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Clinical Evaluation of Medhyarasayana Ghrita along with Vachadi Ghrita Nasya (Pratimarsha) on Senile Dementia

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ABSTRACT

Mind and body are intimately associated with each other. The function of body organs depends on mental makeup of an individual and vice versa. Many factors such as stress, anxiety, depression, negative thoughts, unhealthy life style, unwholesome diet etc., influence mental and physical wellbeing. In senile Dementia progressive deterioration of memory, intellect, attention, thinking, comprehension and personality etc, is encountered during old age with preservation of normal level of consciousness. Medhyarasayana ghrita is a research based newly formulated medicine which contains sankhapushpi, mandukaparni, yastimadhu, guduchi, jyotishmati, kushmanda, ashwagandha, tulsi, bhallatak,kapikachchu and zinc processed with ghee. Vachadi ghrita in form of pratimarsha nasya was administered along with oral Medhyarasayana ghrita. Vachadi ghrita nasya contains vacha, kustha, pippali which also have rasayana property. On Hamilton Anxiety Rating Scale, patients had anxiety, tension, depression, difficulty in concentration & memory and fear. On Hamilton Depression Rating Scale, these patients had anxiety, depression, hypochondriasis and hopelessness. On Brief Psychiatry Rating Scale, psychological factors affected include anxiety, depression, somatic concern and tension etc. Medhyarasayana ghrita along with vachadi ghrita improved clinical features in statistically highly significant ($p<0.001$) manner. The bio-marker serum cholinesterase showed statistically insignificant improvement. The data reflects that disturbed mental health plays an important role in etiopathogenesis of senile dementia.

Key words: Psychological factors, Senile dementia, Alzheimer's disease, vascular dementia.

INTRODUCTION

Ayurveda a complete science of health, not only describes diseases and its management, but also the principles for promotion and maintenance of health in vivid way. It states that a person will be healthy when doshas, agni, dhatus, malas of his body remain in equilibrium condition associated with sensorial, mental and spiritual well being. Hence, an intimate relation always persists between body and mind. Dementia is a type of disease where degeneration of brain particularly in cortical area, takes place and affects mainly elderly persons. As per DSM – IV (Diagnostic and statistical manual of mental disorders), memory impairment is the essential feature of this disease which is characterized by multiple cognitive deficits that includes impairment in memory and at least one of the following cognitive disturbances such as aphasia (language disturbance), apraxia (impaired ability to carry out motor activities despite intact motor function), agnosia (failure to recognize or identify objects despite intact sensory function), or a disturbance in executive

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functioning (i.e., planning, organizing, sequencing, abstracting) and which occurs exclusively without impairment in consciousness. The other cognitive functions that can be affected in dementia include general intelligence, learning, language, problem solving, orientation, perception, attention and concentration, judgment and social abilities. The personality is also affected. Agitation or withdrawal, hallucinations, delusions and insomnia are also common. The diagnosis of dementia, according to DSM-IV, requires the symptoms that result in a significant impairment in social or occupational functioning and that they present a significant decline from a previous level of functioning. Ayurveda states that medha (intellectual power of mind) deteriorates at 4th decade of life and buddhi (power of reasoning) and the activity of mind deteriorate at 9th decade of life normally. Hence, in normal ageing, minor memory problem can occur but it does not become so severe that it will interfere significantly with a person's social or occupational behavior which is commonly found in Dementia and if it is not properly managed, these demented patients may become helpless, hopeless, incapable of remembering the names of close relatives, they may wander into dangerous situations being oblivious of their surroundings and may commit

With the increase in life span and decrease in death rate, the prevalence of dementia is rising all over the world. Of all patients with dementia, 50 to 60 percent have the most common type of dementia i.e., dementia of Alzheimer's type (Alzheimer's disease). Worldwide there is a new case of dementia every seven seconds and more than 35 million people are currently estimated to have dementia with more than 4.6 million new cases diagnosed each year[1]. The number of people suffering from dementia is expected to be 107 million by the year 2050. More than sixty percent of people with dementia currently live in developing countries. Numbers are increasing, especially in rapidly developing and heavily populated regions such as China, India and Latin America. It is estimated that there are already approximately 1.5 million people affected by dementia in India and this number is likely to increase by 300% in the next four decades.

