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A CLINICAL STUDY TO EVALUATE THE EFFECT OF GUDUCHI GHANAVATI IN SMRUTHI BHRAMSHA/ ALZHEIMER'S DISEASE

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ABSTRACT

Objectives: Objective for the study includes answer to the research questions or the hypothesis that is set. Present study was conducted to evaluate the therapeutic effect of *Guduchi ghanavati* in *Smruthi bhramsha*/ Alzheimer's disease. **Method**: Interventional non-randomized open labelled single group study with pre-test and post-test design. Twenty patients diagnosed with *Smruthibhramsha*/Alzheimer's disease satisfying inclusion and exclusion criteria were selected from OPD/IPD of SDM Ayurveda Hospital, Udupi. The selected patients were administered with three capsules of 500 mg of *Guduchi Ghana* in early morning on empty stomach with lukewarm water. Statistical analysis was done using students paired 't' test and Wilcoxon signed rank test. **Result**: Percentage of relief is seen in QOL-informant and patient version is 9.04% and 14.712% respectively. In clinical dementia rating score, dementia severity rating scale and Global deterioration Scale is 19.28% and 7.282%, 9.091% betterment is seen respectively. In parameters like *grahana* 32.727%, *dharana* 33.33%, *smarana* 20.75% improvement is noticed. **Conclusion**: Three capsules of *Guduchi ghanavati* have shown significant improvement in *Smruthibhramsha*/Alzheimer's disease. The efficacy of the medication has been proved with the statistical analysis of the parameters.

KEYWORDS: *Smruthi bhramsha, Alzheimer's disease, Guduchi.*

INTRODUCTION

Aging is both a complex and thought-provoking scientific problem and a fact of universal apprehension. *Smarana* of previously heard, said or seen things is said to be *smruthi*.[1] Derangement in this will lead to *smruthi bhramsha*. Memory is one of the important domain that declines with aging. *Jara* is of two types. One is *kalaja* which is appearing at proper interval even after appropriate fortification and another type is *akalaja* which occurs before the expected phase due to improper care and fortification.[2] *Smruthi bhramsha* in *jara* is not explained as a separate disease entity with *nidana panchaka*. Pathophysiology of *smruthi bhramsa* is a compilation from various reference. Amongst the multiple causes of dementia commonest type of dementia is degenerative dementia and commonest amid degenerative cause is Alzheimer's disease.[3] Alzheimer's disease can manifest as young as the third decade, but it is the most common cause of dementia in the elderly.

Alzheimer's disease is a chronic neurodegenerative condition which is gradually progressive with impairment in one or more cognitive domains (for major neurocognitive disorder, at least two domains must be impaired). It is usually insidious in onset or even earlier.

Smruthi and *bhramsha* are 2 different words. *Smruthi* is a feminine word. It is derived from sanskrit term "*smru+ktin*" applying the *dhatu smru* with the suffix lyut.[4] *'Smr' dhatu* meaning memory, recollection, remembrance.[5] *Bhramsha* is a *purusha shabda*. *Bhramsha* refers to slipping away or downfall.[6] It virtually means going away or slipping away, decline or decrease.[7] Expressions like *smruthibhramsha*, *smruthi hrasa*, *smruthinasha*, *smruthi vibhramsha*, *smruthi vibhrama* denotes similar meaning of altered memory.

A synonym of *jara* "*visrasa*" is derived from the word "*sramsu adahpatane*" which means a degradation / retardation in the physical, physiological and psychological well-being. Though growing old is a natural process, some factors do quicken early aging. Factors like *asatmendriyartha samyoga*, *prajnaparadha* and *parinama* and *manasika* elements like *bhaya*, *shoka*,

krodha, *lobha*, *moha* impacts on *shareera dosha*, besides consumption of *viruddha ahara* or *atimatra* or *heena matra* of *ahara* and *vihara* undeniably have an influence on the early or delayed manifestation of the *jara*.

Free radical theory is one of the most acceptable theory of aging proposes. Multiple factors like genetic, lifestyle and environmental factors impacts on brain functioning overtime causing Alzheimer's disease. In old age, due to influence of depletion of *dhathus* and predominance of *vata*, ability of *grahana* (perception), *dharana* (retention), *smarana* (remembrance), *vachana vijnana* (ability of learning new things) also decline.[8] Alzheimer's disease is marked by diminished memory difficulty in recognition of family member's noticeable difference is seen speech & language, ability to make decision, social & community activity, ability to get from place to place.

