ORIGINAL ARTICLE

Randomised placebo controlled study on *Sarasvata choorna* in generalised anxiety disorder

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Background: Generalised anxiety disorder (GAD) is characterised by a pattern of frequent, persistent worry and anxiety, which is out of proportion to the impact of the event or circumstance that is the focus of the worry. GAD is associated with muscle tension, trembling, twitching, feeling shaky and muscle aches or soreness. Many individuals with GAD also experience somatic symptoms like sweating, nausea and diarrhoea. Epidemiological studies reveal that the prevalence rate of GAD in India is 5.8%. **Objective:** The main objective of the present study was to evaluate the efficacy of *Sarasvata choorna* in the management of GAD. **Materials and Methods:** In this study, a total of 114 patients with GAD satisfying the Diagnostic and Statistical Manual of Mental Disorders – Text Revision (DSM IV – TR) diagnostic criteria were selected and randomly divided; of these, 102 patients completed the course of treatment. In trial group, *Sarasvata choorna* and in control group, placebo (wheat powder) was given with the dose of 1 g thrice a day (i.e. 3 g/day) along with *madhu* (honey) and *ghrita* (cow's ghee) orally for 60 days. Fifteen days of follow up period was kept after treatment. Two assessments were done before and after treatment. Criterion of assessment was based on the scoring of Hamilton Anxiety Rating Scale (HAM-A). Paired and unpaired '*t*'-test was used for statistical analysis. **Results and Conclusion:** In trial group (n = 51), 51.1% improvement and in control group (n = 51), 47.67% of improvement was observed with the significance of (P < 0.001). No statistically significant difference (P > 0.05) was found in between the two groups. *Sarasvata choorna* did not provide better relief compared with placebo.

Key words: Generalised anxiety disorder, placebo, *Sarasvata choorna*

INTRODUCTION

Anxiety disorders constitute the largest group of psychiatric disorders as well as the most prevalent. Generalised anxiety disorder (GAD) is one of the most common anxiety disorders characterised by persistent worrying, anxiety symptoms and tension.[1] Patients with GAD report various symptoms like restlessness, fatigue, muscle tension, worry and sleep disturbances. Patients with GAD experience a multitude of disabilities affecting work, education and social interactions.[2] GAD is the second most frequent of all mental disorders. The prevalence of GAD in general population might actually be as high as 5-8%, whereas among individuals seeing their physicians for psychological problems, 25% of them have a diagnosis of pure GAD.[3]

Medhya Rasayanas (nootropic) are group of medicinal plants described in *Ayurveda* (Indian system of medicine) with multi-fold benefits, specifically to improve memory and intellect by their *prabhava* (specific action). They are *mandukaparni* (*Centella asiatica* Linn.), *yastimadhu* (*Glycirrhiza glabra* Linn.), *guduchi* (*Tinospora cordifolia* (Wild) Miers) and *shankhapushpi* (*Convolvulus pleuricaulis* Chois), specially mentioned with wide range of applications on different systems. Yet in general practice, few more drugs used with same aim are mentioned. They are *brahmi* (*Bacopa monniera*), *jyothishmati* (*Celastrus panniculata*), *kushmanda* (*Benincasa hispida*), *vacha* (*Acorus calamus*) and *jatamamsi* (*Nardostachys jatamamsi*).[4] These are commonly prescribed by the *Ayurvedic* practitioners for treatment of anxiety, depression, cognitive deficits and memory problems.

Sarasvata choorna is mentioned in the treatment of psychiatric problems such as "*durmedhasaam* (dull witted)", "*vichetasaam* (absent mindedness/stupidity)" conditions. In this formulation, *medhya rasayana* drugs such as *vacha, shankhapushpi, brahmi, kushta (Saussurea lappa* C. B. Clarke), *ashwagandha (Withania somnifera* Linn) are present.[5] Anxiolytic (on elevated plus maze test) and anti-depressant activity (on forced swimming test) of *Sarasvata choorna* was proved in animal models.[6] No clinical trial has been conducted on *Sarasvata choorna* in GAD. By considering these facts, the present study

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was planned on *Sarasvata choorna* as trial drug in the management of GAD.

Aims and Objective

To evaluate the efficacy of *Sarasvata choorna* in the management of GAD.

MATERIALS AND METHODS

Study Design

This was a single-blind, randomised and placebo-controlled study.

Selection of Patients

All patients fulfilling the inclusion criteria were selected from the out-patient department (OPD) irrespective of caste, religion and economic status with their written consent.

