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RESEARCH ARTICLE

Clinical Evaluation of *Ashwagandha* and *Mandookaparni* in the Management of *Manodwega* (Generalized Anxiety Disorder)

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ABSTRACT

Introduction: Generalized anxiety disorder (GAD) is a common clinical condition reported at psychiatric hospitals. Reasonable estimates for its one year prevalence range from 3 to 8%. It is characterized by excessive, uncontrollable and irrational worries about day to day events. Most of the features of GAD are similar with that of *chittodwega* in Ayurveda.

Materials and Methods: This study is a prospective randomized open clinical trial conducted in GAD patients. One hundred patients fulfilling the selection criteria were enrolled from the out patient department (OPD) of the institute. They were randomized into two groups of 50 patients each. First group patients ware administered with *Ashwagandha Churna* tablets 1.5 gms (Withania Somnifera Linn), and *Mandookaparni churna* tablets 1.5 gms (centella asiatica) twice daily after food for 12 weeks. In the second group along with the same oral medications *Shirodhara* with *Ksheerabala Taila* was performed for 30 minutes daily for the initial seven days only. Outcome measures were improvement in total and individual constituents of hamilton anxiety rating (HAR) scale which were assessed at baseline and at 28th day, 56th day and 84th day. Paired sample t-test was used to compare mean change in hamilton rating scale (HRS) values from baseline to the 84th day. A p-value of < 0.05 was considered as significant.

Results: At the end of 12 weeks compared with baseline statistically significant improvement was observed in Hamliton rating scale score (p-value < 0.001) in both the groups.The treatment was found to be safe and effective as all the safety parameters were in the stipulated range. No adverse drug reaction or event was reported during the trial period.

Conclusion: Oral administration of *Ashwagandha* and *Mandookaparni churna* in tablet forms with or without combination of Shirodhara were found to be effective in the treatment of GAD patients.

Keywords: *Ashwagandha churna*, GAD, HRS, *Mandookaparni Churna, Manodwega*

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INTRODUCTION

Anxiety disorders are among the most prevalent psychiatric condition in the world. Estimates indicate one year prevalence range from 3 to 8%,[1] and lifetime prevalence between 5 to 8%.[2] The disorder usually has its onset in late adolescence or early adulthood. Occasionally cases are also seen in the older age.

GAD is characterized by persistent excessive anxiety and worries about day to day events or activities at least for a period of 6 months.[3] The worry may be difficult to control and associated with various somatic symptoms.

Patients (50–90%) suffering from GAD will have coexistence of other mental disorder like social phobia, panic disorder or depressive disorder. About 25% of patients associated with panic disorder.[4]

Genetic, biochemical, environmental and psychological profiles form major risk factors for GAD. People having personality traits like anxiety, anger, hostility, impulsiveness, pessimism, and depression are more prone to GAD. Many patients with anxiety disorders report overprotective and unaffectionate parents. Stressful events, disagreements with parents and close relatives, posttraumatic stress syndrome, specific traumatic events in childhood may cause anxiety disorders.

Chronic anxiety disorder may also increase the risk of other non-communicable disease (NCD) related morbidity. Hence, clinicians in psychiatry and other specialties need to make proper diagnosis of anxiety disorder and initiate treatment at the earliest.[3]

As per DSM-IV diagnostic criteria for GAD suffering with excessive anxiety and worry in a day to day events persisting at least for 6 months along with the presence of at least four out of the following six symptoms, i.e., restlessness, fatigue, difficulty in concentrating, irritabil-

ity, muscle tension and Sleep disturbances. The treatment options available in contemporary medicine are pharmacotherapy and psychotherapy in the form of cognitive behavioral therapy and counselling. In *Ayurveda* features chittodwega is similar with that of GAD.

Chittodwega is one among many types of *Manasika Vikara* explained in Ayurveda. *'Anavasthita Chitta'* is explained under 80 types of *Nanatmaja Vata Vikara*. Indriyas and manas get vitiated due to excessive, deficient and improper indulgence and disorders of corresponding sensory perceptions manifest.[4] *Chintana* is the object of mind and when impairment in cognition and decision making occur it results in the manifestation of various types of psychological disorders. Due to *Astmendriyartha samyoga, Prajnaparadha* and *Parinama shareeraka* and *Manasika doshas* get vitiated. *Sthana samshraya* of *Manasika doshas* occurs in *hridaya*. As *hridaya* is the sthana of manas it also gets vitiated resulting in manovaha srotodusti and production of manasika lakshana of chittodwega. Vitiated *Vatadi doshas* impair Agni which inturn vitiate rasadi dhatus. This results in the manifestation of various somatic manifestations observed in *Chittodwega*.[5]