From the vedic period till date understanding of medicine have only changed into better. Regardless, much essentials are yet to be understood and concealed, both in terms of the cause and treatment of dementia. The effective treatment to *Smruthi bhramsha* is *medhya rasayana.*[9] This study is planned to see the efficacy of *Guduchi ghanavati* in the patients of *smruthi bhramsha*/Alzheimer's disease. This present study will analyse the effect of the *shamana* medication in Alzheimer's disease. *Guduchi ghanavati* is selected as it is a single drug therapy, is easily available and is cost effective.

MATERIALS AND METHODS

Objectives of the study

• To evaluate to evaluate the therapeutic effect of *Guduchi ghanavati* in *Smruthi bhramsha*/ Alzheimer's disease.

• To assess the Quality of life in patients with Alzheimer's disease.

Design: An interventional non-randomized single group open label clinical study with pre-test and post-test design.

Sample size: Minimum of twenty patients with a definite diagnosis of fulfilling the diagnostic, inclusion criteria of *Smruthi bhramsha*/Alzheimer's disease were selected for the study irrespective of sex, caste and religion.

Setting: OPD and IPD of Shri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Udupi.

INTERVENTION

Patients will be administered with Guduchi Ghanavati manufactured at SDM Pharmacy, Udupi of 500mg 3 capsules in early morning on empty stomach with lukewarm water.[10]

Duration of clinical study: Total 56days

Intervention: 14 days

Follow up: 28th day

Diagnostic criteria

1) ICD10 Diagnostic Guidelines for dementia due to Alzheimer's disease.
2) Patient who come under mild and moderate type of dementia as per Clinical Dementia Rating.

INCLUSION CRITERIA

1) Patients who have signed consent form for taking treatment.
2) Patients are selected of age group above 40-75, who come under Presenile and Senile dementia which is a characteristic feature of Alzheimer's disease.
3) Patient who meet probable cases and definite cases criteria of Alzheimer's disease.

EXCLUSION CRITERIA

1) Other Degenerative Diseases of the CNS like Pick's Disease, Huntington's disease, Parkinson's disease, Wilsons Disease, Progressive Supranuclear Palsy, Normal Pressure Hydrocephalus, Multiple Sclerosis, Schilder's Disease, Hallervordern-Spatz's disease.
2) Vascular diseases, Intracranial Space occupying lesions, Metabolic disorders, Endocrine disorders, Head injury, Epilepsy, Infections, Toxic causes, Hypoxia conditions, Vitamin deficiency conditions and other Miscellaneous causes like sarcodosis, Histocytosis X, Heat stroke, Electric injury will be excluded.
3) Patients who come under severe category of Dementia.

ASSESSMENT CRITERIA

1) Objective and subjective criteria parameter were scored by standard method and was assessed before and after treatment on 0, 28th, 56th day and were analysed statistically using students paired t test and Wilcoxon signed rank test.
2) Subjective parameters like *Grahana* (perception), *Dharana* (retention), *Smarana* (remembrance) are assessed.
3) Improvement in signs and symptoms according to

a. The Clinical Dementia rating scale.[11]
b. Dementia Severity Rating Scale.[12]
c. Global Deterioration scale for primary Alzheimer's disease.[13]
d. Quality of Life Assessment in Alzheimer's disease.[14]

OBSERVATION

In this study maximum patients belonged to age group of 40-70years. 60% of the patients in study are females. 70% of them belonged to hindu religion. 80.0% of the patients followed mixed diet. Maximum numbers of patients were having *vishamagni* (65%). Amongst 20 patients registered for the study, 70% belonged to *vatakapha prakruti*, while in *manasika prakruti* 55.0% of patients had *tamasika prakruti* and 20.0% belonged to

rajasika prakruti and 25% belonged to *sannipataja prakruti*. 75.0% patients had *madhyama sara*, 80.0% recorded as *madhyama samhanana*, The assessment of *pramana* of the body in 20 patients revealed that 90.0% patients had *madhyama pramana*, 70% has *avara satwa*, 70% has *avara satwa*, 95% of patients had *madhyama satmya*, 90.0% of patients had *madhyama aharashakti*, 60.0% of the patients had *avara vyayama shakti*. In the study 70% of the patient the onset was in between >6 months to <12 months. Amongst patients, all the i.e. 100 % of the patients had difficulty in recalling (*smarana*) of previously learnt things, 100% of the patients had difficulty in retention (*dharana*) of the known things, 45% patient had difficulty in perception (*grahana*) of freshly learnt things, 40% patient had difficulty in doing simple tasks, 25% of the patient had difficulty in recognition of previously known people or things. 15% of the patient had difficulty in *vijnana shakti* and 5% of patients had difficulty in *vachana* i.e. ability to speech and language capability. In this study 100% of the patient's disease was chronic and progressive in nature.