Inclusion Criteria

- Patients who fulfil the Diagnostic and Statistical Manual of Mental Disorders – Text Revision (DSM IV – TR) diagnostic criteria for GAD (300.02)[7]
- Patients aged between 16 and 60 years.

Exclusion Criteria

- Patients presenting with major organic disorders and psychotic disorders
- Patients aged <16 and >60 years.

The study was cleared by the institutional ethics committee. Written consent was taken from the parent or guardian of each patient willing to participate before the start of the study. A detailed history of each patient was taken. A general physical examination of all systems was performed. After establishing the diagnosis, the patients were allocated to trial group and control group. Patients were free to withdraw from the study at any time without giving any reason.

A total of 114 patients were registered in the present study. In the trial group, 57 patients were registered; among them, 51 patients completed the course of treatment and 6 patients discontinued the treatment. In control group, 57 patients were registered; among them, 51 patients completed the course of treatment and 6 patients discontinued. A total of 102 patients completed the course of treatment and 12 patients discontinued.

Laboratory Investigations

Routine haematological tests, biochemical investigations and urine analysis had been carried out before and after the treatment to exclude organic pathology and to assess the general condition of the patient. If any major abnormality was found in their investigation reports, those patients were excluded from the study.

Grouping

The patients satisfying inclusion criteria were selected and randomly divided in to two groups by following computerised randomisation plan.[8]

Method of Preparation of *Sarasvata choorna* and Placebo

All the ingredients [Table 1] were collected from the pharmacy, where the present study has been carried out, and they were powdered after cleaning and drying in a pulveriser separately. All the 11 ingredients except *vacha* were separately weighed and mixed together in equal parts. Then 11 parts of powdered *vacha* was added to it. *Brahmi swarasa* was collected. The powder was kept in fresh *brahmi swarasa* and it was subjected to three *bhavana*'s. After *bhavana*, the powder was dried in a shade. Then again it was powdered and passed through sieve number 60-80 to obtain a homogeneous blend. It was packed in air-tight containers to protect from light and moisture. For the preparation of placebo, wheat powder was collected and it was roasted till it became dark brown in colour. It was packed in air-tight containers.

Intervention

In trial group, 1 g of S*arasvata choorna* mixed with *madhu* (honey) and *ghrita* (cow's ghee) was given three times a day, orally for 60 days. Placebo (roasted wheat powder) with the dose of 1 g thrice a day, orally along with *madhu* and *ghrita* for 60 days was given in control group. Follow up period was kept for 15 days in both groups after the treatment period.

Assessment

Two assessments were carried out, before and after treatment. A criterion of assessment was based on the scoring of Hamilton Anxiety Rating Scale (HAM-A) rating scale. The HAM-A was one of the first rating scale developed to measure the severity of anxiety symptoms, and it is useful in both clinical and research settings.

Table 1: Ingredients of *Sarasvata choorna*

Ingredient	Part used	Quantity
Kushta	Root	1 part
Ashwagandha	Root	1 part
Saindhava lavana		1 part
Ajamoda	Fruit	1 part
Shweta jeeraka	Fruit	1 part
Krishna jeeraka	Fruit	1 part
Sunthi	Rhizome	1 part
Maricha	Fruit	1 part
Pippali	Fruit	1 part
Patha	Root	1 part
Shankhapushpi	Whole plant	1 part
Vacha	Rhizome	11 parts
Brahmi	Whole plant	Quantity sufficient for *bhavana* (tirturation)

The scale consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0-56, where <17 indicates mild severity, 18-24 mild-to-moderate severity and 25-30 moderate-to-severe. This is a widely used scale and an accepted outcome measure in clinical trials.[9] In the present study, this scale has been used for assessment.

Statistical Analysis

The information gathered on the basis of observation was subjected to statistical analysis in terms of mean difference, standard deviation (S.D), standard error (S.E), paired '*t*'-test and unpaired '*t*'-test. The obtained results were interpreted as:

Insignificant - $P > 0.05$
Significant - $P < 0.05$, $P < 0.01$, $P < 0.001$

Overall Effect of Therapy

Overall effect of therapy on 102 patients of GAD was calculated by taking the percentage of relief based on the scores of HAM-A scale and categorised into:

1. 100% relief - Complete relief
2. >75% to <100% - Marked improvement
3. >50% to 75% - Moderate improvement
4. >25% to 50% - Mild improvement
5. 0% to 25% - No relief

OBSERVATIONS AND RESULTS

The demographic data of the present study showed that maximum number of patients, that is 54.4% were female, 34.21% were aged 31-40 years, 85.96% were Hindus, 25.43% were graduates, 40.35% were homemakers, 73.68% were married, 78.95% belonged to nuclear families, 59.64% belonged to middle class, 11.40% were having depression as a co-morbid condition along with GAD, 63.15% were having up to 5 years chronicity and 92.10% were having severe anxiety. Associated symptoms were found in majority of the patients, that is sleep disturbances (91.22%), irritability (81.57%), headache (73.68%), history of precipitating life events (76.31%), positive family history (43.9%), un-satisfaction with job (44.07%) with marital life (24.14%) and with sexual life (41.38%).