Herbs like *Brahmi* (*Bacopa monnieri*), *Mandukaparni* (*Centella asiatica*), *Sankhapushpi* (*Convolvulus pluricaulis*), *Guduchi* (*Tinospora cardifolia*), *Ashwagandha* (*Withania somnifera*) are indicated for treating manovikara. Among these *Ashwagandha* is said to be *rasayana* and *yogavahi*.[6] *Mandookaparni* is a *Medhya Rasayana* having effect in reducing tension and stress.[7] *Shirodhara* is a treatment procedure included under *'moordhataila'* having beneficiary effect in all types of psychiatric disorders.[8] Prior studies conducted with *Ashwagandha* and *Mandookaparni* individually have shown beneficiary effects in GAD patients in small samples. But this study proposes the combined effect in GAD patients with or without *Shirodhara* in a significantly large sample.

Justification for Selecting Trial Drugs and Treatment Procedure

Ashvagandha: It is explained as a rasayana drug which reduces stress, tiredness and promote immune responses. It is explained as anti-stress and adaptogenic drug. Its efficacy is not tested in a randomized control trial earlier in GAD. In a controlled study conducted among stressed adults, the group that was supplemented with *Ashvagandha* had more significant reduction in 'Cortisol' than in the control group. Cortosol is a stress hormone which is released by adrenal glands in response to stress and when blood sugar levels become low.[9]

Ashvagandha also promotes antioxidant activity and reduces oxidative stress.[10]

Mandukaparni: Acts like a tonic and a mood elevator in conditions like stress, anxiety, tension, depression, etc., it is used as a sedative. The effect is mainly due to the 'brahmoside' and 'brahminoside' constituents. Anxiolytic activity is considered to be due to binding to 'cholecystokinin' receptors (CCKB) a group of G protein composed receptors which bind the peptide hormone cholecystinokinin (CCK) or gastrin and were thought to play a potential role in the modulation of anxiety.[11]

Shirodhara: *Shirodhara* is a classical and a well-established Ayurvedic procedure. This procedure induces a relaxed state of awareness that results in a dynamic psychosomatic balance.[12] *Shirodhara* is one of the most powerful treatments to relieve *Vata* (wind) in the mind preoccupied with swarming thoughts, which can lead to inability to handle stress, creating nervousness, anxiety, depression, insomnia, fatigue, psychological disorders.

Scope of work and contribution to the field: Work aims at clinical safety and outcome of Ayurveda formulations and treatment in GAD patients is undertaken.

MATERIALS AND METHODS

The study was a prospective randomized open clinical trial conducted at a unit of Central Council for Research in Ayurvedic Sciences. The study was approved by Institutional Ethics Committee of the Centre and was done in accordance with WHO–good clinical practice guidelines. The clinical trial has also been registered in Clinical Trial Registry of India. (CTRI /2017/07/009095)

Source of Data

A total of 100 participants were enrolled in the clinical trial from the OPD unit of the hospital. Patients were screened in accordance with the inclusion and exclusion criteria mentioned in the protocol and were recruited for the study after obtaining the written informed consent. The enrolled patients were randomly assigned in to two groups of 50 patients each.

Inclusion Criteria

Patients of either sex aged between 18 to 45 years who were diagnosed based on DSM IV diagnostic criteria for GAD, were included in the trial.

Exclusion Criteria

Patients suffering from any other systemic disorders, patients in whom GAD is associated with any other psychiatric illness like depression, social phobias, psychotic disorders, etc. Any abnormalities in values of thyroid profile and electrocardiogram (ECG) were also excluded.

Study Interventions

Trial patients were randomly divided into two groups and the following intervention were done.

Group I: Patients of this group were orally administered with *Ashwagandha churna* in the dose of 1.5 gm (3 tablets of 500 mg) twice daily and *Mandookaparni churna* tablets in the dose of 1.5 gm (three tablets of 500 mg) twice daily with water for 12 weeks after intake of food.

Group II: Patients were administered with similar oral medications as in patients of Group I. In addition they were also subjected to *Shirodhara* with *Ksheerabala taila* for 30 minutes daily for an initial seven days only.

All the medicines used in the trial were procured from good manufacturing practice certified Ayurvedic pharmaceutical industries and standardized following the standards as per ayurveidc pharmacopeia of India.

Timelines (Flow Chart 1)

Total study period	36 months
Period required for pretrial preparation	6 months
Recruitment and follow up period	2 years and 3 months
Treatment period	12 weeks
Successive visit	At every 4 weeks
Statistical analysis	At the end of study period (In last 3 months)

Outcome Measure

Assessment of changes in total and individual constituents of Hamilton anxiety rating scale was adopted for assessment. Ayurvedic factors assessed include *Dashavidha* and *Sroto Pariksha*.