RESULTS

Guduchi ghanavati has made a statistically significant improvement with p<0.001 in QOL-informant and patient version with a reduction of 9.04% and 14.712% respectively. Noticeable reduction was seen in clinical dementia rating score, dementia severity rating scale, Global deterioration scale for primary dementia with p value (<0.001) with 19.28%, 7.282%, 9.01% improvement is seen respectively (Table no 01). Effect of treatment on memory as shown in the DSR scale records a remission by 15.09% and there is a statistically significant difference i.e. P = 0.008. Effect of treatment on Speech & Language records a remission by 7.692%. The change that occurred with the treatment is not great enough to exclude the possibility that it is due to chance (P = 0.250). Effect of treatment on Recognition of family members records a remission by 14.706%. The change that occurred with the treatment is not great enough to exclude the possibility that it is due to chance. (P = 0.063). Effect of treatment on Ability to make decision records a remission by 5.128%. The change that occurred with the treatment is not great enough to exclude the possibility that it is due to chance. (P = 0.500). Effect of treatment on social and community activity records a remission by 4.545%. The change that occurred with the treatment is not great enough to exclude the possibility that it is due to chance (P = 0.500). Effect of treatment on ability to get from place to place records a remission by 8.333%. The change that occurred with the treatment is not great enough to exclude the possibility that it is due to chance (P = 1.000) (Table no 02)

Difficulty in *smarana*, *grahana* and *dharana* shows a marked improvement with p value <0.001 and relief of 20.76%, 32.727%, and 33.33% respectively is noticed which is statistically significant (Table no 03).

Table No. 1: Showing The Statistical Result Depending Upon Assessment Scales.

PARAMETERS	BT Mean	AT Mean	Diff BT-AT	% OF Relief	WILCOXON SIGNED RANK TEST				
					SD	SEM	MEDIAN	Z VALUE	P VALUE
CDR	4.925	3.975	0.95	19.29	BT:2.975 AT : 2.342	0.665 0.524	4.250 3.500	3.236	<0.001
GDS	2.750	2.500	0.250	9.091	BT : 0.789 AT : 0.607	0.176 0.136	3.000 3.00	2.236	0.063
DSRS	17.850	16.550	1.3	.283	BT : 9.126 AT : 8.294	2.041 1.855	17.500 16.00	3.530	<0.001
QOL-INFORMANT	24.400	26.600	2.200	9.016	BT : 6.524 AT : 5.510	1.459 1.232	23.000 25.000	3.409	<0.001
QOL-Patient	23.450	26.900	3.450	14.712	BT : 7.790 AT: 5.893	1.318	21.000 25.000	3.198	<0.001

Table No 02: Showing The Statistical Result Depending Upon Clinical Features As Per Dsrs Scale.

PARAMETERS	BT Mean	AT Mean	Diff BT-AT	% OF Relief	WILCOXON SIGNED RANK TEST				
					SD	SEM	MEDIAN	Z VALUE	P VALUE
MEMORY	2.650	2.250	0.4	15.09	BT:1.309 AT : 1.209	0.293 0.270	2.000 2.000	2.828	0.008
SPEECH & LANGUAGE	1.950	1.800	0.15	7.692	BT : 1.191 AT : 1.005	0.266 0.225	2.000 2.000	1.732	0.250
RECOGNITION OF FAMILY MEMBERS	1.700	1.450	0.25	14.706	BT:0.801 AT : 0.688	0.179	1.000 2.000	2.236	0.063
ABILITY TO MAKE DECISIONS	1.950	1.850	0.10	5.128	BT: 0.999 AT : 1.040	0.223 0.223	2.000 2.000	1.414	0.500
SOCIAL & COMMUNITY ACTIVITY	2.200	2.100	0.100	4.545	BT:0.788 AT: 1.005	0.176 AT: 0.225	2.000 2.000	1.414	0.500
ABILITY TO GET FROM PLACE TO PLACE	1.200	1.100	0.100	8.333	BT :1.105 AT: 0.912	0.247 0.204	1.000 0.000	1.000	1.000

Table No. 03: Showing The Statistical Result Depending Upon Overall Asssessment of Treatment.

