



Review Article

CONCEPT OF *CHARAKOKTA MEDHYARASAYANAS* IN AGE RELATED MILD COGNITIVE IMPAIRMENT (MCI)

Mahajan Madhavi¹, Parauha Saurabh^{2*}, Sawale Surekha³

¹Associate Professor, ²Ph.D. Scholar, ³MD Scholar, Department of Kayachikitsa, College of Ayurveda, BV University, Pune, Maharashtra, India.

ABSTRACT

Life expectancy has increased as a result of advancement in medical science. As a result the number of elderly in the population is also greater than ever and there is a need to tackle their problems. Mild Cognitive Impairment (MCI) is one of the most common clinical manifestations affecting the elderly population. This is a transitional stage between the cognitive decline of normal ageing and the more serious decline in dementia. Timely intervention is awfully important in these cases as they are at a high risk of developing dementia. According to *Sarangadhara Acharya, Medha* (grasping and retention power) deteriorates after the fourth decade of life and this may be considered as a warning signal for further *Smriti* (memory) and *Buddhi* (intellect) deterioration, in the successive years. Ayurveda has a major role to play in this arena. The '*Medhya Rasayanas*' are known to be beneficial to improve the intellectual e.g., *Mandukparni Swaras, Yashtimadhu Churna* with *Ksheer, Guduchi Swaras*, and *Shankhapushpi Kalka. Medhya Rasayana* drugs are used for prevention and treatment of mental disorders of all the age groups. These drugs promote the Intellect (*Dhi*) Retention power (*Dhriti*), Memory (*Smriti*). This review discusses about *Medhya Rasayanas* as a great player for prevention and management of age related cognitive decline.

KEYWORDS: Aging brain, *Jara*, Mild Cognitive Impairment, *Medhya Rasayana*.

INTRODUCTION

The process of aging begins at birth or conception and continues throughout life. This process of ageing brings changes which are unsolicited, irreversible and inevitable.^[1] Current trends in demographics coupled with rapid urbanization and lifestyle changes have lead to an emergence of a host of problems faced by the elderly in India. Age related MCI is the cognitive decline of thinking, memory and reasoning. Normal ageing and Dementia are considered as two opposite ends of a continuum and the area of transition between them has been recognized as "Mild Cognitive Impairment". The individuals fall in under the category of MCI exhibit symptoms, that lie between normal age related cognitive Decline from their past level of functioning and therefore they do not meet criteria for Dementia.

India is in a phase of demographic transition. According to the state of World Population 2019 report by the United Nations Population Fund (UNFPA) released this year, India's population in 2019 stood at 1.36 billion, growing from 942.2 million in 1994 and it has been projected that by the

year 2050, the number of elderly people would rise to about 324 million. India has acquired the label of "an ageing nation" with 7.7% of its population being more than 60 year old. As percentage of the older people increasing worldwide, their health problem is becoming an important public concern. The mental health problems of the older adults need to be recognized. Among these the neuropsychiatric disorders like Dementia, MCI etc. account for 6.6% of the total disability.^[2]

MCI is not mentioned as a disease entity in separate chapters of Ayurvedic classics but sign and symptoms of the MCI can be understood in terms of various Ayurvedic concepts. According to Ayurveda Cognition comes under the concept of *Gyanotpatti, Medha, Buddhi* and *Smriti*. Clinical trials are being conducted on MCI worldwide, but an effective pharmaceutical management is not present till date. Ayurveda believes that *Manas* and *Indriyas* are *Panchbhautika* as well as *Ahankarika*, hence *Dravyabhoota* and *Adravyabhoota Chikitsa* both should be applied in the management of mental disorders. *Rasayana* therapy comes under the

purview of both *Dravyabhoota* and *Adravyabhoota Chikitsa*. Among the *Rasayana* drugs, *Medhya Rasayana* is the special class of *Rasayana* acting over the neurodegenerative disorder like age related MCI.

MATERIAL AND METHOD

Review study- For this all the verses that dealt with age related MCI w.s.r to *Smrutibuddhihrasa* was taken under specific headings. The aetio-pathogenesis, symptomatology were taken from Ayurveda and modern medical texts, research articles, internet sources, Ayurveda data base.

Disease Review

Ageing is fundamentally the outcome of the overwhelming of the evolutionary process of the body mind system by the evolutionary events hallmarked with degenerative changes like physiological disturbances of neurotransmitter secretions, blunting of dendrites and synapse and formation of beta amyloid plaques warranting reparative and rehabilitative care.