This disorder may be progressive or static, permanent or reversible. An underlying cause is always assumed, although in rare cases it is impossible to determine a specific cause. The potential reversibility of dementia is related to the underlying pathological condition and to the availability and application of effective treatment. Approximately 15% dementia is reversible if treatment is initiated before irreversible damage takes place. More women have Alzheimer's disease than men; this may reflect women's longer life spans. In a study, it was revealed that among the people above 65 years, men and women reported to have 0.6% and 0.8% prevalence rate respectively. At age 90, these rates are 21 percent for men and 25 percent for women. The prevalence of moderate to severe dementia in the population over 65 years is approximately 5% and 20 to 40 % in older than 85 years of age.

The prevalence of dementia nearly doubles with every 5 years of age after the age of 60 years. The 1% of people aged 60 to 64 are affected with dementia, 2% of aged 65 to 69 years, 4% of aged 70 to 74 years, 8% of aged 75 to 79 years; 16% of aged 80 to 84, and 30 to 45% of aged 85 and above respectively[2].

According to the 1997 American Psychiatric Association Practice guideline for the treatment of patients with Alzheimer's disease and the dementia of late life, the onset of the disease generally occurs in late life, most commonly in the 60s, 70s and 80s and beyond, but in some instances the disorder appears in the 40s and 50s known as early onset dementia. The second most common type of dementia is vascular dementia, which is usually related to cerebrovascular diseases. Hypertension predisposes a person to the disease. Vascular dementia account for 15 to 30% of all dementia cases and is most common in people between the ages of 60 and 70 years with more common in men than in women. Approximately 10 to 15% of patients have co-existing vascular dementia and dementia of the Alzheimer's type. Dementia affects more

than 4 million Americans and results in a total health care cost of more than $100 billion annually.

Though, Senile dementia has not been described as disease entity in separate chapters in Ayurveda, some Ayurvedic terms can be correlated with Dementia. It has been mentioned in Madhav Nidana that Smritinasha is among the prodromal symptoms of jara. Charak has described the symptom of Smritibhramsha where smriti is vitiated by rajas and tamas[3]. Hence, Senile dementia can be correlated with Jarajanya Smritibhramsha according to Ayurveda.

Today, Dementia has become the burning problem of the old as well as younger persons. But, the causes of dementia of the Alzheimer's type still remain unknown. Some studies have indicated that as many as 40 percent of patients have a family history of dementia of the Alzheimer's type. Thus, genetic factors are presumed to play a part in the development of the disorder,at least in some cases[4]. Regarding treatment, there is no definite drug is yet available. Early diagnosis and timely medication have become difficult due to unavailability of sophisticated equipments and high cost respectively. Moreover, no direct therapy is available which can reverse or retard the pathophysiological processes permanently. Though cholinesterase inhibitors such as tacrine, donepezil, rivastigmine are used since long times but they did not provide satisfactory results.

On the other hand, Ayurveda is gradually gaining fast popularity for its management of complex psychiatric disorders. The concept of Medhya Rasayana is being used successfully in the treatment of various psychiatric illnesses. As Dementia is an Urdhajatrugata Vikara, Nasya especially Pratimarsha nasya in old persons may be beneficial. In Charak Samhita, Chikitsa sthana 9th and 10th chapters deal with neuropsychiatric disorders viz. Unmada and Apasmara and there is a mention of Nasya in their management. In the etiopathogenesis of dementia, particularly of Alzheimer's type, the role of free radicals is very much advocated. Antioxidants are the substances which can prevent oxidation and rancidity of fat or oil. Vitamin C, E, beta carotenes are some well known antioxidants. They have anti-ageing property also.