PARAMETERS	BT Mean	AT Mean	Diff BT-AT	% OF Relief	WILCOXON SIGNED RANK TEST				
					SD	SEM	MEDIAN	Z VALUE	P VALUE
GRAHANA	2.750	1.850	0.9	32.727	BT: 0.639	0.143	3.000	4.243	<0.001
					AT : 0.587	0.131	2.000		
DHARANA	2.700	1.800	0.9	33.33	BT: 0.733	0.164	3.000	4.243	<0.001
					AT:0.696	0.156	2.000		
SMARANA	2.650	2.100	0.550	20.755	BT:0.745	0.1670	2.500	3.317	<0.001
					AT : 0.447	0.1000	2.000		

DISCUSSION

Classics have mentioned many newer strategies for geriatric health care where contemporary science has very less to offer. *Guduchi* being one of the *medhya rasayana* acts on brain to improve memory and intellectual capacity. In this present study, a total of 20 patients suffering from *Smruthi bhramsha/* Alzheimer's Disease were registered and patients were subjected to oral administration of three capsules of *guduchi ghana* before breakfast with *ushnajala* as *anupana* for 28 days.

Mode of Action

Rasayana is the most suitable therapy in geriatrics, as it helps in increasing longevity also ceases ageing. As *Smruti bhramsha* is the condition where one fails to recall, *medhya rasayana* which is *vatahara* and *kaphahara* (where *raja* and *tama* is also treated) should be adopted.

Guduchi (*Tinospora cordifolia*) is one of the *chaturvidha medya dravya* explained in classics. This possess such properties which aids at improving memory and intellectual capacity. In the present study *guduchi ghanavati* formulation prepared by using concentrated *guduchi kashaya* subjected to drying and capsuling. Since method is done by two times extracting of decoction this will only increase the potency of the formulation which would have best nootrophic effect.

Tikta rasa is said to be laghu, medhya and kashaya rasa is said to be srothoshodaka, kelda vishodaka. *Guduchi* is predominated by these 2 rasa, which is beneficial in treating *jarajanya smruthibhramsha*. *Tikta rasa* and has *ushna virya* of the drug acts as *pittakara* there by enhances *grahana* and *smarana* capability of an individual. *Kashaya* rasa along with *usna veerya* with *prabhava* of *rasayana* corrects the *avarana samprapthi* there by relieving *tamas*. On the other hand *usna guna* along with *tridosha nashaka* property have *rasayana* effect which acts on *srothas* there by clearing channels or *margavarana* which is obliterated by *kapha* also tamas, *pitta* along with *raja* and *vata* which is already predominant in *jara avastha*.

Neuroprotective activity of *Tinospora cordifolia* is to repair the oxygen glucose deprivation of cells, so it involves in modulation of the antioxidant system where it alters the free radicals.

It also play an effective role against ischemic brain damage as it attenuate oxidative stress mediated cell injury during oxygen-glucose deprivation especially in hippocampus. In aging brain guduchi which is rich by strong free radical scavenging property against which reactive oxygen and nitrogen species diminishes the expression of inos gene also reduction in thiobarbituric acid reactive substances. It also increases the reduced glutathione catalase and superoxide dismutase (anti-oxidant).

CONCLUSION

Guduchi ghanavati has made a statistically significant improvement with p<0.001 in QOL-informant and patient version with a reduction of 9.04% and 14.712% respectively. Noticeable reduction was seen in clinical dementia rating score and dementia severity rating scale and Global deterioration scale of primary dementia is p value (<0.001) with 19.28%, 7.282% and 9.01% improvement is seen respectively. Difficulty in *smarana*, *grahana* and *dharana* shown percentage improvement of 20.76%, 32.727%, 33.33% respectively along with a marked progress of p value <0.001 is seen.

On comparing overall effect of the therapy 70% of the patients were having average improvement, 30% of patients showed mild improvement. No any ill effects were seen in any of the patients during the course of treatment and even on follow up period. None of the patients reported adverse drug reaction to the medication.

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