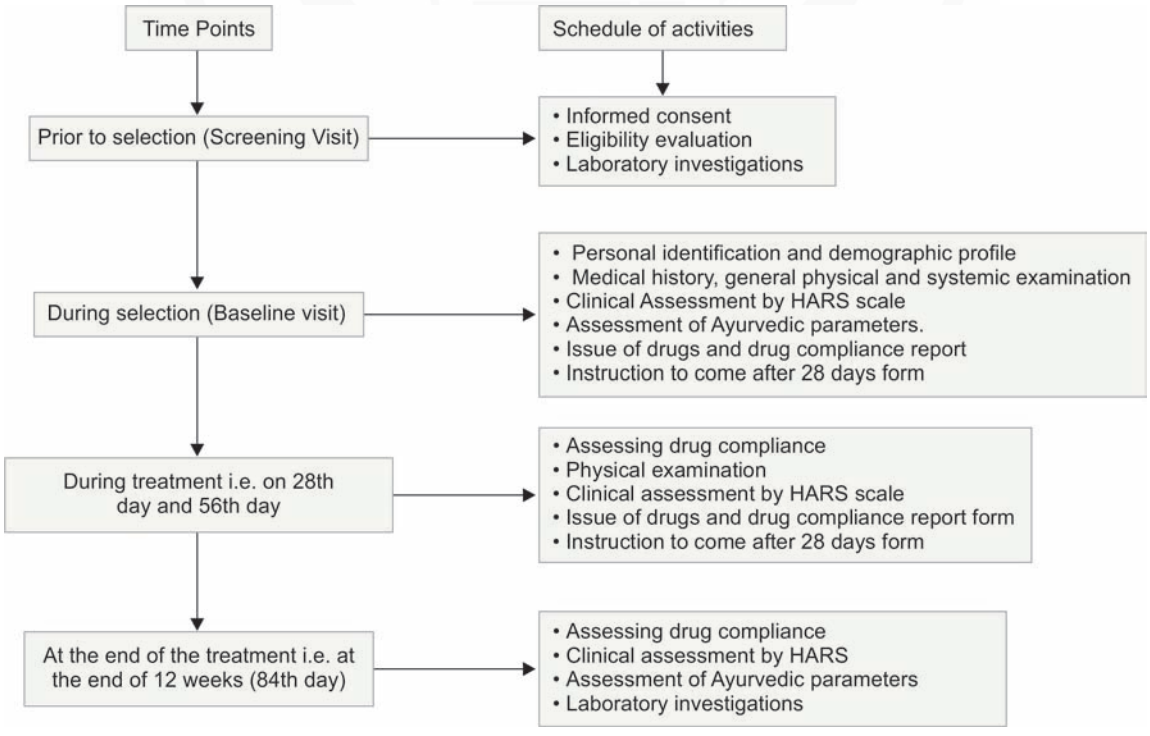
At the study site data of all the patients were recorded in pre-designed case report forms (CRFs) and was also entered in electronic formats (e-formats) designed in ms-excel with many data validation checks to ensure correct data entry. The e-formats and xerox of the CRFs along with the laboratory investigations reports of the patients were sent by the participating center to the council's headquarters on weekly basis for the purpose of clinical trial monitoring.

Out of the total 100 patients, enrolled in the study, 14 were dropped out during the course of the study. Intention-to-treat analysis was done and the data of all those patients who have completed at least 84th day visit were imputed by last observation carried forward (LOCF) method. Hence, data of a total 100 patients was used for statistical analysis.

Statistical Analysis

The outcome measures that are the components of HRS values were analyzed as mean change in the response from baseline to 84th day by using paired t-test. A p-value of <0.05 was considered significant. Analysis was carried out using statistical package for social

Flow Chart 1: Study schedule: Details about the individual time point and schedule of events during the study period



sciences (SPSS) 15.0 version. Patients who reported at least till 28th day are considered for assessment.

RESULTS

Data of a total 100 patients was used for statistical analysis. Majority of the patients were males, i.e., 71%. A demographic profile of the patients showed that 3% of the patients were illiterate and 97% knew how to read and write. Sixty-five percent of the patients used to do desk work, 20% of the patients do field work with physical labor, and 15% of the patients were housewives. It was also observed that the maximum number of patients (78%) were of *Vata pittaja prakriti*. Table 1 shows the basic information and demographic profile of the patients (Flow Chart 2).

Details obtained during history taking showed a majority of patients reports personality traits like anger, hostility, impulsiveness, and pessimism. Among the family-raleated factors, family disputes and stressful environment at home were reported in majority of patients. Failure in academics and financial distress also reported in the majority of cases.

Among the systemic examination findings gastroaintestinal tract related and musculoskeletal symptoms were predominant. *Vata pittaja prakriti* was found in 79% of patients (Tables 2 and 3).