The present study aimed at evaluating the efficacy of Medhyarasayana ghrita along with Vachadi ghrita pratimarsha nasya in Senile dementia.

MATERIAL AND METHODS

Total 35 patients with signs and symptoms suggestive of Senile dementia were registered out of whom 25 patients completed the 3 months' treatment course.

Inclusion criteria

Patients aged within 60 – 90 years attending the OPD of Kayachikitsa Department, I.P.G.T. & R.A, Hospital Jamnagar were screened and those fulfilling the clinical features of Senile dementia based on both Ayurvedic and modern descriptions, were selected.

Exclusion criteria

Patients who were out of the above age group and suffering from psychiatric and neuropsychiatric conditions like Schizophrenia, Parkinsonism, Huntington's disease, Pick's disease etc, persistent endocrine disorders, any other chronic systemic disorders and persons taking psychotropic drugs including alcohol were excluded.

Method of study

The diagnosed dementia patients were subjected to the clinical trial. Before registering the patients, written consent was taken and the study was cleared by Institutional Ethics Committee. The study was conducted as a randomized single blind clinical trial.

Drug, Dose, Duration & Diet

The dementia patients were prescribed Medhyarasayana Ghrita, 10 gm twice daily

in morning & evening for 3 months in empty stomach followed by drinking lukewarm water. Vachadhi ghrita pratimarsha nasya two drops in each nostril twice a day in the morning and evening were also administered for 3 months. Before taking the medicine, patients were advised to take Haritaki churna in a dose of 3-4 gms at bed time for 3-7 days for koshthasuddhi according to the type of koshtha. All the patients were advised to follow appropriate diet as per their Prakriti. They were advised to take Sattvika ahara, to correct their dietary habits and to avoid unhygienic and stale food. *Follow up study:* After completion of treatment patients were observed up for 1 month and all parameters of assessment were assessed.

CRITERIA FOR ASSESSMENT

Subjective criteria

CT scan (if affordable), Mini-mental state examination (questionnaires), Bender Gestalt Motor Visual Test, Hamilton Anxiety Rating Scale, Hamilton Depression Rating Scale, Improvement in clinical features, Brief Psychiatry Rating Scale.

Chief complaints of Senile dementia and others symptoms related to specific rating scales such as Hamilton Anxiety Rating Scale etc., were assessed by 0-4 gradations according to the severity. Visual memory was assessed by Bender Gestalt Motor Visual Test by grading from 0-3 on the basis of severity.

Objective criteria

Serum Choline esterase estimation, Routine haematological and bio-chemical investigation, Urine and stool examination.

OBSERVATION AND RESULTS

Effect of therapy on chief complaints: Suicidal thoughts were relieved by 72.22% which is statistically highly significant ($p<0.001$) followed by 68.75% relief in irritability ($p<0.001$) where as improvement in intentional tremor, assistance in personal care, disturbed sleep, mislaying of objects, losing valuables, impaired attention, forgetting names, forgetting numbers, decreased efficiency in household tasks, making mistake in accounts, forgetting food cooking on stove, difficulty in preparing food/ meals, recognition of family faces and surrounding, forgetfulness and gait difficulty was 68.42% ($p<0.001$), 61.53% ($p<0.05$), 59.61% ($p<0.001$), 59.21% ($p<0.001$), 59.15% ($p<0.001$), 35.13% ($p<0.05$), 56.06% ($p<0.001$), 56.75% ($p<0.001$), 51.02% ($p<0.001$), 49.05% ($p<0.001$), 52.38% ($p<0.05$), 50% ($p<0.05$), 56.09% ($p<0.001$), 47.27% ($p<0.001$) and 55.55% ($p<0.001$), respectively. Therapy showed moderate improvement in most patients (64%). These findings are suggestive for psycho activity of the Ayurvedic formulation. The nourishment of mind provided by Medhyarasayana ghrita can increase physical and mental capacity and can decrease weakness and fatigue and can increase self confidence. However, results also indicate important role of counseling in Senile dementia.