MCI is considered as prodromal stage of an impending Dementia, particularly AD. There is no proper cutoff point to separate MCI from Dementia. But this is the stage to decide the management's protocols of present and forthcoming consequences.

Nidana and Samprapti

The exact cause and mechanism by which age related MCI develops is still unknown. But the main postulates are:

1. Genetic causes/gene mutations^[3]
2. Oxidative damage to the nerve cells^[4]
3. Aggregated protein's in the nerve bodies^[5]
4. Mitochondrial abnormalities^[6]
5. Abnormal neuronal cell death^[7]
6. Impairment in axonal transport^[8]
7. Cytotoxicity^[9]

Diagnostic Criteria for MCI^[10]

1. Memory complaint, preferably qualified by an informant
2. Memory impairment for age
3. Preserved general Cognitive function
4. Intact activities of daily living
5. Not demented

Ayurvedic Concept of Age related MCI

Maharshi Charak states

"Laksanam Manaso Jnanasyabhaobhava Eva Cha"
(Charak sharir 1/18)

Manas is the important factor in the origin of *Prajnya* and hence, all activities (*Karmas*) which are being done. *Manas* and *Indriya* are also involved in the process of *Gyanotpatti*. *Manas* is considered as sensory as well as motor entity.^[11] However, *Manas*

itself is regulated by *Vata* and in old age (*Vriddhavastha*), *Vatavaigunya* is already present hence functions of *Manas* is also affected physiologically to a great extent.

Ageing is a slow and continuous process, which affects various bodily tissues at different times. There are no two opinions regarding the inclusion of declining in *Medha* (intellect) as part of ageing. In this way the process of brain ageing, according to Ayurveda, definitely begins in the fourth decade of life, which includes neurodegeneration. Therefore, neurodegeneration starts in the 4th decade as a part of normal phenomena of aging.^[12]

When the rate of the aging process is disproportionate to the age of individual, the appearance of signs and symptoms of ageing (*Jara*) before the normal age occur that are mentioned under the *Aswabhavika* aging or *Kshaya*. It has been termed as *Akalaja Jara*. This type of ageing may be of greater intensity and rapidly progressing if no care is taken to check it.

In Ayurvedic literature, the etiological and risk factors for *Aswabhavika Kshaya* has been clearly described by *Acharya Charaka* and *Vagbhata*, under the heading of *Gramya Ahara Vihara* and clearly state that, regular practicing of these etiological factors (*Nidanas*) lead to different types of diseases related with premature aging including *Smritibuddhihrasa*. It is obvious from the above description that the majority of etiological factors resulting in premature aging because of disproportionate degeneration of body tissues with age and *Smritibuddhihrasa* are mainly related with the diet, lifestyle and psychological status. They are *Vatavriddhikara*, *Dhatu Ojokshayakara*, *Abhishyandi*, *Srotovarodhaka* and *Raja* and *Tamaguna Vriddhikara*. Thus, they are causing one or more of the following effect in the body *Srotovarodha*, *Dhatukshaya*, *Ojokshaya*, *Manas Dushti*, *Smritibuddhihrasa*, *Vatic* diseases etc. During the old age *Vata* remains in its increased form which may vitiate any time even by the slight indulgence in the causative factors of *Vata*.

Neurological disorders are mainly due to imbalance in *Vata* and partial involvement of *Pitta* and *Kapha*. *Vata* is responsible for movement of impulses through the brain and the nerves which control both voluntary and involuntary functions. *Vata* derangements always results in some weakness, disturbance, or hypersensitivity of the nervous system resulting in, problematic conduction, dryness and death of neurons. Likewise, *Pitta* which is responsible for digestion and assimilation plays a vital role in either accumulation or clearing out of neuro fibrillary tangles and *tau* proteins. *Kapha* which provides nourishment and sliminess to the

synapses helps in proper conduction which is also compromised in the pathogenesis.^[13]

Ojas which is nourished by nutrients is also responsible for the compactness of body elements by providing adequate nutritional defense against body elements. *Ojakshaya* i.e. inadequate nutritional diffuse against body elements is very much responsible for aging and age related cognitive impairment.^[14]

There is "Selective alteration" in neurons of the brain termed as sites of "*Khavaigunya*". This alteration is produced due to deviated metabolism created by the malfunctioning of *Agni* (*Agnivaishamya*). Because *Agni* is responsible for each and every catabolic and anabolic activity, this leads to down regulation of cholinergic receptors like acetyl choline esterase that are prodromal cause of cognitive impairment and by accumulation of neuro fibrillary tangles and increase the pathology of the disease.

