



ORIGINAL RESEARCH ARTICLE

ROLE OF SARPAGANDHA VATI IN NIDRANASHA (PRIMARY INSOMNIA)

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Abstract

Background: Insomnia is the most common of all sleep disorders, in which there is inability to fall asleep or to stay asleep as long as desired. In comparison to the therapeutic procedure of different systems of medicine, Ayurveda has good approach towards the treatment of Insomnia in terms of both internal and external therapies. The drug Sarpagandha (*Rauwolfia serpentina* Benth ex.kuntz) has been widely used in the management of hypertension and insomnia, no study has been carried out to prove its efficacy in insomnia as a single drug. **Aim:** To evaluate the efficacy of *Sarpagandha Vati* in *Nidranasha* (Primary Insomnia). **Study design:** A single group, open labeled, uncontrolled, prospective clinical study with minimum 30 patients with pre and post test design. **Methods and Material:** Study was conducted on 30 patients of *Nidranasha* (primary Insomnia) who fell under inclusion criteria. Sarpagandha tablets of 500mg each were prepared with one Bhavana of Sarpagandha Moola Kashaya (root decoction). One tablet was advised in the morning after breakfast and at night, before bedtime with water for the duration of one month. **Statistical analysis used:** Friedman's test was used to analyze the significance of change in Subjective parameters. Wilcoxon signed rank test with Bonferroni correction was done for post hoc, to interpret the time of significant change. Paired t test was done to analyze the change in objective parameters. **Results:** Highly significant improvements were observed in chief complaints like sleep initiation ($p = <0.001$), maintaining sleep ($p = <0.001$) early morning awakening ($p = <0.001$). Significant improvement were seen in *Angamarda* ($p = <0.001$), *Shirogaurava* ($p = <0.001$), *Jrumbha* ($p = <0.001$), *Tandra* ($p = <0.001$) etc associated complaints from before treatment to after treatment. **Conclusions:** The chief mechanism of action of Sarpagandha (*Rauwolfia serpentina*) seems to be due to its *Prabhava* (specific action or unexplained action). Among other alkaloids reserpine is the one that decides the action of the drug. Hence it can be concluded that *Sarpagandha Vati* can be effectively used in the management of *Nidranasha*.

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Key words: *Nidranasha*, Insomnia, sleep, Sarpagandha, *Rauwolfia serpentina*, Hypertension

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INTRODUCTION

We spend about one third of our lives asleep¹. Through the ages, sleep has occupied a special place in human concern. Ayurveda has given more importance to sleep by considering it as one among *Trayopasthambhas*². It has been rightly stated by *Acharya Charaka* that happiness & misery, proper & improper growth, strength & weakness, potency & sterility, knowledge & ignorance and life & death of an individual depend on proper and improper sleep. Insomnia is the most common of all sleep disorders, in which there is inability to fall asleep or to stay asleep as long as desired. Insomnia has been thought of both as a symptom and as a sign. Aristotle wrote a monograph about insomnia "De Insomnia" in the Greek Antiquity. After that time, our knowledge about sleep remained unchanged until the middle of the last century³.

Need for the study

Among Insomnia patients about 15% are suffering from primary insomnia where the causes are unknown⁴. One out of every twenty Indian suffers from sleep disorder. 16% of the population suffered from insomnia in India not far from the 20% that suffer from insomnia in the West. Indian women (6.5%) outnumber men (4.3%), when it comes to disturbed sleep. 5%-6% of people aged 50 years and above may be affected by sleep disorders in India⁵.

In comparison to the therapeutic procedure of different systems of medicine, Ayurveda has good approach towards the treatment of *Nidranasha* in terms of both internal and external therapies. Medicines used in contemporary science for treating insomnia are fast acting and may provide temporary relief but long term usage may lead to toxicity, adverse drug reaction even drug dependency. By taking into consideration of the above facts, this study of single drug *Sarpagandha* (*Rauwolfia serpentina*) which has *Nidrajanaka Karma* (sedative) as *Prabhava* (specific action) was taken. Even though it is widely used in the management of hypertension and insomnia, no study has been carried out to prove its efficacy in insomnia as a single drug.