As Kapha dosha is found increased in maximum number of patients (51.42%), all the above signs and symptoms may be due to the obstruction of manovaha srotas by increased kapha dosha. Medhya rasayana ghrita contains maximum drugs having medhya, kapha vata shamak,rasayana and pitta vardhak properties, with ushna virya and madhura vipaka. Go-ghrita has yogavahi property. Hence, by these properties, this formulation can act over manovaha srotas, pacify increased kapha and stabilize vata dosha to increase dhi, dhriti and smriti. Moreover, vachadi ghrita administered as nasya contains vacha, pippali. kustha. These drugs have shirovirechana property which can remove vitiated kapha dosha from shiro sthana and thus, absorption of nutrients at tissue level may be increased. These drugs have rasayana property and some drugs have medhya prabhava also, which can improve the above mental qualities too. Recent clinical studies showed that, maximum drugs of medhya rasayana ghrita (Sankhapushpi, Jyotishmati, Mandukaparni etc.) are

established as vasodilators which can increase blood supply to the brain to improve its function

Table 1: Effect of therapy on doshavriddhi lakshana

Dosha	No.of patients	Paired 't' test						
		Mean Score		% relief	S.D	±S.E	't'	'p'
		BT	AT					
Vata	5	12.4	6.8	45.16	3.57	1.6	3.5	<0.05
Pitta	7	11.14	5.42	51.28	2.13	0.08	7.07	<0.001
Kapha	13	11.84	5.38	54.54	2.96	0.82	7.86	<0.001

BT-before treatment, AT-after treatment, SD-standard deviation, SE-standard error

viz memory, intellect, concentration etc. Go-ghrita by its lipophilic action can transport all properties of the drug into target organs of brain like Hippocampus, Hypothalamus, Amygdala by crossing blood- brain barrier and can help them to show their effect.

In Vata vriddhi lakshanas, Medhyarasayana ghrita with Vachadi ghrita provided 45.16% relief which is statistically significant ($p<0.05$) where as 51.28% and 54.54% relief in pitta vriddhi lakshana and kapha vriddhi lakshanas respectively which are statistically highly

Table 2: Effect of therapy on sroto dushti

Srotas	No. of patients	Paired 't' test						
		Mean Value		% relief	S.D	±S.E	't'	'p'
		BT	AT					
Annava-ha	8	3.5	1.75	50	0.70	0.25	7	<0.001
Rasavaha	16	5.62	3.12	44.44	2.25	0.56	4.44	<0.001
Asthivaha	22	4.27	1.81	57.44	1.22	0.26	9.40	<0.001
Majjavaha	24	4.91	2.16	55.93	2.41	0.49	5.57	<0.001
Purishavaha	15	2.93	1.06	63.63	1.40	0.36	5.13	<0.001

BT-before treatment, AT-after treatment, SD-standard deviation, SE-standard error

significant, because most of the drugs have vata and kapha shamak properties and also has tikta rasa predominance. Moreover, Go-ghrita has specially pittashamak property.

Medhyarasayana ghrita orally with Vachadi ghrita nasya provided 55.93% relief in majjavaha sroto dusti lakshanas and 57.44% in asthivaha sroto dusti lakshanas. The 44.44% relief was obtained in rasavaha sroto dusti lakshanas. Annavaha sroto dusti lakshanas were relieved by 50% where as purishavaha sroto dusti lakshanas by 63.63%. All results were statistically highly significant ($p<0.001$). The drugs of the formulation have rasayana, balya properties and madhur vipaka, hence, it can provide proper nutrition to all dhatus, as a result majja and asthi dhatu dusti lakshanas were relieved. Moreover, most of

the drugs have ushna virya and tikta rasa so, it can enhance digestive power and increase appetite, thus annavaha sroto dusti lakshanas were decreased.