Chief complaints faced by the patients suffering from GAD were assessed by hamilton rating scale. Efficacy of the treatments in both groups on individual components of HRS was calculated by using 'wilcoxon signed ranks test (Tables 4 to 7).

Response of Patients Towards the Treatment at Baseline and 84th day in both groups

The response of the patients towards individual components of the Hamilton rating scale is tabulated in the following Table 7. In all the components the number of patients in severe status has been changed to mild or moderate or none status.

Effect of the Drugs on Safety Parameters

The effect of this treatment on liver function tests (LFT) and renal function tests (RFT) was assessed at baseline and at 84th day. The values are within normal range before and after trial period (Table 8). These observations validate that the trial medicines are safe for human use. Further, no adverse drug effect or adverse events were reported during the treatment period.

DISCUSSION

In the manifestation of *Manodwega*, both *Vata* and *Manas* are involved. *Vata* and *Manas* are interdependent and gets vitiated together. The predominant *doshas* of the *Manas* are *Raja* and *Tama*.[13] The *nidanas* which vitiate *Vata, Raja* and *Tamas* are considered as etiological factors of *Manodvega*. Any intervention selected for the management should aim to control these three factors.

Acharya charaka explained three types of therapies for the management of physical and mental disorders, i.e., *Daiva vyapashraya* (spiritual therapy), *Yukti vyapashraya* (pharmacotherapy) and *Satvavajaya* (psychotherapy).[14] *Yukti vyapasraya chikitsa* in the form of oral medications and *shirodhara* are employed in this trial. *Acharya charaka* also advices *Medhya rasayana* to promote the mental health and to treat mental disorders like *Chittodvega* (GAD), etc. A *rasayana oushadhi* imparts the body with the longevity of life, memory, intelligence, disease free status and delayed aeging.[15]

Both *Ashwagandha* and *Mandukaparni* are considered as *Rasayana oushadhi* and with therapeutic effects

Flow Chart 2: Outflow of the patients in the study

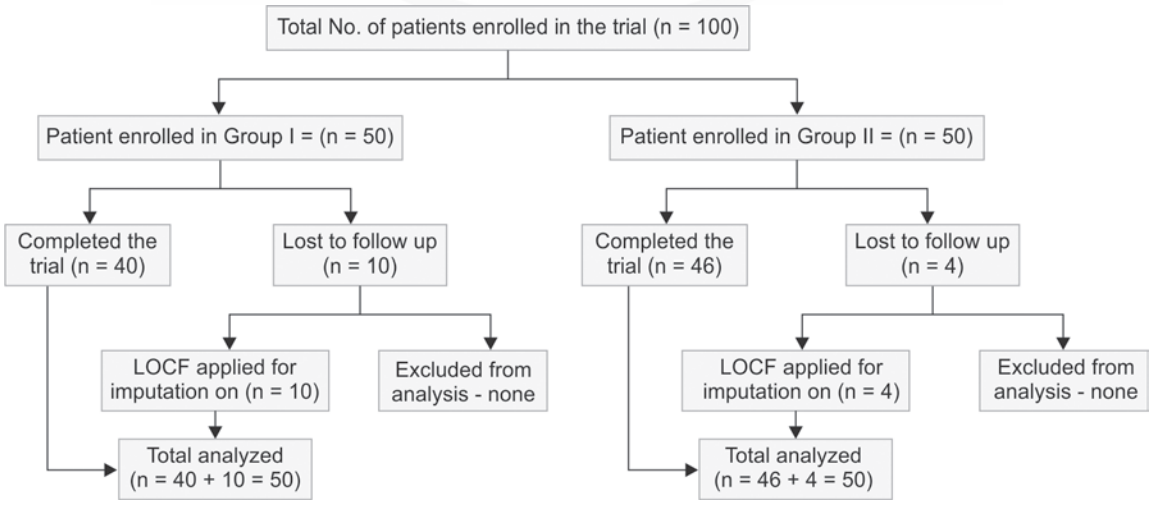


Table 1: Demographic profile of the patients in both the groups

Demographic profile		
Factor	*Group I (n = 50)*	*Group II (n = 50)*
Sex:		
Male	38 (76)	33 (66)
Female	12 (2)	17 (34)
Educational status		
Illiterate	0 (0)	3(6)
Read and write	50 (100)	47 (94)
Socio economic status		
Above poverty line	43 (86)	40 (80)
Below poverty line	7 (14)	10 (20)
Occupation		
Desk work	33 (66)	32 (64)
Desk work with physical labor	10 (20)	10 (20)
Household work	7 (14)	8 (16)
Habitat		
Urban	32 (64)	32 (64)
Semi urban	16 (32)	16 (32)
Rural	2 (4)	2 (4)
Dietary habits		
Vegetarian	13 (26)	18 (36)
Mixed diet	37 (74)	32 (64)
Disturbed Sleep	46 (92)	46 (92)
Irregular bowel habits	20 (40)	21 (42)
Impaired memory	47 (94)	41 (82)