So this study was taken.

OBJECTIVES OF THE STUDY

To evaluate the efficacy of *Sarpagandha Vati* in *Nidranasha* (Primary Insomnia).

MATERIALS AND MATHED

Study design: A single group, open labeled, uncontrolled, prospective clinical study with minimum 30 patients with pre and post test design.

Study Population: General population of Hassan city located in Southern India was selected for the study.

Sampling: Data for the study was collected as per convenience sampling method and treated in single group.

Study sample

Single group of 30 clinically diagnosed patients of *Nidranasha* were recruited for the study. Below stated inclusion and exclusion criteria were used for registration of the patients for present clinical trial.

Sample size: 30 patients fulfilling the diagnostic and inclusion criteria were selected for the study.

Study setting: Study was conducted in Shri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan District, Karnataka, India which is an Academic Institution. Patients visiting outpatient and inpatient department of college were included in the study.

Diagnostic criteria :

For the diagnosis detailed medical history and physical examination was done according to both Ayurvedic and modern clinical methods along with ICD -10 guidelines⁶.

Inclusive criteria

Individuals between the age group of 25 to 60 years of both sexes having insomnia of minimum one month to maximum 5 years duration were selected randomly for the study.

Patients of Insomnia with mild hypertension without any complications were included for the present study.

Exclusive criteria:

Patients with moderate and severe hypertension and hypotension and any other systemic disorders were excluded.

Patients with any major psychiatric disorders where insomnia is found secondary to that were not registered.

Patients of hyperacidity and peptic ulcer were excluded from the study.

Patients with *Nidranasha* due to *Madatyaya* (alcoholism) and *Abhighata* (injury) were excluded.

Patients under hypnotic medications or other drugs which are known to cause drowsiness were not included.

Insomnia associated with physiological conditions like pregnancy, lactation and puerperal stage were left out from the study.

Ethical considerations: Ethical clearance was obtained from the institutional ethical committee (IEC) of SDM College of Ayurveda and Hospital (IEC No: SDMCAH/EC/46/13-14; dt.10th April, 2013). Informed consent was obtained from the participating patients.

Selection of the drug: After considering the symptoms and patho-physiology of *Nidranasha* the drug *Sarpagandha* was selected. It has *Tikta, Kashaya Rasa* (bitter and astringent taste), *Ushna Veerya* (hot in potency); *Vatakapha Shamaka* (passifying) and due to its *Prabhava* (specific action or unexplained action) it acts as *Nidrajanaka* (sedative).

Method of Preparation of Sarpagandha Vati:

Drug was prepared in SDM Teaching Pharmacy. *Sarpagandha* roots were washed, sun dried and powdered into fine and course powders. Course powder was used to prepare *Kashaya* (decoction) which was used as *Bhavana Draya* (drug used for trituration) to reduce the dosage and increase the effectiveness. They were made into pills of 500mg each.

Lab investigations: To confirm or to exclude the other medical disorders routine hematological and urine investigations were carried out.

Technique of Data Collection: Data was collected by means of case records consisting of diagnostic questionnaires and Insomnia Severity Index Scale.

Intervention

Drug: Sarpagandha Vati

Dose: 500mg BD dosage

Anupana: water

Time of administration: one tablet in the morning after breakfast and one at night before bedtime

Duration: one month

Follow up: After treatment period, for one month follow up was done.

