



A COMPARATIVE EVALUATION FOR ANXIOLYTIC ACTIVITY OF MEDHYA RASAYANA GHRITA ADMINISTERED BY NASYA (NASAL ROUTE) VERSUS SHAMANA SNEHAPANA (ORAL ADMINISTRATION) ON OCCUPATIONAL STRESS. - A STUDY PROTOCOL

Ayurveda

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ABSTRACT

Background: "Occupational stress" is the harmful physical and emotional response that can happen when the employee is unable to meet job demands. strenuous work environment, shift variations, inadequate manpower, lack of moral independence, harassment at the workplace, job insecurity, strict deadlines, lack of personal and professional growth, relationship with administrators or coworkers, and difficulty in managing personal and professional strategies. etc. All of these factors contribute negative and serious impacts on personal health and job performance. Occupational stress is an alarming risk factor for many psychological, physical and behavioral disorders and if left untreated can leads to many health hazards like depression, drug abuse, social withdrawal, insomnia, suicidal tendencies cardiac disorders, diabetes, obesity, etc. So, the present Project aims to assess and treat occupational stress among nursing professionals working at Datta Meghe Institute of Medical Sciences, Wardha through the holistic approach of Ayurveda using Rasayana and Panchakarma Treatment. **Methodology:** The sample size will be calculated after the pilot study. For the pilot study, 30 patients will randomly select and divided into two groups. In Group A, after Deepan, Pachana, and srotoshuddhi, Shamana Snehapana with Medhya Rasayana Ghrita in a dose of 20 ml BD. will be given for 21 days. In Group B, after Deepan, Pachana and srotoshuddhi Nasal administration (Nasya) of Medhya Rasayana Ghrita 8 drops in each nostril will be given for 21 days. follow up will be taken for the next 21 days with oral administration of a Placebo capsule of 500 mg BD. The statistical analysis will be done at the end of the trial period to compare the changes in the assessment parameters from the baseline. The study is approved by the Institutional ethics committee and registered in CTRI with registration number CTRI/2023/01/048791. **Expected Results:** Change in subjective Parameters on the basis of the stress symptoms scale & objective Parameters on the basis of the Occupational Stress Index and serum cortisol level will be observed and recorded. **Conclusion:** Results and conclusions will be drawn according to the data obtained.

KEYWORDS

Medhya Rasayana, Nasya, Shamana Snehapana, Occupational stress.

INTRODUCTION:

In this 21st century Stress is an inevitable part of one's life. Some sort of stress is important in life as it provides energy and motivation to face challenges and achieve goals in life. However, it becomes very difficult to handle the situation when symptoms are out of proportion or if they are continued for longer. In the globe, around 3 million employees are suffering from occupational stress-related problems^[1]. A finding in review studies showed that occupational stress is responsible for 70–90% of productivity-related losses. Globally, the prevalence of occupational stress in nursing professionals varies between 9.2% and 68.0%^[2]. In India, this prevalence is 54.2%^[3]. In recent crises of the Covid 19 pandemic, nursing professionals are exposed to infection and have deteriorated mental health due to high workload, fatigue, fear of getting an infection, dealing with patients having negative emotions, and frustration due to long distance from family^[4]. In routine practice, also they are stressed due to the strenuous work environment, shift variations, harassment at the workplace, job insecurity, strict deadlines, lack of personal and professional growth, relationship with administrators or coworkers, and difficulty in managing personal and professional strategies. etc. All of these factors contribute negative and serious impacts on personal health and job performance.

According to the DSM-5, occupational stress is studied under adjustment disorders^[5]. The diagnostic criteria of adjustment disorders include emotional or behavioral symptoms within three months of expressing specific stressors in life. This stress is more than normally experienced in response to a stressful life event. And it is not a result of another mental disorder or a part of normal grieving. The stress is accompanied by cognitive, physical, and behavioral symptoms like headache, irritability, restlessness, feeling of depression, impaired concentration, fatigue, diarrhea, stomach aches, muscle aches and difficulty in sleeping, and so on^[6].