Manasa pariksha bhava are discussed vividly in Ayurveda. Various parameters for mental health are utilized as subjective criteria. Improvement was observed for in Bhaya (63.15%), Krodha (50%), Shoka (66.66%), Priti (42.10%),Virya (41.17%),Vijnana (33.33%), Medha (37.83%), and Smriti (29.72%) after a course of therapy. The improvement in bhaya, krodha, shoka, medha and smriti were found statistically highly significant ($p<0.001$) whereas in priti, virya and vijnana, it was statistically significant ($p<0.05$). Total 60% were mildly improved where as 20% moderately improved.

DISCUSSION

Shankhapushpi, guduchi, yastimadhu and mandukaparni are known medhya drugs. Most of the ingredients of medhyrasayana ghrita have ushna virya and madhura vipaka. Hence, by ushna virya, these drugs can pacify increased kapha and vata doshas and clear the obstruction of manovaha srotas, by madhura vipaka pacify the increased pitta dosha and by medhya property, it improves dhi, dhriti, smriti. Go- ghrita has yogavahi property and is also medhya.Vachadi ghrita nasya drugs have shirovirechana property which can remove vitiated kapha dosha from shiro sthana and thus can increase absorption of nutrients at tissue level. Recent clinical research establishes that antioxidant drugs can retard ageing process by eliminating free radicals from the body and can improve mental functions deteriorated due to ageing.

On Hamilton Anxiety Rating Scale, improvement was found on fear (72.72%), insomnia (56.75%), difficulty in concentration and memory (44.89%) and somatic sensory (50%), anxious mood (40.47 %,), depressed mood (46.66 %,), gastro intestinal symptoms (44.44 %,), tension (24.24%), general somatic (44%) and in behavioral change at interview (44.18 %,). In tension, the improvement was statistically significant ($p<0.05$) but on all other symptoms statistically highly significant improvement ($p<0.001$) was achieved. In total effect, therapy showed mild improvement in 44% patients and moderate improvement in 36% patients. The drugs of the formulation have anti-stress, adaptogenic and tranquilizing effect on brain. One of the ingredients Kushmanda fruit juice containing tryptophan (20-515 ppm) is useful in Anxiety[5].

Maximum drugs of the formulatios have memory enhancing, anxiolytic and antidepressant properties which may increase acetylcholine and acetylcholine esterase in brain and thus help in synaptic transmission of impulse through neurons.

On Hamilton Depression Rating Scale improvement was found in suicidal thoughts (68.75%), depressed mood (36.84 %,), insomnia late (23.07 %,), anxiety psyche (38.46%), anxiety somatic (16.66 %,), hopelessness (43.75%) and hypochondriasis (36.36 %,). Suicidal thoughts, depressed mood, hypochondriasis and anxiety psyche improved in statistically highly significant manner ($p<0.001$ each) and hopelessness improved in statistically significant manner ($p<0.05$). In total effect, therapy showed mild improvement in 36% patients and moderate improvement in 20% patients. The medhya property of the drugs and tranquilizing effect to brain can give soothing effect on abnormal thoughts and thus, may be effective in suicidal thoughts.

On Brief Psychiatry Rating Scale, improvement was noted in somatic concern (51.02%), disorientation (40.74%), tension (39.13%) and depressed mood (40.47%). Somatic concern, tension and depressed mood improved in statistically highly significant manner ($p<0.001$ each) whereas disorientation in significant manner ($p<0.05$). Above symptoms may occur due to vata and kapha vriddhi. Hence, due to us hna virya property and madhura vipaka of most of the drugs of Medhyarasayana ghrita along with vata shamak property of vachadi ghrita, the above symptoms were improved. Vacha, kustha and pippali have anti depressant properties. Based on the parameters marked improvement was observed in 8% patients, moderate

improvement in 24% patients and mild improvement in 48% patients.