Values are expressed as n (%)

Table 2: Occurrence of genetic factors/personality traits

Factor	*Group I (n = 50)*	*Group II (n = 50)*
Personality traits		
Anger	41 (82)	46 (92)
Hostility	14 (28)	15 (30)
Impulsiveness	4 (8)	3 (6)
Pessimism	30 (60)	28 (56)
Family related factors		
Unaffectionate parents	4 (8)	4 (8)
Family dispute/ unrest	18 (36)	23 (46)
Disagreement with parents	5 (10)	8 (16)
Stressful environment	49 (98)	48 (96)
Emotional stress	39 (78)	33 (66)
Traumatic events		
Loss of loved ones	4 (8)	10 (20)
Physical/ psychological abuse	14 (28)	10 (20)
Financial distress	28 (56)	28 (56)
Failure in academic activities	14 (28)	16 (32)

Table 3: Ayurvedic parameters

Parameters	*Group I (n = 50)*	*Group II (n = 50)*
Type of *Prakriti*		
Vata pittaja	36 (72)	42 (84)
Pitta kaphaja	12 (24)	7 (14)
Type of Saara		
Rakta saara	22 (44)	28 (56)
Mamsa saara	17 (34)	12 (24)
Rasa saara	6 (12)	6 (12)
Asthi saara	5 (10)	4 (8)
Samhanana		
Madhyama	45 (90)	41 (82)
Avara	5 (10)	6 (12)
Sattva		
Madhyma	37 (74)	36 (72)
Avara	11 (22)	11 (22)
Ahara shakti		
Madhyma	38 (76)	36 (72)
Avara	10 (20)	10 (20)
Pravara	2 (4)	4 (8)
Vyayama shakti		
Madhyma	39 (78)	34 (68)
Avara	8 (16)	11 (22)
Pravara	3 (6)	5 (10)

to pacify *Vata* and *Rajoguna* which are major factors involved in the pathogenesis of *Manodwega*. The probable mode of action of *Ashwagandha* and *Mandookaparni* can be interpreted as follows.

Mandukaparni is one of the best *Medhya dravya*. It has sedative, hypotensive and anxiolytic actions. It enhances memory and grasping power and is used as a brain tonic. It is beneficial in Alzheimer's disease, anxiety and depression. In a previously conducted randomized placebo-controlled study on 100 patients suffering from minor disturbances of cerebral higher mental functions observations showed the increased feeling of wellbeing with mental and physical fitness, attention, memory, calculation, abstract thought, visual and body perception.[16] According to scientific interpretation, *Mandookaparni* is likely to increase the CNS alpha wave activity and simultaneously decrease beta wave activity. Increase in alpha wave activity in the EEG is shown to be associated with a state of relaxation of the body and mind and reduces the fluctuations of mind. There by concentration ability and improvement in overall positive mental health occur.[16]

Medhya rasayana drugs like *Mandookaparni* and *Brahmi* possesses similar action like that of nootropic agents

Table 4: Effect of treatment on chief complaints in Hamilton rating scale

Hamilton anxiety rating scale score individual symptoms	*Group I (n = 50)*		*Group II (n = 50)*	
	Baseline	*84th day*	*Baseline*	*84th day*
Anxiousness	2.7 (0.544)	1.92 (0.488)	2.50 (0.647)	1.70 (0.505)
Tension	2.40 (0.571)	1.52 (0.677)	2.22 (0.679)	1.42 (0.609)
Fear	2.06 (0.620)	1.52 (0.614)	1.82 (0.691)	1.28 (0.701)
Insomnia	2.04 (0.570)	1.46 (0.613)	1.9 (0.678)	1.38 (0.602)
Intellectual (Cogn)	1.82 (0.482)	1.38 (0.490)	1.76 (0.657)	1.34 (0.717)
Depressed mood	1.2 (0.756)	1.12 (0.659)	1.24 (0.716)	1.22 (0.737)
Somatic-Muscular	1.66 (0.626)	1.30 (0.580)	1.58 (0.609)	1.16 (0.584)
Somatic-Sensory	1.42 (0.609)	1.22 (0.737)	1.20 (0.700)	1.02 (0.654)
CV symptoms	0.64 (0.663)	0.70 (0.735)	1.02 (0.654)	0.64 (0.663)
Respiratory symptoms	0.42 (0.642)	0.54 (0.579)	0.62 (0.567)	0.68 (0.551)
GIT symptoms	0.86 (0.808)	0.60 (0.606)	0.92 (0.829)	0.76 (0.687)
Genitourinary symptoms	0.34 (0.593)	0.36 (0.485)	0.38 (0.567)	0.44 (0.611)
Autonomic symptoms	1.0 (0.535)	0.66 (0.479)	0.98 (0.515)	0.68 (0.513)
Behavior at interview	0.82 (0.523)	0.72 (0.536)	0.86 (0.405)	0.76 (0.434)