Many Previous Researchers co-relates occupational stress with 'chittodvega'. According to Ayurveda, 'Chittodvega' is one of the *Mansik vikaras* in which affliction of mind by anxiety, fear, and agitation are seen^[7]. Etiological factors for *Chittodvega* described in Ayurveda are *Asatmendriyarthasamyoga* (primarily abnormal perception through senses), *pradnyapradha* (unwholesome activities), and *Parinama* (the effect of time stage of disease and complication)^[8].

Due to the above factors, there is a derangement of understanding by the mind is seen that leads to the vitiation of *Manas Dosha (Rajas and Tamas)*, then one goes through several Physiological and behavioral changes as the misuse of mental capability begins. This pathological state of mind is considered as *Chittodvega*^[9]. In Ayurveda Preventive as well as curative aspect is adopted for stress management. The stress can be prevented by avoiding the factors inducing stress or by increasing the coping capacity of the body through lifestyle drugs and dietary modifications. All these are well organized under the umbrella of *Rasayana* (Rejuvenation) therapy. *Nasya* is considered the best treatment for *Mansik vikara*. Many experimental studies have been carried out in modern medicine which show the nasal route has been explored as an alternative route of drug administration as target drugs reach directly into the brain and provide rapid drug absorption and quick onset of action^[10]. Keeping these principles in mind, a polyherbal formulation of neurotrophic drugs (*Medhya Rasayana*) is administered through the nasal as well as the oral route in the management of occupational stress in Nursing Professionals.

RATIONALE:

The disease burden of mental disorders has increased to double in the last few decades, so India needs to invest heavily in mental health services. According to the World Health Organization (WHO), the Global Burden of Disease Survey estimates that mental disease, including stress-related disorders, will be the second leading cause of disabilities by the year 2020^[11].

Although the prevalence of occupational stress among nursing professionals has increased in the last 2-3 years due to the covid-19 pandemic, many observational studies are carried out carried to find out the stress aggravating factors. however, very less clinical trials are conducted due to a lack of awareness and early management of occupational stress. so, it is most important to carry out more and more clinical trials to relieve stress among healthcare workers and improve the quality of the healthcare system.

Routine tests for stress like exercise, nuclear stress tests, and echocardiograms are tedious and costly^[12]. The Prolonged medication causes an economic burden to already stressed individuals. However, herbal medicines are easily available and cost-effective. The modern system of medicine is still in want of effective antistress agents.

Though drugs like diazepam and fluoxetine are claimed to have an anti-stress activity they have many side effects like loss of memory, poor concentration, blur vision, headache, loss of coordination, Problems in speech, stomach upset, etc.^[13] However, herbal medicines are having a broad spectrum of action with minimum side effects. Various oral medications and Panchakarma therapies like Shirodhara, Shiro Basti, shirobhyanga, shirolepa, Shiro Pichu, Nasya, etc. are effective in psychosomatic disorders. Among Panchakarma, Shirolepa and Shiropichu take more time to achieve the desired therapeutic effect and it is a localized treatment.^[14] Shirodhara has promising results over stress but it is a very costly and time-consuming procedure. however, Nasya is easy to administer, a cost-efficient procedure, and shows desired therapeutic action in less period of time as the Nasal route is considered the best route over the oral or systemic route in psychosomatic disorders.

The polyherbal formulation i. e, Medhya Rasayana Ghrita^[15] used in this study contains only 4 ingredients (Guduchi, Yastimadhu, Mandookparni, and Shankhapushpi) which are easily available and cost-effective and each drug has proven anxiolytic, Rejuvenation and anti-oxidant properties through many experimental and clinical studies. So, it may probably reduce the stress when given in combination with the appropriate route of administration. Considering all these facts, the Nasal administration of Medhya Rasayana is selected for occupational stress disorder in nursing professionals.

AIM AND OBJECTIVES:

AIM:

To assess and compare the Anxiolytic activity of nasal and orally administered *Medhya Rasayana Ghrita* in the management of occupational stress in health care Professionals.