Dhatukshaya and *Margavarodha* are the cardinal aetiologies for the vitiation of *Vata Dosha*.^[15] The accumulation of protein can be understood as collection of *Aama* at the cellular level. *Margavarodha* may be caused of the formation of *Aama* precipitated by *Vishamagni* which was formed due to *Vatadushti*. *Kaayagni* is the end process of metabolism occurring in tissue level involving bio enzymes which determines the proper formation of *Saara* (nourishment) and *Kitta* (waste) in that level. The proper functioning of *Vata* in cellular level will make use of nutrients for building tissues and removing wastes from the system. *Vikruti* of *Kaayagni* and *Vata* at the level of neurons is the cause of production of *Aama* which leads to AD. This accumulation of waste as *Aama* which can be correlated with protein aggregation can disturbs the equilibrium and leads to degenerative changes. This degeneration further vitiates *Vata* and it goes on in a vicious circle. The possibility of *Avarana* of *Vata* should also be considered logically as in *Pranaavrita Samana* there will be difficulty in speech, slurring speech and even dumbness.^[16] If *Vyana Vata* is occluded by *Prana Vata*, then there will be loss of functions of all the senses and there will be loss of memory as well as strength.^[17]

Treatment

The patient should be given proper counseling and mental support i.e. nothing but the *Satvavajaya Chikitsa* as it is the best in management of *Manovikara* (psychological disturbances). This will be very helpful to manage the behavioral symptoms of patient of MCI. *Rasayana* therapy including *Medhya Rasayan* and *Achara Rasayana* must be planned for the MCI because it helps us in strengthening the host

defense mechanism. It is very beautifully says about right mental and physical conduct, which when followed lead to a disease free life. A regulated lifestyle, wholesome diet, appropriate behavior, and following ideal code of conduct as quoted in Ayurveda are best to prevent and manage the Neurodegenerative diseases in general and age related MCI in particular.^[19]

Management of MCI is challenging and gratifying despite the absence of cure or a robust pharmacologic treatment. Although Donepezil shows significant impairment in condition of MCI and Alzheimer's disease but it is accompanied with a lot of side effect.

Many new scientific studies have been conducted showing that the Ayurvedic *Rasayana* therapy is very useful in the prevention of prognosis of cognitive impairments and other neurodegenerative disorders. Among the *Rasayana* drugs, *Medhyarasayana* are the special class of drugs described for prevention and management of *smritibuddhihrasa* and simultaneously managing the consequences of aging. *Charakokta Medhyarasayana* drugs mentioned are *Mandookaparni*, *Guduchi*, *Yastimadhu*, and *Shankapushpi* may have pharmacological action similar to the nootropic agents.^[20] It may have effect on cerebral circulation and may enhance oxygen consumption and glucose utilization by the brain cells. Potentially it may be useful in cases of degenerative brain disorders. Early detection of the problem and early starting of the appropriate *Rasayanas* is required to prevent the progress of the condition. *Medhya* drugs are useful in the prevention and management of cognitive impairments and effective in improving not only the quality of life of the patient, but also the care givers/family members in broader sense. Thus in conclusion, the control of aging and prevention of cognitive impairments is possible by *Rasayana* by which some or the other way improve the life expectancy.

Utility of *Medhya rasayana*^[21]

Medhya Rasayana has a specific purpose of benefitting *Medha* in particular and they do not have broad spectrum of action like other *Rasayanas*. As per *Acharya Susruta*, the benefits derived from *Medhya Rasayana* and their applied aspects are enlisted below.

1. *Shruta Nigadi* (Power of retention of scriptures)
2. *Smrutiman* (Endowed with good memory)
3. *Medhavi* (Becomes genius)
4. *Grantham Ipsitam utpadayati* (Develops enthusiasm to read the scriptures)

5. *Nastam cha Pradurbhavati* (Power to recollect the forgotten)
6. *Dvirucchaaritam shatamapi avadharayati* (Capable of retaining 100 words spoken only twice)
7. *Moorthimaticcha enam vagdevyanupravishyati* (Goddess of speech enters one's body)
8. *Sarvaischa enam shrutayaupatishtanti* (All the srutis remain within)
9. *Shruta dharaya panchavarsha shatayur bhavati* (Power of remembering the scriptures and a life of 500 years)
10. *Shrotram vivriyate* (Endowed with good hearing capacity)
11. *Dvirabhyasat smrutiman bhavati* (Endowed with good memory)
12. *Trirabhyasat shrutamadatte* (Retains the scriptures in one's mind)
13. *Sarvam tarati kilvisham* (Gets rid of all blemishes)

