

Critical Review on *Medhya* Drugs as an Adjuvant to Overcome Adverse Effect of Long Term Use of Anticonvulsant Drugs in Children

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Abstract

Cognition is the mental process which incorporates memory, calculation, understanding and making dialect, reasoning, attention of operating, problem solving and higher cognitive process. High-quality kid development centres within the world have placed priority on children's intellectual learning.

The rates of unfavourable impacts could be a basic issue while endorsing antiepileptic medicinal drug (AED's), as a large portion of the anticonvulsant drug have unfriendly impact on psychological feature of youngsters.

Present paper is an audit to overhaul learning on range of adverse effects on psychological feature coupled to a range of newer and older anticonvulsant medication used to control seizures, trailed by a discussion relating to *medha/ buddhi* (intellect), *medhyarasayana* and use of Ayurvedic *medhya dravya* to minimize adverse drug reactions (ADR's), major chemical constituents, therapeutic actions, pharmacologic properties, and doable mode of action of the chosen herbs from Ayurvedic literature. At the same time, it conjointly reveal for additional analysis and use of *medhya rasayana* (nootropic herbs) as an adjuvant therapy to minimize or conquer adverse impact of long run use of antiepileptic medication in kids.

Keywords

Cognition, Antiepileptic drugs, Medhya rasayana & Adverse effect



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INTRODUCTION

Intelligence is the discriminative capability of an individual that makes him completely different from animals. Language, observations, analytical mind, analysis ability and plenty of additional contributed for human intellect. For the successful survival of man during this competitive world there's a desire for promotion of mental state. It becomes invariably essential to own nice skills in terms of memory and intelligence right from the childhood itself.

There is a robust affiliation between the event a baby undergoes early in life and the level of success that the kid can expertise later in life. Here development is especially concerned with psychological development of a baby. Epilepsy is a common disorder in medicine practice that demands usually long term medical care. There are only a few medicine studies relating to incidence of epilepsy from India. A recent study conducted in Kolkata's urban population showed an annual incidence rate of 27.27 per 100,000 per year¹. A recent rural epilepsy surveillance program from Uttarakhand showed a prevalence rate of 2 or more unprovoked seizures to be 7.5 per 1000². This can be more than the prevalence

rate in Kerala, wherever prevalence rate is 4.9/1000³.

The ultimate aim in treating epilepsy ought to be complete management of seizures, while not inflicting any untoward reaction as a result of the medication. A large variety of drugs are presently on the market for the treatment of epilepsy. Effective treatment of epilepsy depends on medication compliance across a time period, and studies indicate that drug tolerability could be important limiting factor in medication maintenance. Available anticonvulsant medication (AED's) have the potential to exert harmful effects on psychological feature operate and thus compromise patient wellbeing.

Antiepileptic medication decrease membrane excitability, increase postsynaptic inhibition or alter synchronization of neural networks to decrease excessive neuronal excitability related to seizure development. Common side effects of decreasing neuronal excitability, however, are slowed motor and activity speed, poorer attention and mild memory impairment⁴ (Meador, 2005). Unlike adults, psychological side effects in children occur against the scene of normal cognitive and psychosocial development, and treatment decisions made in childhood might have long effects. Adults who

developed epilepsy during their childhood tend to own less education, ablated rates of employment and employment at lower job levels, lower rates of wedding, poorer physical health, and enhanced incidence of psychiatric disorders⁵. Significantly, these long term adverse effects are present in adults who aren't any longer taking medications. The persistence of those effects when termination of AED treatment suggests a role of either seizure etiology, accumulative effects of continual seizures or AED treatment permanently altering the course of development.

Ayurveda has its own principle which may prove an excellent answer for several of the issues involved with mind and body. The

description concerning the construct of *Medhya Rasayana* is one such idea which needs reconsideration and application in present situation because it may be a robust answer for several of the psychological and cognitive issues.

MATERIALS AND METHODS

In this current literature, we reviewed studies in terms of range of effects on cognition connected to a range of newer and older agents used to control seizures (Table

no.1). These embody key alterations in both executive and broader neuropsychological functions, which may exert essential influence on children's quality of life and well-being. As a result of drug side-effect profiles are typically associated with patient characteristics, this review is followed by an essential discussion concerning idea of *medha*, *medhyarasayana* and use of Ayurvedic medication to minimize ADR's, which can provide recommendations for prescribing medication each in general and in respect to a lot of specific clinical cases. Finally, we valuate reviewed studies in terms of knowledge improving actions, toxicity, interaction of Ayurvedic medication, providing essential steerage for using it in clinical practice.