OBJECTIVES:

- Among nursing professionals having occupational stress
- To determine the Efficacy of *Nasya* i. e. nasal administration of *Medhya Rasayana Grita* in the management of occupational stress.
- To determine the Efficacy of oral administration of *Medhya Rasayana Ghrita* in the management of occupational stress.
- To compare the efficacy of nasal & oral administration of *Medhya Rasayana Ghrita* in the management of occupational stress.
- To assess and compare the efficacy of nasal and oral administration of *Medhya Rasayana Ghrita* on serum cortisol level in occupational stress.

MATERIALS & METHODS:

Study Type: Interventional study

Trial Design: Randomized, Reference Standard, Controlled, Single-blind (Assessor), superiority clinical trial.

Case Definition- Diagnosed cases of Occupational stress according to

1. DSM V diagnostic criteria for adjustment disorder.
2. Raised serum cortisol Level
3. Occupational stress Index Score^[16] (Score 128-150) and those having moderate stress.

Research Question:

whether *Medhya Rasayana Ghrita* administered by the Nasal route more efficacious than the oral route in managing occupational Stress?

Methodology:

Study Setting:

The study will be conducted in Mahatma Gandhi Ayurveda College Hospital and Research Centre (MGACH&RC), Salod (Hirapur) Wardha, Maharashtra.

Eligibility criteria:

Inclusion Criteria

- Participants willing to give informed consent.
- Participants have an age group between 25 to 40 years irrespective of their sex and socioeconomic status.
- Subjects fulfilling DSM-5 criteria for diagnosis.
- Participants were screened with Occupational Stress Index and those having moderate stress. (Score 128-150).
- Participants having Samagni and Madhyam Koshtha [17].

Exclusion Criteria:

- Participants having age less than 25 and more than 40 years of age of either sex.
- Person suffering from other psychiatric illnesses and using other anti-psychiatric medication^[18].
- Patient suffering from any systemic chronic illness. e.g., Asthma, COPD, Anemia, hepatic dysfunction, renal dysfunction, and Resistant hypertension. Etc^[19].
- Participants with a history of alcoholism and drug abuse^[20].
- Pregnant, breastfeeding, or planning to become pregnant during the study.
- Women in the peri-menopausal age group^[21].
- Participants having hypersensitivity to trial drugs.
- Patients having Nasal obstructive Pathology like congestion, Deviated Nasal septum, Nasal polyps etc .
- Patients contraindicated for Nasya according to classics^[22].
- Patients contraindicated for Shamana Snehapana^[23].

Method of Randomization, Allocation & Intervention:

It is the Randomized, Reference Standard, Controlled, Single-blind (Assessor), superiority clinical trial. The study design is as per (Fig.1). In this study, A simple Randomization will be done using SPSS software, and participants will be randomized in both groups in a 1:1 ratio. Participants in group A are allocated to intervention i.e Nasal administration of *Medhya Rasayana Ghrita*. Participants in group B are allocated to control group i.e Oral administration of *Medhya Rasayana*. The detailed methodology of the Intervention is as per mentioned in (Table 1).

The formulation used for this study i.e *Medhya Rasayana Ghrita* will be prepared according to classical textual references at the Pharmacy department of Mahatma Gandhi Ayurved College, Wardha (Table.2). The raw material for the Preparation of Ghrita will be procured from Manas Ayurved, Nagpur. Plant identification will be made by the institute's staff botanist. All raw materials are GMP-certified as per Food and pharma norms. Physico-chemical characterization and High-performance thin layer chromatography (HPTLC) will be done at Authorized Pharmacognosy Department.