Values are expressed as mean and standard deviations. The scores on individual symptoms of HAM-A were compared by using Wilcoxon signed rank test at baseline and 84th day, *p-value of <0.05 has been considered as significant

which enhances the oxygen supply and better glucose utilization in brain cells. The altered blood supply ensures better psychostimulation producing positive effects on cerebral higher functions like memory, intelligence and learning abilities.[16]

Ashwagandha is said to have anti-stress, adaptogenic, aphrodisiac, sedative, diuretic, antispasmodic, germicidal and anti-inflammatory actions. It is a nervine tonic and enhances immunity. Due to its anxiolytic effect, it decreses stressful situation and is effective in Insomnia. Its *Tikta rasa* and *Ushna veerya* alleviates *Vata* and *Kapha. Ashwagandha* is a rejuvenative and has has a calming effect on anxiety symptoms when compared to the drug lorazepam (a sedative and anxiety medication). A study published in the journal Phytomedicine showed that the herb had the ability to reduce anxiety levels. A clinical study conducted previously to assess the anti stress effect of *Ashwagandha* (*Withania somnifera)* established improvement in a physical feeling of well being and psychological improvement in terms of reduced anxiety level, adjustment, memory span, mental fatigue rate, sleep pattern, etc. Improvement was observed in significant reduction of anxiety level suggesting marked tranquillity state of mind.[17] In another clinical study conducted with *Ashwagandha leha* on 156 apparently healthy individuals for assessing *rasayana* effect showed highly significant result in imroving quality of life, visual analog scale (VAS) score, Hamilton depression rating scale score and PGI memory scale score.[18]

The neuro-physiological mechanism of the effects of *Shirodhara* on the psycho-physiological changes may be related to the tactile stimulation of the skin or hair follicles innervated by the first branch of the trigeminal nerves (ophthalmic nerve). The impulses would be transmitted to the thalamus through the principal nucleus and forward to the cerebral cortex (somatosensory field) or limbic system.[19] In the procedure of *Shirodhara,* a particular pressure and vibration is created

Table 5: Effect of treatment on chief complaints assessed by Hamilton anxiety rating scale in both the groups

HAR Scale Score	*Group I (n = 50)*			*Group II (n = 50)*		
	Mean (SD)	*t-value*	*p-value*	*Mean (SD)*	*t-value*	*p-value*
Baseline	19.38 (4.318)			18.62 (4.802)	____	____
28th day	17.32 (4.483)	12.291	<0.001	16.26 (4.650)	12.938	<0.001
56th day	15.70 (4.550)	11.688	<0.001	14.76 (4.502)	12.940	<0.001
84th day	15.02 (4.520)	12.683	<0.001	14.38 (4.629)	13.139	<0.001

In Group I Mean score of Hamilton rating scale was decreased from 19.38 at baseline to 15.02 at 84th day. In Group II Mean score of Hamilton rating scale was decreased from 18.62 at baseline to 14.38 at 84th day.

Table 6: Analysis of change in HARS score between the groups

HARS Score	*Group*	*N*	*Mean (SD)*	*$t-value*	*p-value*
Difference of baseline and 84th day score	I	50	4.36 (2.431)	0.255	0.800
	II	50	4.24 (2.282)		

$ Compared using independent sample t-test

Table 7: Effect of the treatment on chief complaints in both groups (only selected parameters where significant reduction was observed in complaints)