Cognitive deficits that are secondary to adverse effect of many of antiepileptic drugs (as explained in table no 1) demand use of *medhya dravya* (nootropics) to boost cognitive abilities. Recently there is a tremendous urge to explore medicinal plants on global platform for improving cognitive function owing to their less adverse effects. Ayurveda provides concept of *medhya rasayana* to boost up the cognition of an individual.

CONCEPT OF MEDHA AND MEDHYARASAYANA

In different Sanskrit/English dictionaries following terms are used for *medha*-

A form of *Saraswati*, retentive faculty/retentiveness of memory, intellect, and intelligence in general, strength, mental power or vigor, prudence, wisdom and intelligence personified.

Medha is considered as a form of *buddhi* itself²³. *Buddhi* is a functional unit of human body which perceives the stimulus either from sense organs or from memory and imaginations. The man with proper *buddhi* gets proper impulses from the interior or exterior world and *buddhi* gets involved with *indriyas* and *manas* and perceives the knowledge.

Measures to improve *medha*

There are many methods by which *medha* can be manipulated. Some methods are concerned with the maintenance of equilibrium status of body and mind, there by facilitating the normal physical and psychological functions. Some other measures are directly acting on the psychological entities by which *medha* can be improved.

Specific Measures

Treatment modalities according to Ayurveda can be explained as- *Svasthanasyaurjaskara & arthasayaroganut*²⁴.

Urjaskarachikitsa is mainly concerned with preventive and promotive medicine where *asrogranut* deals with curative therapy. *Rasayana* and *Vajeekarana* are the two forms of *Urjaskarachikitsa*²⁵. Though *Rasayana* is one among the eight branches of Ayurveda, it has its applicability in all the branches of Ayurveda. *Rasayana* is the most applied specialty of Ayurveda.

Use of *medhyarasayanans* is specifically meant for improving the *medha*. Charaka samhita mentions about four *medhyarasayanans* as *mandukaparni*, *yashtimadhu*, *guduchi* and *shankhapushpi*²⁶. Sushruta Samhita mentions in detail about *medhayushkameeyarasayanans*²⁷.

In Kashyapa Samhita there is mentioning of preparations such as *Brahmighrita*, *Panchagavyaghrita*, *Kalyanakaghrita* and *Samvardhanalehya* having *medhya* effect²⁸.

Commonly indicated drugs for Cognition improvement in Ayurveda classics with their active ingredients are explained in Table no 2.

Table 1 Commonly used AED's (Anti-epileptic drugs) with their cognitive adverse effects (CAEs)

| Sr. No. | Name of drug | cognitive adverse effects (CAEs) | References |
|---------|-----------------------------------|--|--|
| 1 | Phenobarbital | lower IQ ⁶ , more adverse effects on motor performance and attention/concentration tests ⁷ , attentional and memory difficulties ⁸ impaired attention ⁹ . | 6- Farewell et al. 1990 7- Smith et al. 1987 8- Riva and Devoti 1996 9- Mannie et al. 1993 |
| 2 | Phenytoin | Poor concentration, memory, visuomotor functions and mental speed & more detrimental effects on memory than carbamazepine ¹⁰ slowed performance on information processing tasks with phenytoin in comparison with carbamazepine ¹¹ . | 10- Pulliainen and Jokelainen, 1995; 11- Aldenkamp et al. 1994 |
| 3 | Carbamazepine | deterioration in measures of information processing speed and attention, ¹² detrimental effects on memory, ¹³ worse arithmetic performance ¹⁴ | 12- Wesnes et al. 2009 13- Shehata et al. 2009 14- Kang et al. 2007 |
| 4 | Sodium valproate and ethosuximide | detrimental impact on cognitive function, ¹⁵ subtle changes in cognitive function, ¹⁶ relationship between plasma concentration and cognitive performance in children ¹⁷ | 15- Sun et al. 2008 16- Prevey et al. 1996 17- Brouwer et al 1992 |
| 5 | Topiramate | impaired concentration, ¹⁸ cognitive dulling, ¹⁹ psychomotor slowing, ²⁰ detrimental effects on short-term memory ²¹ reduced IQ score ²² | 18- Froscher et al. 2005 19- Coppola et al. 2008 20- Tatum et al. 2001 21- Gomar et al. 2007 22- Sun et al. 2008 |