Criteria for Assessment

- To assess the psychological intactness, mental status examination was carried out.
- The subjective and clinical improvement of *Nidranasha* was assessed by adopting Insomnia Severity Index scale⁷. (Table 1& 2)

Table 1: Insomnia Severity Index with grading of symptoms

| Insomnia problem | Non e | Mild | Moderate | Severe | Very severe |
|--------------------------------|-------|------|----------|--------|-------------|
| 1. Difficulty falling asleep | 0 | 1 | 2 | 3 | 4 |
| 2. Difficulty staying asleep | 0 | 1 | 2 | 3 | 4 |
| 3. Problem waking up too early | 0 | 1 | 2 | 3 | 4 |

4. SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

| | | | | |
|----------------|-----------|----------------------|--------------|-------------------|
| Very satisfied | Satisfied | Moderately satisfied | Dissatisfied | Very dissatisfied |
| 0 | 1 | 2 | 3 | 4 |

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing

| the quality of your life? | | | | |
|---------------------------|----------|----------|------|-------------------------|
| Not at all noticeable | A little | Somewhat | Much | Very much noticeable |
| 0 | 1 | 2 | 3 | 4 |

6. How WORRIED/DISTRESSED are you about your current sleep problem?

| | | | | |
|-----------------------|----------|----------|------|----------------------|
| Not at all worried | A little | Somewhat | Much | Very much worried |
| 0 | 1 | 2 | 3 | 4 |

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

| | | | | |
|---------------------------|----------|----------|------|--------------------------|
| Not at all Interfering | A little | Somewhat | Much | Very much interfering |
| 0 | 1 | 2 | 3 | 4 |

Table 2 : Total Score interpretation:

| Score | Interpretation |
|-------|---------------------------------------|
| 0–7 | No clinically significant insomnia |
| 8–14 | Subthreshold insomnia |
| 15–21 | Clinical insomnia (moderate severity) |
| 22–28 | Clinical insomnia (severe) |

- Associated symptoms of *Nidranasha* like *Angamarda* (Malaise), *Apakti*(Indigestion), *Shirogurava* (Heaviness and Headache), *Jrumbha* (Yawning), *Jadyata* (Lethargy), *Glani* (Tiredness), *Bhrama*(Giddiness), *Tandra* (Drowsiness) were assessed before and after the therapy. Pulse and Blood

pressure were recorded before and after the treatment as *Sarpagandha* has its effect on these parameters

Statistical analysis :

- Statistical analysis was done using SPSS VERSION 16

- Friedman’s test was used to analyze the significance of change in Subjective parameters.
- Wilcoxon signed rank test with Bonferroni correction was done for post hoc, to interpret the time of significant change.
- Paired t test was done to analyze the change in objective parameters.

OBSERVATIONS

Demographic data: Out of 30 patients of *Nidranasha* every age group had approximately same number of patients. Maximum number of patients were of Males (58.8%), of Hindu religion (97.1%), Married (91.2%), Educated up to higher secondary (44.1%), belonged to middle economical status (55.9%) and were Home makers (32.4%). Majority of patients did not have familial disposition (91.2%), were Addicted to Coffee (44.1%). Maximum number of patients were of *Kapha-Vataja* body constitution (47.1%) with *Rajo Guna* predominant *Manasika Prakruti* (67.6%) (mental constitution) and *Vikruthi* wise (vitiation) *Vata Pitta* predominant (91.2%) with majority of them having *Chinta*(worry) as *Nidana* (causative factor)

(55.9%) and *Madhyama Satva* (moderate mental strength) (91.2%).

Clinical observations: Chief complaints like reduction in sleep hours was present in all patients(100%); where as 97.1% had difficulty in staying asleep; 94.1% had inability to sleep after getting up; 91.2% had difficulty to fall asleep and 44.1% had complaints of early morning awakening.

Associated complaints like *Angamarda* was present in 82.4%; *Apakti* in 70.6%; *Shirogaurava* in 82.4%; *Jrumbha* in 52.9%; *Jadyata* in 73.5%; *Glani* in 50%; *Bhrama* in 41.2% and *Tandra* in 76.5% out of 30 patients of *Nidranasha*.