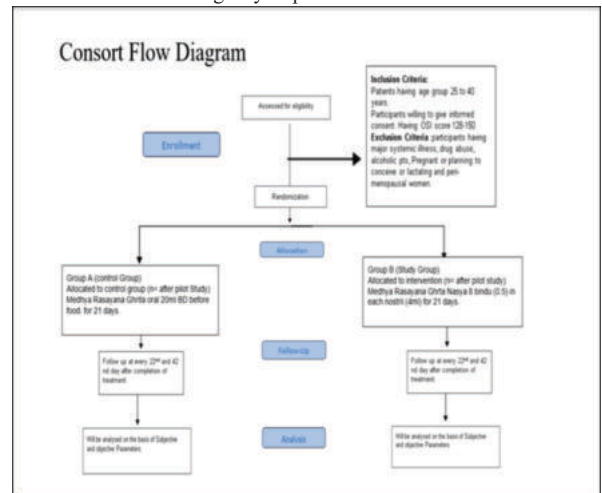


Table 1. Methodology Of The Study

No. Of Days	Study and Intervention
0 th day	1. Complete history taking 2. Initial assessment 3. Informed consent 4. Physical examination and case paper recording. Investigation- Serum cortisol level
1 st to 3 rd day	Deepan-Pachan with Trikatu Churna- 3gm after meal twice a day up to Niramavastha and Agnideepan Lakshana's. Koshthashuddhi- Erandbhrishtha Haritaki Churnna – 5gm at night after the meal with lukewarm water.
4 th to 24 th day	In Group A- Poorvakarma: Lactal Abhyang with Til Taila and swedan Pradhan Karma- Nasya with <i>Medhya Rasayana Ghrita</i> - 8 Bindu in each nostril. (1 bindu=0.5 ml). 4ml in each nostril for 21 days. Paschat Karma- Swedan (fomentation) and Gandush (Gargling) and Dhoompana.

	In Group B- Shamana Snehapana with Medhya Rasayana Ghrita in a dose of 20 ml BD before food for 21 days.
25 th day to 46 th day.	Follow up with the administration of a Placebo capsule in a dose of 500 mg twice daily after food with water for a period of 21 days.
47 th day	Assessment of all investigations and parameters after treatment.

Table 2. Content of Interventional Drugs & Details of Drug Preparation:

Medhya Rasayana Ghrita content & Preparation					
S.N.	Content	Latin Name	Part used	Form	Ratio
1	Mandookaparni	Centella asiatica	Leaf	Swaras	8 parts
2	Yasthimadhu	Glycyrrhiza glabra	Roots	Churna	1 part
3	Guduchi	Tinospora Cardifolia	Steam	Swaras	8 parts
4	Shankhapushpi	Convolvulus pluricaulis	All Parts	Kalk	1 part
5	Go-Ghrita				4parts

8 parts of Mandookaparni Patra Swarasa added with 8 parts of Guduchi steam Swarasa, it is then added with 4 parts of Go-Grita and 1 part of Shankpushpi Kalk and 1 part of yasthimadhu root churna, the mixture then heated on low flame. The mixture will heat until attains Snehā siddhi lakshana.

Criteria For Discontinuing Or Modifying Allocated Interventions:

- Patients willing to quit in between are allowed to quit and will be replaced.
- If the patient develops an acute illness during the trial will be withdrawn.
- Withdrawn patients will be replaced.

Follow up- 25th day, 46th day

Assessment Criteria:

A. For Subjective Parameters: The clinical features of stress will access according to the stress symptoms scale^[24]. It consists of a total 41 symptoms of stress and they are rated from 0 (never) to 3 (very often) according to the frequency with which the symptoms are experienced in the last two weeks.

Score- Ranges from 0 to > 50

Score	Rating
0-19	Lower than average
20-39	Average
40-49	Moderately higher than average
50 and above	Much higher than average

B. For objective Parameters:

1. Occupational stress Index is widely used to assess occupational stress. It contains 46 statements with 5 alternative responses i.e. from strongly agree (5 scores) to strongly disagree (1 score) based on 5-point Likert scale. The total score on this scale was considered for the severity of occupational stress.

2. Serum cortisol level. – Blood samples will be taken at 11 am. In the morning to assess the cortisol level before and after treatment.

Outcomes:

Primary: Reduction in Occupational stress index score and serum cortisol level.

Secondary: Reduction in symptoms of stress.

Participant Timeline: 21 days of treatment and follow-up on the 25th and 46th day after treatment.

Sample size: It will be calculated after the pilot study by using the formula for superiority Randomised controlled Trial.

$$N = 2 \times \left(\frac{z_{1-\alpha} + z_{1-\beta}}{\delta - \delta_0} \right)^2 \times s^2$$

N= No. of size in each group

Z=standard deviation for both sides of the Mean

S²= Polled standard deviation of both comparison group

δ: clinically admissible margin of superiority

δ₀= a clinically acceptable margin.

