



Refractory seizures in children

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ABSTRACT

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Epilepsy is described as a heterogeneous clinical syndrome results from various cerebral destructions. It is categorized to partial and generalized forms. Degree of neural system impairment and affected area determine the severity and pattern of symptoms. Patients might experience sensory, motor, or both signs and symptoms. About 60% of epileptic patients suffer from partial type. It is estimated that up to 30% of epilepsy cases would not be controlled adequately despite sufficient and proper management. Anacyclus pyrethrum, Citrus aurantium var. amara, Paeonia officinalis, Rosa Damascena and Nigella Sativa are some of herbal drugs which have antiepileptic effect. Natural agents are valuable sources to treat chronic diseases and a huge number of world's population believe herbs are effective and safe for daily primary health care needs. There is not enough evidence about their efficacy and safety obtained from randomized control trials.

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Introduction

Convulsion is the most common form of neurologic disease in childhood. Single seizure episode might happen in 4 to 10 percents of children younger than 16 years (1). Childhood seizures might be a transient feature. Convulsions should be differentiated from epilepsy, because they happen due to a wide spectrum of disorders

such as metabolic diseases, electrolyte imbalances and trauma, etc. When seizure attacks become recurrent, they are called epilepsy. Fifty million of world population are affected by this disease (2). Epilepsy is described as a heterogeneous clinical syndrome, results from various cerebral destructions. It is categorized to partial and

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generalized forms. Degree of neural system impairment and affected area determines the severity and pattern of symptoms. Patients might experience sensory, motor or both signs and symptoms. About 60% of epileptic patients suffer from partial type. It is estimated that up to 30% of epilepsy cases would not be controlled adequately despite sufficient and proper management (3). Resistance epileptic cases, who do not respond properly to antiepileptic drug (AED), are considered as DRE (drug resistant epilepsy). Between 6 to 35% of seizures would be refractory. It is estimated that about 70000 children suffer from DRE in Iran and there are some diagnostic and therapeutic challenges about it (4).

With recent technical revolutions, different medications and therapeutic methods are introduced to control DRE, such as Levetiracetam, Topiramate and different surgical methods. Promotion of herbal and Chinese medicine leads to extensive application of traditional drugs for untreated controversy issues (5).

On the other hand some fruit and food could influence the bioavailability of antiepileptic drugs, for example there are several researches about ketotonic diet and its effect on epilepsy. Grapefruit juice inhibits CYP3A4 enzymes and increases the bioavailability of carbamazepine (6). Although there are different and effective drugs for epilepsy, a number of patients still have seizures with proper treatment and also a proportion of patients have to discontinue medication because of severe side effects. Modern therapeutic agents are expensive so they might not be prescribed for all patients. It has been shown that synthetic antiepileptic drugs cause some various side effects and complications such as liver toxicity, teratogenicity, psychological disorders and GI problems. Plant derived medications might have less side effects,

so they have been considered as safe agents especially in childhood (7).

Epilepsy is a historical issue in Iran, and different traditional methods were described for its treatment. In recent years traditional medicine has been revised so again herbs have been proposed for epilepsy treatment, particularly for DRE (4). *Anacyclus pyrethrum*, *Citrus aurantium* var. *amara*, *Paeonia officinalis*, *Rosa Damascena* and *Nigella Sativa* are some of the herbal drugs which have antiepileptic effects (8).

Valeriana officinalis has been used in convulsion management which might have an impact in adenosine system activation (9).

Discussion

In recent years the role of herbal medicine has been established in some chronic diseases like epilepsy and some botanical drugs have been approved by FDA. Herbal drugs are more acceptable in our country because of Iranian culture (9). On the other hand Iran is a developing country that economic factor might influence the treatment method and herbs are available and cheaper. Other complications such as sleep disorders and gastrointestinal malfunctions are also common in patients with epilepsy, particularly in children and herbal drugs might reduce all of their problems (8). In Table 1 the effect of herbal medicine is shown in childhood refractory seizure in different parts of world.

Some different herbal medicines that have been described as antiepileptic agents are mentioned as below: Debnath showed that the *Terminalia chebula* ethanolic extract could reduce seizures duration in mice (10). The anticonvulsive and neuroprotective effects of *Pimpinella anisum* were revealed in another study (11).

Agher Gherha or *Anacyclus pyrehrun* could increase seizure threshold. *Laurus*

Table 1. The effect of herbal medicine in childhood refractory seizure

Author	Publication year	Title	Type of seizure	Treatment method	Outcome
Ashrafzadeh (7)	2007	Effect of Rosa Damascena oil as adjunctive treatment for refractory seizures in children	Refractory seizures	Rosa Damascena	Antiepileptic effect
Carvalho-Freitas (12)	2002	Anxiolytic and sedative effects of extracts and essential oil from Citrus aurantium L	Epilepsy	Citrus aurantium L	Increased the latency period of tonic seizures
Hung-Ming (13)	2002	Antioxidant and anticonvulsant effect of a modified formula of chaihu-longu-muli-tang	Refractory seizures	Chaihu-longu-muli-tang	Reduce the seizure frequency
Ma (14)	2003	Clinical observation on 930 child epilepsy cases treated with anti-epilepsy capsules	Epilepsy	Anti-epilepsy capsules	Reduce the frequency and duration of seizures
Akhondian (15)	2011	The effect of thymoquinone on intractable pediatric seizures (pilot study)	Refractory seizures	Thymoquinone	Anti-epileptic effects
Wang (16)	1996	Effects of Chinese medicine zhenxianling in 239 cases of epilepsy	grand mal epilepsy	Zhenxianling	Effective rate of 97.2%
Akhondian (17)	2007	The effect of Nigella sativa L. (black cumin seed) on intractable pediatric seizures	Intractable pediatric seizures	Black cumin seed	Antiepileptic effects

nobilis oil might have an anticonvulsant effect in tonic seizures (18,19). Piper longum is an antioxidant which could be used as an anticonvulsant medication by influencing the GABA system (20).

Ostokhodoss could act as diazepam and is sedative (21,22). Efficacy of some herbal drugs such as Nigella sativa and Piper longum have been proved in childhood refractory epilepsy by randomized control trials and there are several reports about anticonvulsant effect of plant derived agents in animal models (23).

Herbal drugs were important in Asian and African folk medicine. Traditional drugs are derived from the flowers, leaves, roots, or other parts of plants. Some herbs could be used directly as medication, but most of them need to be processed to become

applicable. Extracting and drying are the first stages of processing the herbal medicine. Although ancient science described many antiepileptic agents, it is found that none of them are useful. One of the herbal drugs limitations is that their dosage might not be cautiously adjusted. All of their side effects and interactions are not well known too (22).

It is crucial to know that some herbs could induce seizure such as ginkgo, ginseng, and evening primrose. Some traditional medicine might interact with antiepileptic drugs and increase or decrease their serum level and efficacy.

Conclusion

Natural agents are valuable sources to treat chronic diseases and a huge number

of world's population believe herbs are effective and safe for daily primary health care needs. But there is not enough evidence about their efficacy and safety obtained from randomized control trials.

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Conflict of Interest

The authors declare no conflict of interest.

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