In the present study, 45.61% of the patients were having *vata pitta prakriti*, 59.14% were having *rajasik prakriti* and 35.96% of the patients were having *avara satva*. Recurrence of the symptoms during follow up period was observed in 54.34% of the patients.

In trial group, maximum relief was observed in, behaviour (72.38%), insomnia (64.93%), genito urinary symptoms (63.63%) and respiratory symptoms (56.94%), which were statistically significant ($P < 0.001$) [Table 2]. In control group, maximum relief was observed in, behaviour (66.03%), insomnia (61.11%), depressed mood (52.45%) and anxious mood (52.09%), which were statistically significant ($P < 0.001$) [Table 3]. Comparison between the two groups revealed that there was statistically no significant difference ($P > 0.05$) in all items [Table 4].

On total score of HAM-A rating scale, trial drug provided 51.1% of relief after treatment period, whereas control drug provided 47.67% of relief ($P > 0.001$) [Table 5]; however, the difference between the two groups was statistically insignificant ($P > 0.05$) on total score of HAM-A rating scale. In trial group, maximum percentage of patients (37.25%) got mild relief, whereas in control group, maximum patients (39.22%) got moderate relief [Table 6].

Table 2: Effect of therapy on Hamilton Anxiety Rating (HAM-A) scale in trial group (*n*=51)

HAM-A	Mean score BT**	Mean score AT*	M. Diff	% of relief	SD***	*t* value	*P* value
Anxious mood	3.31	1.66	1.64	49.70	0.80	14.60	<0.001
Tension	2.52	1.09	1.43	56.58	0.97	10.52	<0.001
Fears	1.29	1.01	0.27	21.21	0.57	3.42	<0.01
Insomnia	3.01	1.05	1.96	64.93	0.90	15.51	<0.001
Difficulties in concentration and memory	1.76	0.96	0.80	45.55	0.77	7.41	<0.001
Depressed mood	2.56	1.23	1.33	51.90	0.84	11.28	<0.001
General somatic symptoms muscular	2.56	1.41	1.15	45.03	0.83	9.91	<0.001
General somatic symptoms sensory	2.62	1.45	1.17	44.77	0.89	9.37	<0.001
Cardiovascular symptoms	1.96	1	0.96	49	0.93	7.32	<0.001
Respiratory symptoms	1.41	0.60	0.80	56.94	0.89	6.40	<0.001
Gastro-intestinal symptoms	2.64	1.49	1.15	43.70	0.90	9.14	<0.001
Genito-urinary symptoms	1.29	0.47	0.82	63.63	1.09	5.37	<0.001
Autonomic symptoms	1.86	1.07	0.78	42.10	0.87	6.43	<0.001
Behaviour during interview	2.05	0.56	1.49	72.38	0.76	13.95	<0.001

AT* – After treatment; BT** – Before treatment; SD*** – Standard deviation

Table 3: Effect of therapy on Hamilton Anxiety Rating (HAMA) scale in control group (*n*=51)

HAM-A	Mean score BT**	Mean score AT*	M. Diff	% of relief	SD***	*t* value	*P* value
Anxious mood	3.27	1.56	1.70	52.09	0.88	13.81	<0.001
Tension	2.45	1.29	1.15	47.2	0.84	9.72	<0.001
Fears	1.27	1	0.27	21.53	0.64	3.06	<0.01
Insomnia	3.17	1.23	1.94	61.11	1.15	11.95	<0.001
Difficulties in concentration and memory	1.54	0.88	0.66	43.03	0.74	6.42	<0.001
Depressed mood	2.39	1.13	1.25	52.45	0.94	9.90	<0.001
General somatic symptoms muscular	2.64	1.54	1.09	41.48	0.88	8.84	<0.001
General somatic symptoms sensory	2.66	1.54	1.11	41.91	0.82	9.68	<0.001
Cardiovascular symptoms	2	1.07	0.92	46.07	0.76	8.58	<0.001
Respiratory symptoms	1.47	0.80	0.66	45.33	0.79	5.99	<0.001
Gastro-intestinal symptoms	2.88	1.68	1.19	41.49	0.87	9.77	<0.001
Genito-urinary symptoms	1.41	0.80	0.60	43.05	0.87	4.94	<0.001
Autonomic symptoms	1.96	1.05	0.90	46	0.86	7.46	<0.001
Behaviour during interview	2.07	0.70	1.37	66.03	0.75	12.96	<0.001