		Group I		*Group II*	
Parameter	*Severity*	*Baseline*	*84th day*	*Baseline*	*84th day*
Anxiousness	Mild	1 (2%)	8 (16%)	2 (4%)	17 (34%)
	Moderate	14 (28%)	38 (76%)	26 (52%)	28 (56%)
	Severe	34 (68%)	4 (8%)	22 (44%)	1 (2%)
Tension	Mild	2 (4%)	17 (34%)	4 (8%)	23 (46%)
	Moderate	26 (52%)	28 (56%)	28 (56%)	24 (48%)
	Severe	22 (44%)	1 (2%)	17 (34%)	0 (0%)
Fear	Mild	8 (16%)	24 (48%)	11 (22%)	22 (44%)
	Moderate	31 (62%)	23 (46%)	31 (62%)	21 (42%)
	Severe	11 (22%)	2 (4%)	6 (12%)	0 (0%)
Insomnia	Mild	4 (8%)	24 (48%)	11 (22%)	25 (50%)
	Moderate	37 (74%)	23 (46%)	30 (60%)	22 (44%)
	Severe	8 (16%)	1 (2%)	8 (16%)	0 (0%)
Intellectual (cogn)	Mild	11 (22%)	31 (62%)	9 (18%)	22 (44%)
	Moderate	37 (74%)	19 (38%)	35 (70%)	21 (42%)
	Severe	2 (4%)	0 (0%)	3 (6%)	1 (2%)
Depressed mood	Mild	23 (46%)	28 (56%)	22 (44%)	21 (42%)
	Moderate	17 (34%)	14 (28%)	20 (40%)	20 (40%)
	Severe	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Somatic (muscular)	Mild	15 (30%)	29 (58%)	15 (30%)	32 (64%)
	Moderate	31 (62%)	18 (36%)	32 (64%)	13 (26%)
	Severe	2 (4%)	0 (0%)	0 (0%)	0 (0%)
Somatic (sensory)	Mild	23 (46%)	21 (42%)	24 (48%)	29 (58%)
	Moderate	24(48%)	20 (40%)	18 (36%)	11 (22%)
Autonomic symptoms	Mild	36 (72%)	33 (66%)	37 (74%)	32 (64%)
	Moderate	7 (14%)	0 (0%)	6 (12%)	1 (2%)
Behavior at interview	Mild	35 (70%)	32 (64%)	41 (82%)	37 (75.5%)
	Moderate	3 (6%)	2 (4%)	1 (2%)	0 (0%)

over the forehead. The vibration is amplified by the hollow sinus present in the frontal bone. The vibration is then transmitted inwards through the fluid medium of cerebrospinal fluid (CSF). This vibration along with little temperature may activate the functions of thalamus and the basal forebrain which then brings the amount of serotonin and catecholamine to the normal stage inducing the sleep. The procedure of *Shirodhara* brings the *Sanjnavaha Srotas* in a peaceful state of rest which helps in inducing sleep. The process of *Shirodhara* also produces a meditation effect which helps to overcome the complaint of insomnia.

Table 8: Effect of the treatment on safety parameters in both groups

	Group I (n = 50)				*Group II (n = 50)*			
Parameters	*Baseline*	*84th day*	*$t-value*	*p-value*	*Baseline*	*84th day*	*$t-value*	*p-value*
Blood urea (mg/dL)	18.28 (4.64)	18.55 (4.85)	0.477	0.636	19.1 (6.24)	18.74 (5.30)	0.488	0.627
Serum uric acid (mg/dL)	5.83 (2.51)	6.07 (3.097)	0.897	0.374	5.84 (1.64)	5.98 (2.28)	0.559	0.579
Serum creatinine (mg/dl)	0.98 (0.366)	0.96 (0.37)	1.872	0.067	0.91 (0.142)	0.91 (0.13)	0.98	0.923
SGOT (IU/L)	26.77 (10.97)	28.48 (14.17)	1.285	0.205	26.35 (9.22)	27.3 (10.19)	0.71	0.48
SGPT (IU/L)	27.98 (17.06)	27.28 (17.31)	0.608	0.546	26.53 (15.27)	26.80 (19.21)	0.11	0.90
Total protein (g/dL)	7.29 (1.00)	7.42 (0.39)	0.955	0.344	7.47 (0.43)	7.42 (0.47)	0.866	0.391
Serum total bilirubin (mg/dL)	0.803 (0.445)	0.787 (0.388)	0.328	0.745	0.87 (0.45)	0.82 (0.43)	0.863	0.392
Serum alkaline phosphatase (U/L)	86.62 (23.90)	85.78 (28.68)	0.279	0.781	90.70 (31.99)	93.01 (34.02)	0.673	0.504

Values are expressed as mean (SD), $ Compared using paired t-test at baseline and 84th day, *p-value of < 0.05 has been considered as significant

In the present clinical trial as evident from results there is a significant reduction observed in the intensity of Hamilton rating scale parameters in treated patients of both groups (Table 4). Statistically significant reduction (p-value <0.001) was observed in components of HRS like anxiousnessness, tension, fear, insomnia, intellectual (cognitive), somatic (muscular) and autonomic symptoms in both the treated groups. There was no significant improvement observed in a depressed mood, Somatic (sensory), cyclic vomiting syndrome (CVS) symptoms, GIT symptoms, respiratory and genitourinary symptoms.

The result of the indipendant sample 't test' conducted between the groups shows that both the treated groups show a significant reduction in values of Hamilton rating scale (Table 6). But the efficacy between the groups is not significant. The interpretation is that in both the groups the efficacy is almost identical.