RESULTS

The clinical study conducted on 30 patients showed following improvements.

Effect of *Sarpagandha Vati* on insomnia severity index: *Sarpagandha Vati* provided significant improvement in sleep initiation (p=<0.001), maintaining sleep (p=<0.001) early morning awakening (p=<0.001), Improvement in satisfaction towards sleep pattern, quality of life and interference with daily functioning (p= <0.00) due to *Nidranasha*. (Table 3)

Table 3: Showing significant change chief clinical symptoms

| Parameter | X ² | P value | Remarks |
|------------------------------|----------------|---------|---------|
| Difficulty in falling asleep | 46.32 | <0.001 | HS |
| Difficulty to stay asleep | 44.24 | <0.001 | HS |

| | | | |
|--|-------|--------|----|
| Early Morning awakening | 18.5 | <0.001 | HS |
| Satisfaction with current sleep pattern | 45.53 | <0.001 | HS |
| Noticability to others in terms of impairing QOL | 49.57 | <0.001 | HS |
| worry about sleep problem | 46.10 | <0.001 | HS |
| Interference with daily functioning | 51.7 | <0.001 | HS |

Effect of *Sarpagandha Vati* on associated symptoms: The effect of *Sarpagandha Vati* on improvement of associated symptoms like *Angamarda* (p = <0.001), *Apakti* (p = <0.001),

Shirogurava (p = <0.001), *Jrumbha* (p = <0.001), *Jadyata* (p = <0.001), *Glani*(p = <0.001), *Bhrama*(p = <0.001) and *Tandra*(p = <0.001) were highly Significant.(Table 4)

Table 4: Showing improvement in associated clinical symptoms

| Parameter | X ² | P value | Remarks |
|--------------------------|----------------|---------|---------|
| <i>Angamarda</i> | 36.28 | <0.001 | HS |
| <i>Apakti</i> | 28.00 | <0.001 | HS |
| <i>Shirogurava</i> | 29.20 | <0.001 | HS |
| <i>Jrumbha</i> | 30.00 | <0.001 | HS |
| <i>Jadyata</i> | 27.90 | <0.001 | HS |
| <i>Glani</i> | 22.6 | <0.001 | HS |
| <i>Bhrama</i> | 38.96 | <0.001 | HS |
| <i>Tandra</i> | 38.96 | <0.001 | HS |
| <i>Total sleep hours</i> | 31.22 | <0.001 | HS |

Effect on pulse and blood pressure: *Sarpagandha Vati* provided 8.4% reduction in pulse, 7.37% reduction in systolic blood

pressure and 8.33% reduction in diastolic blood pressure. (Table 5)

Table 5: Showing Effect of *Sarpagandha Vati* on Pulse and Blood pressure

| Parameters | Mean | | St.deviation | St.Error | T value | P value | Remarks |
|------------|------|----|--------------|----------|---------|---------|---------|
| | BT | AT | | | | | |
| | | | | | | | |

| | | | | | | | |
|--------------|--------|--------|------|------|------|--------|----|
| Pulse | 78.53 | 71.93 | 5.06 | 0.92 | 7.14 | <0.001 | HS |
| Systolic BP | 128.33 | 118.87 | 7.16 | 1.30 | 7.24 | <0.001 | HS |
| Diastolic BP | 87.27 | 80.00 | 6.37 | 1.16 | 6.24 | <0.001 | HS |

DISCUSSION:

Total 30 patients of *Nidranasha* fulfilling the criteria were registered. Though it is said that Insomnia is common in old age in this study patients were distributed in all groups between 25-60 years. In 36-45 and 46-55 age group *Nidranasha* may be due to increased family liabilities and job related problems. In 25-35 age group emotional changes and stress or failure related to establishment may be the cause of Insomnia. In the study dominance of male sex of middle class with agricultural occupation were found affected more. This may be due to the physical & mental stress for better life. Most of the patients belonged to the Hindu religion may be because of the dominance of Hindu population in the area where hospital is located. Study revealed that married suffer more than unmarried may be due to marital commitments, children care and other family problems.