AT* – After treatment; BT** – Before treatment; SD*** – Standard deviation

Table 4: Comparison of effect of therapy on Hamilton Anxiety Rating (HAM-A) scale in between the two groups

HAM-A	Trial group		Control group		*t* value	*P* value
	M. Diff	SD*	M. Diff	SD		
Anxious mood	1.64	0.80	1.70	0.88	0.36	>0.05
Tension	1.43	0.97	1.15	0.84	1.56	>0.05
Fears	0.27	0.57	0.27	0.64	0	>0.05
Insomnia	1.96	0.90	1.94	1.15	0.09	>0.05
Difficulties in concentration and memory	0.80	0.77	0.66	0.74	0.94	>0.05
Depressed mood	1.33	0.84	1.25	0.94	0.45	>0.05
General somatic symptoms muscular	1.15	0.83	1.09	0.88	0.35	>0.05
General somatic symptoms sensory	1.17	0.89	1.11	0.82	0.35	>0.05
Cardiovascular symptoms	0.96	0.93	0.92	0.76	0.24	>0.05
Respiratory symptoms	0.80	0.89	0.66	0.79	0.84	>0.05
Gastro-intestinal symptoms	1.15	0.90	1.19	0.87	0.23	>0.05
Genito-urinary symptoms	0.82	1.09	0.60	0.87	1.13	>0.05
Autonomic symptoms	0.78	0.87	0.90	0.86	0.70	>0.05
Behaviour during interview	1.49	0.76	1.37	0.75	0.80	>0.05

SD* – Standard deviation

Table 5: Effect of therapy on total score of HAM-A rating scale

Group	Sample size (*n*)	Mean score BT**	Mean score AT*	M. Diff	% of relief	SD***	*t* value	*P* value
Trial	51	30.92	15.11	15.80	51.10	7.01	16.09	<0.001
Control	51	31.25	16.35	14.90	47.67	6.67	15.95	<0.001

AT* – After treatment; BT** – Before treatment; SD*** – Standard deviation; HAM-A – Hamilton Anxiety Rating

Table 6: Overall effect of the therapy based on HAM-A rating scale

Result	Trial group (*n*=51)		Control group (*n*=51)		Total	
	No.	%	No.	%	No.	%
Complete remission (100%)	0	0	0	0	0	0
Marked improvement (>75 to <100%)	7	13.73	6	11.76	13	12.74
Moderate improvement (>50 to 75%)	19	37.25	17	33.33	36	35.29
Mild improvement (>25 to 50%)	19	37.25	20	39.22	39	38.24
Unchanged (<25%)	6	11.76	8	15.69	14	13.73

HAM-A – Hamilton Anxiety Rating

DISCUSSION

In the present study, maximum numbers of patients were female. Community surveys done previously indicate a 2:1 female to male preponderance of GAD.[10] Maximum number of patients in this study were in the age group of 31-40 years. The prevalence of GAD was highest in the primary care attendee's aged between 35 and 60 years.[1] In the present study, similar findings were also observed. Maximum patients were married. Married patients are more prone to anxiety because of marital commitment, child care and other family problems. Un-married and divorcees are also prone to disease because of lack of emotional outlet.

A previous study found higher rates of neurotic disorder in people who live separately.[11] In the present study, similar findings were also observed. Majority of the patients in the present study belonged to middle and lower-middle class. Lower socioeconomic status is the predictor of worse outcome. Lower social class, no access to cars, home renting and low educational attainment were all associated with higher prevalence of neurotic disorder.[11]

In the present study, depression, other anxiety disorders such as phobia and obsessive compulsive disorder (OCD) were observed as common co-morbid conditions. GAD is particularly co-morbid with depression. The general health survey confirmed these findings and reported that co-morbidity of GAD includes other anxiety disorders in 55% of cases and depression in 59% of cases.[1] The present study findings are also similar to these views.