Probable mode of action of *Medhya Rasayana*

The *Medhya* effect of *Rasayana* can be considered as *Prabhava janya* (unthinkable and unimaginable). This attribution holds good since the action of *Medhya dravya* cannot be related to a particular quality of the drug. Maintaining of normal functioning of *Sadhaka pitta* and *Tarpaka kapha* is the desired action of any *Medhya* drug. *Medhya* drugs also act on *Manasika bhavas* (faculties of mind) there by relieving anxiety, stress etc. They are having *Mastishka balya* (nourishing brain) property. It is very difficult to conclude the mode of action of *Medhya Rasayanas* as the mechanism of *Medha* is very complex one and the properties of *Medhya Rasayana* are also not uniform.

Mandukaparni (Centella asiatica Linn.)

1. Major constituents of it are saponins, medacoside, asiaticoside, medacassoside and asiatic acid, a new triterpenic acid.^[22]
2. They act on behavior besides being neuro-protectives and brain growth promoters. Dendritic arborization is supposed to be the neuronal basis for improved learning and memory.^[23]
3. Anti-seizure activity may result from direct or indirect modulation of ATPase activity. *Centella asiatica* Linn. inhibits the memory impairment induced by scopolamine through the inhibition of AChE.^[24]
4. Methanol extract of *Centella asiatica* Linn. showed highest free radical scavenging activity that can be attributed to the presence of polyphenols and flavonoids as this fraction contains maximum amount of these secondary

metabolites (0.07mg/ml). These two namely poly phenols and flavonoids are responsible for potent anti-oxidant activity and terminate free radicals.^[25]

5. *Centella asiatica* Linn. extract selectively decreases amyloid beta levels in hippocampus of Alzheimer's disease animal model.^[26]
6. *Centella asiatica* Linn. accelerates nerve regeneration upon oral administration and contains multiple active fractions increasing neurite elongation in-vitro.^[27]

Yasthimadhu (Glycyrrhiza glabra Linn.)

1. The roots and rhizomes of *G. glabra* have been studied with respect to spatial learning and passive avoidance, preliminary free radical scavenging, cerebral ischemia and antioxidant capacity towards LDL oxidation.^[28]
2. *Glycyrrhiza glabra* Linn. aqueous extract markedly improves anti-hypoxic effects induced by sodium nitrite in rats and this effect may be mediated by its antioxidant properties.^[29]
3. The roots and rhizomes of *Glycyrrhiza glabra* Linn. is an efficient brain tonic; it increases the circulation into the CNS system and balances the sugar levels in the blood.^[30]
4. Liquorice has significant action on memory enhancing activity in dementia. It significantly improved learning and memory on scopolamine induced dementia.^[31]

Guduchi (Tinospora cordifolia (Willd) Miers.)

1. Its root is known for its anti-stress, anti-leprotic and anti-malarial activities.^[32]
2. Chemical constituents' classes are alkaloids, diterpenoid lactones, glycosides, steroids, sesqui terpenoids, phenolics, aliphatic compounds and polysaccharides.^[33]
3. Neuro protective and ameliorative properties are due to their antioxidant and trace element contents.^[34]
4. *Tinospora cordifolia* (Willd) Miers. is known to be a rich source of trace elements (Zinc and Copper) which act as antioxidants and protects cells from the damaging effects of oxygen radicals generated during immune activation.^[35]
5. It increases the blood profile and has lead scavenging activity.^[36]
6. *Tinospora cordifolia* (Willd) Miers. has been claimed to possess learning and memory enhancing and antioxidant activities.^[37]
7. *Tinospora cordifolia* (Willd) Miers. enhanced the cognition in normal and cognition deficit animals in behavioural test Hebb William maze and the passive avoidance task. Mechanism of cognitive

enhancement is by immune stimulation and increasing the synthesis of acetylcholine, this supplementation of choline enhances the cognition.^[38]

8. Myriad actions of *Guduchi* may be attributed to its antioxidant and immune modulatory properties.^[39]

Shankhapushpi (*Convolvulus pleuricaulis* Chois.)

