. Of these, he has discussed five examples: Valerian (European traditional botanical), *Passiflora incarnata* (native North and South American botanical), Kava kava (Pacific native botanical), *Piper nigrum* (traditional Chinese medicine), and *Withania somnifera* (Ayurvedic medicine). He has further stated that scientific studies and clinical experience with these botanicals is very limited and formal clinical trials are desirable to assess their efficacy.

Acupuncture and Epilepsy

A growing number of people with epilepsy are realizing that this ancient treatment helps control seizures. Acupuncture, which has been practiced in China for over 3,000 years, is often used as a synonym for Chinese medicine;[25] however, traditional Chinese medicine also includes diet modification, herbal remedies, and exercises.

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How to cite this article: Saxena VS, Nadkarni VV. Nonpharmacological treatment of epilepsy. Ann Indian Acad Neurol 2011;14:148-52.

Received: 19-02-11, **Revised:** 22-11-10, **Accepted:** 23-05-11

Source of Support: Nil, **Conflict of Interest:** Nil

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