Majority of the patients were having complaints of sleep disturbances, irritability, restlessness, fatigue, unable to concentrate and muscle tension. According to the diagnostic criteria, patients must find it difficult to control their worry and must report at least three of six somatic or cognitive symptoms. Such symptoms include feelings of restlessness, fatigue, muscle tension and insomnia.[12] In addition to various parameters of worry, findings from several recent studies indicate that GAD may be allied with a set of associated symptoms that foster its distinction from other anxiety disorders. Previous studies indicated that patients with GAD suffer with the symptoms like irritability, restlessness or feeling keyed up, muscle tension, fatigability, sleep disturbance and concentration difficulties;[10] In the present study also similar findings were observed.

Maximum number of patients in the present study reported positive history of some sort of psychiatric abnormality in their family, drug addiction, history of suicide and other problems in their families. Previous works proved that GAD occurs more frequently in patients with a family history of anxiety and depression.[13]

In the present study, maximum patients were un-satisfied with their job and having un-satisfactory relationship with co-workers. This is most notable in terms of diminished functioning, both socially and at work. GAD has been found to be associated with significant impairment in social and occupational functioning. Individuals with GAD report greater disability and more absence from work than individuals without a mental disorder.[11] In the present study, similar findings were also observed. In the present study, maximum patients were un-satisfied with their marital and sexual life. Women with GAD perceive their marriages to be less satisfying than other married women.[14] Any kind of inter-couple hostility and depressive symptoms obviously inter-personal problems, such as sexual problems, may be the cause or the result of dysfunctional or un-satisfactory relationships.[15] Recent studies suggest that persons with GAD may experience significant difficulties in interpersonal functioning such as prevalent worry themes, co-morbid social anxiety, insecure relationships and marital dissatisfaction.

Sarasvata choorna is a *medhya* compound formulation, which is indicated in *durmedhas, vichetas* like conditions and for improving the cognitive functions. All *medhya* and *medhya rasayana* drugs are claimed to be nutraceutical agents. They are called *medhya* because they are beneficial for *medha* (i.e. intellect). All such herbs have been found to possess nootropic effect besides varying degrees of anxiolytic activity. In addition to other aspects of the *rasayana* effect, they bring about anti-stress effect, improves the memory and cognitive functions.[16]

Sarasvata choorna contains various ingredients that have different properties such as anxiolytic (*vacha, brahmi, shankhapushpi, ashwagandha*), anti-depressant (*shankhapushpi, ashwagandha, vacha, brahmi, sunthi [Zingiber officinale* Roscoe]), muscle relaxant (*patha [Cissampelos pareira* L], *brahmi*), tranquiliser or sedative (*vacha, ashwagandha*) anti-stress and adaptogen (*ashwagandha, shankhapushpi, brahmi*, etc.) *deepana and paachana* (*sunthi, pippali* [*Piper longum* L], *maricha* [*Piper nigrum* L], *ajamoda* [*Apium graveolens S*], *saindhava lavana* [*Rock salt*], *krishna jeeraka* [*Carum carvi L*], *sweta jeeraka* [*Cuminum cyminum L*], etc.), analgesic (*ajamoda, ashwagandha, sunthi, maricha*, etc.), *rasayana and medhya rasayana* (*brahmi, shankhapushpi, vacha, ashwagandha, kushta*, etc.), *unmadahara (vacha, brahmi, kushta, shankhapushpi*, etc.).[17] Based on these properties, *Sarasvata choorna* was found effective on various items of HAM-A such as anxious mood, tension, insomnia, difficulties in concentration and memory, depressed mood, general somatic muscular, sensory, cardiovascular symptoms, respiratory symptoms, gastro-intestinal symptoms, genito-urinary symptoms and autonomic symptoms.

Previous studies on placebo proved that it may show the effects such as anxiolytic, anti-depressant, analgesic by conditioning or learning or by anticipation or positive expectancy effects or by altering various central nervous system (CNS) activities or autonomic nervous system (ANS) activities or by altering neurotransmitter release or by altering hypothalamic pituitary adrenal (HPA) axis or by changing mood, motivation or by making various psycho neuro immunological changes.[18] Based on these actions, placebo was found effective in various items of HAM-A scale such as anxious mood, tension, insomnia, difficulties in concentration and memory, depressed mood, general somatic muscular, sensory, cardiovascular symptoms,

respiratory symptoms, gastro-intestinal symptoms, genito-urinary symptoms and autonomic symptoms.

CONCLUSION

Individually, both the drugs, S*arasvata choorna* and placebo, were found effective in the management of GAD. There was no significant difference found in between the two drugs. *Sarasvata choorna* is not better than placebo in GAD.

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