On anthropometric parameters, therapy showed 2.65% reduction on body weight, 0.73% increase in ponderal index and 1.39% reduction in body surface area which was statistically insignificant.

On Mini Mental State Examination (MMSE), 11.31% increase was found in Scores in MMSE which is statistically highly significant. Therapy successfully improved the orientation, attention, calculation, immediate and short term memory, corrected the language problem and increased the ability to follow the simple commands with statistically significant results. Most of the drugs have memory enhancing and vasodilator properties, so improvement may be due to increased blood supply to the brain.

On Bender Gestalt Motor Visual test, 44.44% increase in Scores was found in this test which is statistically significant ($p<0.05$). On hematological and biochemical parameters,therapy showed improvement in haemoglobin (0.72%), total leucocyte count (4.86%), neutrophil count (1.49%) which was statistically insignificant ($p>0.05$). The 3.33% and 6.02%, decrease were found in lymphocyte and eosinophil respectively which were statistically insignificant ($p>0.05$). The 9.64% decrease was found in monocyte which was statistically significant ($p<0.05$). The 3.448% decrease was found in ESR which was statistically insignificant ($p>0.05$). On biochemical parameters, the 1.54% increase was found on fasting blood sugar and 0.082% increase in Serum Cholesterol which were statistically insignificant. Serum Creatinine (7.51%) and Serum Urea (8.07%) were found to increase whereas Serum Triglyceride was decreased (6.27%), all the values were statistically insignificant ($p>0.05$). Mild increments were found in hematological and biochemical parameters after treatment but within the normal range. This change seems to be due to fluctuations which are observed normally and though due to therapeutic effect but they are not so apparent to consider.

On Biomarker - Serum Cholinesterase, 1.16% increase was found which is statistically insignificant. Serum Cholinesterase level is generally decreased than normal in Senile Dementia[6]. Recent studies show that in Alzheimer's disease[7], the ratio of Butyrylcholinesterase to Acetylcholinesterase changes dramatically in cortical regions from 0.2 up to as much as 11 and it is found that Acetylcholinesterase is lost up[8] to 85% in specific brain regions, whereas Butyrylcholinesterase[9] levels rise with disease progression. Hence, in total Acetylcholinesterase is decreased in Alzheimer's disease.

The medhya drugs of the formulation may enhance acetylcholine as well as serum cholinesterase concentrations in brain and may help in synaptic transmission of impulse through neurons and retard disease process. Therapy showed 1.58% decreased in puss cells in urine examinations ($p>0.05$) and 12.5% decreased in cyst in stool examination ($p>0.05$).

The oral Medhyarasayana ghrita with Vachadi ghrita nasya showed overall mild improvement in 64% patients and moderate improvement in 36% patients. It may be due to the synergistic actions of 12 potent rasayana and medhya drugs (mandukaparni, jyotishmati, sankhapushpi, kushmanda etc.) including Go-ghrita which directly act through hypothalamo-pituitary-adrenal axis to improve memory and other cognitive impairment such as attention, concentration, judgment, intellect etc,. The Vachadi ghrita can clear the srotas of shiro sthana and can eliminate the morbid doshas from shiro pradesha and can help medhyarasayana ghrita to act directly through the above axis to achieve the needed objective.

CONCLUSION

The depressed mood, negative thoughts and abstinence from sadvritta and swasthavritta disturb one's psychological health and play an important role in dementia in old age by vitiating rajas and tamas manasika doshas, prana, udana, vyana vayu, rasavaha, majjavaha and manovaha srotas and ojas. Patients who reported manovighatakara

bhava like bhaya, chinta, shoka, dvesha, krodha and moha and taking vatakaphaprokopa ahara vihara are at a high risk for developing smritibhramsha. Dementia is a progressive degenerative disease of brain. There is no definitive treatment for this disease till now. Thus, Ayurvedic rasayana drugs may be efficacious in the management of senile dementia.

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