**Pilot Study: Group A- Medhya Rasayana Ghrita Oral (15 patients)
Group B- Medhya Rasayana Ghrita Nasya (15 patients)**

Data Collection, Management, And Analysis Methods:

Observations will be made after completion of the study, according to the data collected with the help of the following: I. Case registration Form with detailed history and examination II. Follow Up Assessment Proforma.

A. Data monitoring:

The Data coding will be done by the PI and supervisor

B. Statistical Analysis:

Observation and results will be computed statistically to know the significance level and obtain the conclusions for the study by using the Statistical Package for Social Sciences (SPSS) 20.0 version. Data will be analyzed by a superiority trial applicable statistical method.

Ethics and dissemination:

The trial will be conducted as per ICMR guidelines involving human participants (2017) and in accordance with the ethical principles of the Declaration of Helsinki for biomedical research. IEC certificate, obtained vide Ref No. MGACHRC/ IEC/ June 2022/516 dated 30.06.2022. The trial is also registered in CTRI with registration number CTRI/2023/01/048791.

Consent:

Written informed consent will be taken from the patient before starting the study. During the study, the confidentiality of each patient will be maintained.

DISCUSSION:

"Occupational stress" is the harmful physical and emotional response that can happen when the employee is unable to meet job demands^[25]. It is associated with various biological reactions in the body including mental deterioration, heart attack, high blood pressure, and other systemic disorders. Due to the global crisis of Covid 19 pandemic, the prevalence of occupational stress is increasing day by day among healthcare professionals. As nursing professionals are an integral part of the healthcare system and mainly deal with intensive care of patients the sound status of the mental health of nurses is important. According to Ayurveda, the stress symptoms can be co-related to 'Chittodvega'. In Charak Samhita Chittodvega is mentioned as Manasik vikara^[26]. The symptoms are mainly due to Vata prakopa along with Raja, Tama dushti, and Oja Kshya Lakshana^[27]. In Charak Vimansthana Acharya Charaka mentioned Manasik bhavas (criteria for assessment of mental status) to assess the mental status of the individual. These factors are incorporated as the scale for the assessment of occupational stress in this study.

The present study is planned to establish the effect of Medhya Rasayana Ghrita on Occupational stress through two different routes of administration, assuming that being Rasayana the formulation will work on Saptā Dhatus, improving oja Kshya and Vata vrudhhi, Medhya (improving intellect) ingredients used in this formulation already proved their anxiolytic effect through various experimental studies. As Medhya It will also work on Raja and Tam Dosha. The formulation used in Ghrita (Ghee) form helps to enhance the therapeutic outcome. Nasal administration of this formulation helps to provide rapid drug absorption and quick onset of action.

The results of this trial may provide evidence of the safety and effectiveness of this formulation on occupational stress. It also helps in widening therapeutic options for the management of occupational stress through the holistic approach of Ayurveda.

Trial status:

The recruitment of study participants has been started in February 2023. The study is in progress. The trial results will be published through national/ international peer-reviewed journals after the completion of the study.

REFERENCES:

1. Eleni M, Fotini A, Maria M, Ioannis ZE, Constantina K, Theodoros CK. Research in occupational stress among nursing staff-a comparative study in capital and regional hospitals. Sci J Hell Regul Body Nurses. 2010;3(3):79-84.
2. Kaburi B.B., Bio F.Y., Kubio C., Ameme D.K., Kenu E., Sackey S.O., Afari E.A. Psychological working conditions and predictors of occupational stress among nurses, Salaga Government Hospital, Ghana, 2016. The Pan African Medical Journal. 2019; 33:320