Assessing the personal data showed that maximum number of patients were of *Vata-Kaphaja Prakruti* (body constitution) with *Rajas* predominant *Manasika Prakruti* (mental constitution). Generally *Vata-Pitta Pradhana Prakruti* have less sleep or disturbed sleep. Causative factors leading to insomnia can

easily provoke *Vata, Pitta* and *Rajas* – which is called as *Pravartaka*; because of which it causes arousal. In this study *Vata* seems to vitiate *Rajas* causing *Tamo Dosha Kshyaya* by which person has *Nidranasha*. But while analyzing *Vikruta Dosha Vata-Pitta Dushti* along with *Rajo Dosha Vriddi* was observed. After the course of one month of treatment subjects having *Vatapitta Pradhana Prakruti* seem to have more relief than other *Prakruti*.

Even though most of the patients were of *Madyama Satva, Madhyama Samhanana* (moderate compactness) and *Madhyama Sara*(moderate excellence of Dhatus); unavoidable stress and situations might have caused Insomnia. Majority of the patients had coffee (44.1%) and tea (29.4%) addictions. It has been reported that caffeine competes with adenosine receptors causing cortisol arousal which leads to Insomnia⁸.

Causative factors of *Nidranasha* in majority was *Chinta* (worry) (55.9%), *Udvega* (17.6%) (anxiety) and *Bhaya* (fear) (5.88%). *Chinta* causes *Vata Vriddhi* (increase in *Vata*), *Udvega* does *Vata Pitta Vriddhi*, *Bhaya* again Causes *Vata Vriddhi* along with *Rajas Vriddhi* resulting in *Nidranasha*.

Chief complaints: Among 30 patients of *Nidranasha* reduction in sleep hours was present in all patients(100%); where as 97.1% had difficulty in staying asleep; 94.1% had inability to sleep after getting up; 91.2% had difficulty to fall asleep and 44.1% had complaints of early morning awakening. This may be due to different causative factors, like in *Chinta* there will be difficulty in initiation of sleep, in *Udvega* both initiation and maintaining sleep will be lost; but in all case there will be reduction in sleep time irrespective of the causes due to *Rajas Vata* and *Pitta Dushti* (vitiation).

Associated complaints: Associated complaints like *Angamarda* (Malaise) was present in 82.4%; *Apakti* (indigestion) in 70.6%; *Shirogurava* (Heaviness and Headache) in 82.4%; *Jrumbha* (yawning) in 52.9%; *Jadyata* (lethargy) in 73.5%; *Glani* (tiredness) in 50%; *Bhrama* (giddiness) in 41.2% and *Tandra* (drowsiness) in 76.5% out of 30 patients of *Nidranasha*. These *Lakshanas* were due to *Dusti* of *Vata*, *Pitta* and *Rajas* individually or together and also as secondary to *Nidranasha*. Once *Nidranasha* was managed there was reduction in the associated complaints.

Probable mode of action of *Sarpagandha*: The drug *Sarpagandha* selected for the study mainly has *Tikta*, *Kashaya* taste, *Laghu Guna*, *Ushna Virya*(potency), *Katu Vipaka* and *Vata-Kaphahara* properties⁹. Even though because

of *Tikta* and *Kashaya Rasa* it does *Pitta Shamana* (passifying) and due to the *Ushna Veerya* it does *Vata Shamana*; the *Nidrajanaka karma* is because of its *Prabhava*⁹. We don't have any explanations regarding *Prabhavaja Karma* in our classics but with the help of contemporary science *Prabhavaja Karma* of *Sarpagandha* can be vaguely understood by analyzing its action on neurotransmitters.