1. Important chemical principles are microphyllic acid, shankhapushpin, kaempferol kaempferol-3-glucoside, 3, 4 dihydroxycinnamic acid and sitosterols. Neuro-protective and intellect promoting activity is implicated to the free radical scavenging and antioxidant properties.^[40]
2. BR-16A (Mentat) a poly-herbal combination containing *Shankhapushpi* significantly reversed the social isolation stress-induced prolongation of onset and decrease in pento barbitone induced sleep, increased total motor activity and stress induced anti nociception in experimental model.^[41]
3. Ayushman-8 (containing *Shankhpushpi*, *Brahmi* and *Vacha*) reported to be effective on *Manasa mandata* (mental retardation).^[42]
4. *Shankhapushpi* compound containing *Shankhapushpi*, *Sarpagandha*, and *Gokshura* in equal quantities are studied to be effective in *Chittodvega* (anxiety disorders).^[43]
5. *Shankhapushpi* is effective in relieving signs and symptoms of *Chittodvega* (anxiety disorders).^[44]
6. Herbalists believe that *Shankhpushpi* calms the nerves by regulating the body's production of the stress hormones, adrenaline and cortisol.^[45]
7. Few investigations report that *Shankhpushpi* has potent depressive action in mice.^[46]
8. *Convolvulus pleuricaulis* Chois. whole plant extract, shows the highest inhibitory activity against *Helicobacter muridarum*.^[47]
9. *Convolvulus pleuricaulis* Chois. aqueous extract possesses neuro protective potential, thus validating its use in alleviating toxic effects of scopolamine.^[48]

DISCUSSION

Regarding administration of *Medhya rasayana* Acharya Charaka suggests taking it as *Vatatapikarasayana*, as the description is found in '*Kara prachiteeya rasayana pada*' which mainly deals with *Vatatapika rasayana*. Whereas as per Acharya *Susruta* almost all *Medhya Rasayanas* mentioned are to be administered in *Kutipraveshika vidhi*. So both the methods of administration can be considered in the context of *Medhya Rasayana*. Early morning before food is preferred as the ideal time for the

administration of *Medhya Rasayana*. In *Yoga Ratnakara*, '*Prabhata*' is the word used for the time of administration for the four *Medhya* formulations. *Medhya* drugs are mainly *Madhura* and *Sheeta dravyas*, but there are many *Medhya* drugs which do not possess these qualities. It is observed that main *Medhya Rasayanas* (*Mandukaparni*, *Yasthimadhu*, *Guduchi* and *Sankhapushpi*) are *Madhura vipaki dravyas*. Majority of them are *Seeta veerya dravyas*. *Medha* is the *karma* given to *Prakrita pitta*. This can be related to orientation and grasping power. *Guduchi*, being *Madhura vipaka* and *Ushna virya* can help in enhancing grasping power as its constitution is ideal for *Karma* of *Pitta*, especially *Sadhaka pitta*. It can stimulate neuronal functions due to the *Pachana karma*. The *Madhura vipaki* and *Seeta virya dravyas* can help the function of *Tarpaka kapha* to go on smoothly owing to its constitution that is favourable for *Kapha karma*. *Dhruiti* i.e., *Dharana shakthi*, memory retention capacity can occur in the presence of only *Seeta virya*. Pharmacological studies reveal that *Mandukaparni* has neuroprotective, brain growth promoter, anti seizure activities and free radical scavenger (antioxidant) properties and is helpful in subsiding neurodegenerative changes that occur with Alzheimer's disease and also accelerates repair of damaged neurons; It has been found that *Yasthimadhu* is an anti-oxidant, memory enhancer and improves antihypoxic effects; *Guduchi* has got neuroprotective, antioxidant, memory enhancing, anti-stress, antileprotic and antimalarial properties; It is observed that *Shankhapushpi* has got antistress, neuroprotective and antioxidant properties.

CONCLUSION

Promotion of mental health is the need of the hour. Ayurveda a holistic science provides solutions for memory related disorders in a fruitful way. System of Ayurveda with its longest clinical experiences can do a lot for preventing and management of MCI and other neurodegenerative disorders. Ayurveda treatments like *Medhya Rasayana*, *Acharya Rasayana*, *Satvavajaya Chikitsa* etc. can effectively reduce the progression of disease and provide a better quality of life to patients of MCI. In the present scenario *Medhya Rasayana* drugs of Ayurveda can be used to obtain effective results in memory related disorders. Hence attempt has been made to think logically in the aspect of memory promotion in a view to seek greener pastures.

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***Address for correspondence**

Dr Parauha Saurabh

Ph.D. Scholar (Kayachikitsa),
Department of Kayachikitsa, College
of Ayurveda, BV University, Pune,
Maharashtra.

Mo. no. 9039920250

Email: sparauha5@gmail.com

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