The effect of the treatment on LFT and RFT was assessed at baseline and at 84th day. The values are within normal range before and after trial period (Table 8). These observations validate that the trial medicines are safe for use. Further, no adverse drug effect or adverse events were reported during the treatment period.

Combination of *Ashwagandha churna* and *Mandukaparni churna* with or without combination of shirodhara performed with ksheerabala taila was found to be effective in the management of GAD which could be ascertained by its effect on the outcome parameters. Tables 5 and 6 show the effect of these two ayurvedic formulations on the outcome measures.

CONCLUSION

Since ages, *Ashwagandha* and *Mandookaparni* have been used by Ayurvedic physicians in the treatment of *Manodwega* (GAD), *Vishada* and other neuropsychiatric disorders. Even though the drugs have been studied individually in psychiatric disorders, there has not been any systematic attempt to document the effect of this combination on specific subjective and objective outcome measures based on HARS. This trial has established that 84 days of treatment with this combination of medicines administered with or without *Shirodhara* helps in reducing anxiety levels in patients suffering with GAD. Results have shown efficacy in reducing anxiousnessness, tension, fear, insomnia, intellectual (cognitive), somatic (muscular) and autonomic symptoms. The medicine combination is also safe to use as there was no significant influence on safety parameters which is evident by post-treatment renal and hepatic function tests. Since GAD patients require long-term medical intervention, *Ashwagandha* and *Mandookaparni* can be effective and safe in its management.

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Previous studies on *Manodwega* (GAD)

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हिंदी सारांश

"मनोद्वेग (जी ए डी) के प्रबंधन में अश्वगन्धा और मण्डूकपर्णी का नैदानिक मूल्यांकन"

[1]जी. वी. रमणा, [2]हेमन्त कुमार गुप्ता, [3]सुधाकर डी., [4]रेणु सिंह, [5]राकेश राणा, [6]रीचा सिंघल

भूमिकाः सामान्य रूप में मनोद्वेग रोग को चिंता विकार (जी.ए.डी,) के रूप में जाना जाता है। इस विकार से लगभग 5% संख्या प्रभावित है। आयुर्वेद में इसे चित्तोद्वेग के नाम से उल्लेख मिलता है।

अभिप्राय और उद्देश्यः मनोद्वेग (जीएडी) विकार से पीड़ित रोगियों में क्षीरबला तैल से शिरोधारा एवं अश्वगन्धा चूर्ण और मण्डूकपर्णी चुर्ण की प्रभावकारिता और सुरक्षा का मूल्यांकन करना मुख्य उद्देश्य है।

सामग्री और पद्धतिः सीसीआरएएस, नई दिल्ली के अधीनस्थ संस्थान ए.सी.ए.एम.एच.एन.एस, निम्हान्स, बेंगलूरु में मनोद्वेग (जी ए डी) विकार से पीड़ित रोगियों का एक खुला स्तर पर नैदानिक परीक्षण किया गया। इस केंद्र के बाह्य रोगी विभाग में अध्ययन के लिये 100 मनोद्वेग (जी.ए.डी,) रोगियों का पंजीकरण किया गया। इन 100 रोगियों को दो समूहों में विभाजित करके (प्रत्येक का 50–50 रोगियों), एक समूह को 12 सप्ताह तक खाने के बाद अश्वगन्धा चूर्ण टेबलेट 1.5 ग्रा. और मण्डूकपर्णी चूर्ण टेबलेट 1.5 ग्रा. दिन में दो बार दिया गया। दूसरे समूह के रोगियों को उपर्युक्त औषधियों के साथ एक सप्ताह तक प्रतिदिन 30 मिनट क्षीरबला तैल से शिरोधारा कि गयी। इस उपचार के परिणाम का मूल्यांकन हेमिल्टन रेटिंग स्केल द्व ारा 28, 56 एवं 84 दिनों के बाद मूल्यांकन किया गया।

परिणामः अध्ययन अवधि में दोनों समूहों में उपचार सुरक्षित और प्रभावी पाया गया एवं सभी सुरक्षा मानक निर्धारित सीमा में थे। परीक्षण अवधि के दौरान औषधि का कोई प्रतिकूल प्रभाव नहीं पाया गया।

निष्कर्षः मनोद्वेग (जी ए डी) विकार से पीड़ित रोगियों पर शिरोधारा एवं अश्वगंधा चूर्ण और मण्डूकपर्णी चूर्ण टेबलेट प्रभावी और सुरक्षित पाये गये।

कीवर्डः आयुर्वेद, अश्वगन्धा चूर्ण, मण्डूकपर्णी चूर्ण, जी.ए.डी, मनोद्वेग, एच.आर.एस