Table 2 Common drugs indicated for Cognition improvement in Ayurveda classics with their active ingredients

| Sr. no | Drug | Classical Indication ²⁹⁻³⁰ | Active ingredient |
|--------|---------------|---|---|
| 1 | Shankhapushpi | <i>Kalka</i> (fine paste) of whole plant highly regarded as <i>Medhya</i> | Microphylllic acid, shankhapushpin, kaempferol & its glucoside, 3, 4 dihydroxycinnamic acid, sitosterols. |
| 2 | Yashtimadhu | <i>Choorna</i> (fine powder) of dried root is used by oral route with milk for therapeutic purpose as <i>Medhya</i> . | Glycyrrhizine, flavonones, isoflavones, glycyrrhetic acid, many phenolic compounds. |
| 3 | Brahmi | whole plant juice is recommended for increasing <i>Medha</i> (intellect) | Saponin, jujubogenin, bacopasaponin G, and glycoside, bacopasides III, IV and V |
| 4 | Guduchi | <i>Swaras</i> (Juice) of whole plant is used therapeutically as <i>Medhya</i> . | Alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides. |
| 5 | Mandukparni | <i>Swaras</i> (fresh whole plant juice) is used for therapeutic purposes as <i>Medhya</i> (cognitive enhancer) | Saponin (medacoside, asiaticoside, medacassoside, asiatic acid & triterpenic acid. |
| 6 | Jatamamsi | Rhizome is used for medicinal purposes in different psychiatric illness as it has | Terpenoid ester, nardostachysin I |

Bhutaghnaor Manasa Doshahara (relieves of psychiatric problems) and *Medhya* properties.

Evidences from different researches

MANDOOKPARNI (*Centella Asiatica*)

- Mandookparni has shown brain growth promoter activity³¹.
- Dendritic arborisation activity of *mandookparni* is supposed to be the neuronal basis for improved learning and memory³².
- Anti-seizure activity of *Mandookparni* may result from direct or indirect modulation of ATPase activity³³.
- *Centella asiatica* inhibits the memory impairment induced by scopolamine through the inhibition of AChE³⁴.

SHANKHAPUSHPI (*Convolvulus pleuricaulis*)

- Pre-clinical research on BR-16A (Mentat- polyherbal compound containing shankhapushpi) has established that it enhances cognition and also protects rats against amnesia (anterograde and retrograde amnesia) induced by electroconvulsive shock³⁵.
- **Learning, memory and behavior**³⁶ - The ethanolic extract of shankhapushpi has shown significant improvement in learning and memory in rats

using various laboratory models for learning and memory assessment.

- **Anticonvulsant activity**- water soluble portion of ethanolic extract of shankhapushpi decreased spontaneous motor activity and the fighting response. It has also seen that, electrically induced convulsive seizures were antagonized by the extract of Shankhapushpi³⁷.

Animals treated with the methanolic extracts of whole plant of shankhapushpi, showed significant protection against tonic seizures induced by transcorneal electroshock, which was comparable with that of standard drug phenytoin³⁸.

YASHTIMADHU (*Glycyrrhiza glabra*)

- The roots and rhizomes of Yashtimadhu (*Glycyrrhiza glabra*) is an efficient brain tonic; it increases the circulation into the CNS system³⁹.
- Liquorice has shown significant action on memory enhancing activity in dementia. Improved learning and memory on scopolamine induced dementia was observed⁴⁰.

GUDUCHI (*Tinospora Cordifolia*)

- *Guduchi (Tinospora cordifolia)* has been claimed to possess learning and memory enhancing activity⁴¹.
- *Tinospora cordifolia* enhance the cognition in normal and cognition deficits animals in behavioural test Hebb William maze⁴².
- Cognitive enhancement mechanism of *Tinospora cordifolia* is by immune stimulation and increasing the synthesis of acetylcholine⁴³.

BRAHMI (Bacopa Monniera)

- Brahmi has Cognitive enhancer properties⁴⁴.
- Alcoholic extract of Brahmi increases cognitive function and retention capacity, decreases retrograde amnesia. Protection from phenytoin -induced cognitive deficit in the Rats was also observed⁴⁵.
- Brahmi (Bacopa Monniera) mainly utilized in the treatment of memory and attention disorders⁴⁶.

JATAMAMSI (Nardostachys jatamamsi)

- *Jatammsi* is proven to have effect on improving learning and memory in mice⁴⁷.
- An acetone extract of *N. jatamansi* has shown significant inhibition of benzoyl peroxide-induced cutaneous oxidative stress in mice⁴⁸.

- Roots and rhizomes of *N. jatamansi* are used to treat epilepsy, hysteria, and convulsions⁴⁹.

- The *kwath* (decoction) of the *Jatamamsi* is also used in neurological disorders, insomnia and disorders of cardiovascular system⁵⁰.

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DISCUSSION & CONCLUSION

Data obtainable thus far support procognitive activity of herbs explained in Samhita within the context of medhya rasayana; at a similar time demand substantial evidences and revalidation in humans. Above aforementioned herbs act on the premise of antioxidant, adaptogenic or essential trace components present in them. Their activity on modulation of biological axis and neurotransmitters needs additional investigation so as to use them as an adjuvant medical aid.

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