3. Nayak s, sahu P, A cross-sectional analysis of prevalence and factors related to depression, anxiety, and stress in health care workers amidst the COVID-19 pandemic, *BMJ*.2021 ;11(4)
4. Aziziaran, S. Basharpour The role of rumination, emotion regulation and responsiveness to stress in predicting of Corona anxiety (COVID-19) among nurses. *Quarterly journal of nursing management*.2020; 9 (3); p.8-18
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders DSM-V*, 5th ed. (Text Revision). New Delhi: Jaypee Brothers Medical Publishers (p) Ltd;2000 p.435-6
6. Classification and diagnosis of Mental disorder, American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders DSM-V*, 5th ed. (Text Revision). New Delhi: Jaypee Brothers Medical Publishers (p) Ltd;2000
7. Pragyaprasad UR. Understanding of occupational stress through principles of Ayurveda. *Ayurpub.com*. 2020;5(4); p.1523-1534.
8. Charak Samhita, Cakrapani commentary, Yadavaji Trikamaji Acharya. Sutrasthana, Traisraishniya adhyaya 11:37; Reprint edition.Varanasi; Chaukhamba Orientalia publishers; 2009. 165 P.
9. Charak Samhita, Cakrapani commentary, Yadavaji Trikamaji Acharya. Sutrasthana, Traisraishniya adhyaya 11:41; Reprint edition.Varanasi; Chaukhamba Orientalia publishers; 2009. 167 P.
10. Michel Ikechukwu Ugwoke,et.al The biopharmaceutical aspects of nasal mucoadhesive drug delivery, 2001, *journal of pharmacy and pharmacology*, 53(1),p. 3-22
11. SL Buka, Psychiatric Epidemiology, Reducing the global burden of Mental illness. *American journal of Epidemiology*.2008; 168 ,9(1), p 977-979
12. C Yogita, R Anitta , K iikal stress-A psychological disorder and its management in Ayurveda-a review; *Ayurpub* 3(4), 970-80, 2018
13. C Yogita, R Anitta , K iikal stress-A psychological disorder and its management in Ayurveda-a review; *Ayurpub* 3(4), 970-80, 2018
14. Pragyaprasad UR. Understanding of occupational stress through principles of Ayurveda. *Ayurpub.com*. 2020;5(4); p.1523-1534.
15. Charak Samhita, Cakrapani commentary, Yadavaji Trikamaji Acharya. chikitsasthana, Rasayana adhyaya pada 3, 1:30,31; Reprint edition.Varanasi; Chaukhamba Orientalia publishers; 2009. 30 P.
16. Occupational Stress Index by Shrivastava and Singh, BHU, Uttar Pradesh, 1984.
17. Vasant Patil et.al., further clinical study on standardization of Shodhnang Abhyantar Snehana, Jamnagar, 2006
18. Self-Medicating depression, Anxiety and stress. Helpguide.
19. Andre M, et a Stressful life events and the onset of chronic diseases among Australian adults: findings from a longitudinal survey. 24(1), Feb 2014 .p 57-72.
20. Self-Medicating depression, Anxiety and stress. Helpguide.
21. April M Falconi, The longitudinal relation of stress during Menopausal Transition to Fibrinogen concentration. *PMC*, 23(5). May 2016, 518-527.
22. Charak Samhita, Cakrapani commentary, Yadavaji Trikamaji Acharya. sidhhisthana,, Panchakarmiya siddhi adhyay 2,;22; Reprint edition.Varanasi; Chaukhamba Orientalia publishers; 2012. p.974.
23. Charak Samhita, Cakrapani commentary, Yadavaji Trikamaji Acharya. sutrasthana, Snehaadyay 13(3) Reprint edition.Varanasi; Chaukhamba Orientalia publishers; 2012 p. 128
24. Elkin, A. (1999). *Stress Management for Dummies*. New York, NY: Wiley Publishing, Inc.
25. Henry O, Evans AJ. Occupational Stress in Organizations and its effect on organizational performance. *Journal of Management Research* 2008; 8 (3); p.123-35.
26. Acharya YT, ed. *Charaka Samhita of Agnivesha, Sutra Sthana*, Vol. 1
27. Anonymous. *Indu commentary on Astanga Samgraha of Vagbhata, Sutra Sthana*, Vol. 1, Ch. 13, Ver. 3, 9th ed. Varanasi: Choukhamba Orientalia; 2005. p. 280.