Vata is known to regulate endocrinal functions of the body; and also influences *Pitta* and *Kapha* functions¹⁰. Sleep being an endocrinal function gets influenced by *Vata*. *Vata Shamakatva* (passifying action of *Vata*) and *Nidrajanana Prabhava* (sedative action) of *Sarpagandha* corrects the sleep pattern.

Vata and *Rajas* are mainly involved in late initiation of sleep and *Pitta* along with *Rajas* is responsible for repeated waking in the night. *Tikta* (bitter) and *Kashaya* (astringent) taste and *Prabhava* of the drug may function as *Pitta Shamaka* and *Nidrajanana*.

Once *Nidranasha* was corrected most of the associated complaints like *Angamarda*, *Apakti*, *Jrumbha* etc were brought back to normal. Other than previously mentioned actions, *Sarpagandha* has *Agnivardhaka* (Improving the appetite) property due to *Tikta Rasa* and *Ushna Veerya* may be because of which it helped in improving symptoms like *Apakti*, *Shirogurava* etc.

Mode of action through Neurotransmitters

The drug Rauwolfia serpentine's pharmacological action is mainly because of its alkaloids chiefly like reserpine, deserpidine, ajmaline, yohimbine etc. Sleep is a complex process which involves various neurotransmitters. Sleep wake pattern is regulated by Norepinephrene, 5-hydroxytryptamine and GABA mainly.

Reserpine, has its pharmacological properties as sedative and tranquilizing agent. Reserpine increases GABA receptor binding acts as GABA-ergic¹¹. Activation of GABA-ergic cells in the basal forebrain and preoptic area appear to coordinate sleep onset through direct effects and/ or through inhibition of cells promoting cortical activation i.e. inhibition of neurotransmitters like norepinehrine and serotonin which promote wakefulness. Reserpine separately depletes 5-hydroxytryptamine, noredrenaline and dopamine from brain tissue¹².

Yohimbine - another alkaloid present in Sarpagandha has *alpha* 2 receptor blocking (anti dopaminergic) action by which hypnotic action can be explained¹³.

Tranquilizing action of reserpine is also by inhibiting serotonin reuptake, enhancing GABA binding and by blocking catecholamine receptors. Because of blockage of catecholamine, it also acts as hypotensive agent¹⁴.

Notable Events:

- 2 patients reported sour belching, burning sensation of chest region and one patient had nasal blockage after 2 days of intake of *Sarpagandha Vati* which may be due to side effect of the drug.
- 3 patients experienced excessive drowsiness on taking 2 tablets of 500mg.
- Some researches (Lipsett MB *et.all*) conclude adverse effects if observed were mild and took as long as 8 months with continuous usage¹⁵. Depression, suicidal ideations etc were not found in any of the study subjects. This may be because the drug was given for short period and whole root was used as medicine but not the extract.
- No withdrawal/habit forming tendencies were reported.

SCOPE AND LIMITATIONS

- Needs further research with larger sample size for longer duration.
- Comparative long term clinical study can be done with benzodiazepines to know the efficacy as drug does not possess any dependency or much adverse effects.
- To fix the dosage further study can be done with different dosages.
- Further study can be done to know the *Nidrajanaka* effect of *Sarpagandha* on patients of different types of *Prakruti*.

CONCLUSION

The disease *Nidranasha* altogether affects *Tridoshas* and *Trigunas*(three mental faculties) leading to impaired quality of life and acts as predisposing factor for diseases. The selected herbal drug *Sarpagandha* is considerably safe, without dependency or much adverse effects. The results have shown significant improvement in signs and symptoms of *Nidranasha* with better life. After the administration of *Sarpagandha* tablet for one month 33.3% patient's severity came down to clinically not significant insomnia, 60% patients had mild insomnia and only 6.6% had moderate insomnia which is better than before treatment. Hence it can be concluded that *Sarpagandha Vati* can be effectively used in the management of *Nidranasha*.

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