

“A COMPARATIVE CLINICAL STUDY ON THE EFFICACY OF INDIGENOUS COMPOUND AND PLACEBO IN THE MANAGEMENT OF NIDRAJODAVARTA W.S.R TO SLEEP DEPRIVATION”

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ABSTRACT

Nidrajodavarta is the *Udavarta* (abnormal movement of Vata Dosha) caused due to imbalance in the quality and quantity of *Nidra* (Sleep) leading to *Jrumbha* (yawning), *Angamarda* (discomfort due to pains in the body), *Anga Shiro Akshi Jadya* (feel of heaviness in the body, head and eyes along with decreased performance and alertness in daily routine) and *Tandra* (fatigue). *Nidrajodavarta* can be closely correlated to Sleep Deprivation explained in the contemporary science due to similarities between both conditions. Sleep Deprivation is the condition of not having enough Sleep (Qualitative and Quantitative) or suffering from lack of Sleep. Since past few decades the incidence and prevalence rates of Sleep deprivation have been found increasing not only in India but also worldwide.

In this study an attempt is made to study the efficacy of an indigenous compound in effectively combating *Nidrajodavarta* in comparison to placebo. It is a single blind randomized comparative clinical study with pre and post evaluation where in 60 subjects of either sex diagnosed with *Nidrajodavarta* were randomly assigned into two groups, each comprising of 30 subjects. The subjects in Group 01 were administered with 12 grams of Indigenous compound once at night along with 150 ml of warm milk and the subjects in Group 02 were administered with 12 grams of Placebo once at night along with 150 ml of warm milk for 21 days with every 07 days review and review on every 07 days up to 21 days after the trial. The observed data was subjected to appropriate Statistical analysis. The statistical results showed significant effect in Group 1 than in Group 2.

Adverse reaction of drugs were not noted in any subject during and after study.

Keywords: *Nidrajodavarta*, Sleep Deprivation, *Nidra*, *Udavarta*, Indigenous compound, Placebo

INTRODUCTION

“Sleep is the golden chain that ties health and our bodies together”.

Man often in laudable arrogance accompanied by blinding ignorance, has always attempted to exceed the limits of his own nature. Modern civilization appears to be racing to eliminate sleep. In fact, sleep (*Nidra*) is one of the most significant human behaviour occupying roughly one third of human life and is considered as one among the three *Upasthambas*. A detailed discussion about *Nidra* and its related aspects are available in Ayurvedic literature.

Due to the hampered life style, sleep disturbance has been a major concern especially since few decades.

Worldwide 20% of people are sleep deprived due to lifestyle changes. Nearly 93% of Indians are sleep deprived due to changing life style and intrusion of modern gadgets. 72% of Indians are waking up one to three times per night and 87% of them have lack of sleep which is affecting the health. On the impact on productivity, more than 58% of Indians believe their work suffers due to lack of sleep. On an average 20.3% patients examined by doctors ask for sleeping pills, which is almost 1 out of 5 of the patients who are suffering from sleeping disorders.

The management of *Nidrajodavarta* emphasizes on handling both *Nidranasha* and *Udavarta* simultaneously. *Dravyas* possessing both *Vatahara* and *Nidrajanaka gunas* plays a vital role in this aspect. Thus, the present study is aimed to evaluate the efficacy of Indigenous compound (*Ashwagandha*, *Draksha* and *Sita*) possessing both *Vatahara* and *Nidrajanaka* properties and Placebo (starch powder). Indigenous compound comprises of *Choorna's* of *Ashwagandha*, *Draksha* and *Sita* in combination. They all have *Snigdha guna* in common. *Ashwagandha* possess *katu tikta kashaya rasas*, *laghu guna*, *ushna veerya* and *Katu vipaka*, *Draksha* possess *madhura rasa*, *guru guna*, *sheeta veerya* and *madhura vipaka* and *Sita* possess *madhura rasa*, *guru guna*, *sheeta veerya* and *madhura vipaka*. Effect of Placebo has focussed on the relationship of mind and body and has significant effect in Sleep disorders. *Ksheera* possessing *Madhura rasa*, *Madhura Vipaka*, *Snigdha guna*, *Jeevaniya*, *Dhatu Vardhaka*, *Ojaswi*, *Balya*, *Shrama Klama hara*, *Vata-Pitta-Shonita-Manasa Vikarahara*, *Udavartahara* and *Shoolahara* properties has been chosen as *Anupana*.

AIMS AND OBJECTIVES

- To analyse the efficacy of Indigenous Compound (*Ashwagandha*, *Draksha* and *Sita choorna's*) with *Ksheera* (milk) as *Anupana* in the management of *Nidrajodavarta*.
- To analyse the efficacy of Placebo (Starch powder) with *Ksheera* (milk) as *Anupana* in the management of *Nidrajodavarta*.
- To compare the therapeutic efficacy of Indigenous compound (*Ashwagandha*, *Draksha* and *Sita choorna's*) with Placebo (Starch powder) in the management of *Nidrajodavarta*.

MATERIALS AND METHODS

1. **Research design:** Single blind Randomized Comparative clinical study with pre and post study evaluation.
2. **Sampling Process**
 - a. **Sample size:** A total of 60 subjects diagnosed with *Nidrajodavarta* were selected and randomly categorized into two groups each comprising of 30 subjects.
 - b. **Sampling technique:** Random allocation was made in blocks in order to keep the sample size equal in both treatment groups. The block size is calculated as $2 \times n$ where 'n' is number of treatment groups.

Data Collection

- A. **Source:** All the classical and contemporary science information, recent advances through various information sources including internet, the published scientific

papers in reputed journals both in printed and online media about mentioned diseases and drugs in the present study were thoroughly reviewed and recorded.

B. Methods

a. Inclusion Criteria

- ❖ Subjects diagnosed with *Nidrajodavarta* based on classical signs and symptoms of either sex, aged 16 to 60 years were selected.
- ❖ Subjects with Signs and symptoms of Sleep deprivation were selected.

b. Exclusion Criteria

- ❖ Subjects with underlying Systemic diseases which interfere with the treatment were excluded.

c. Diagnostic Criteria

- ❖ Subjects with signs and symptoms of *Nidrajodavarta* as mentioned in Classical and Contemporary texts such as: *Jrumbha* (yawning), *Angamarda* (discomfort due to pains in the body), *Anga shiro akshi jadyam* (feel of heaviness in the body, head and eyes along with decreased performance and alertness in daily routine) *Tandra* (fatigue), Sleeplessness, Sleep quality, Total sleep time (in hours) and Wakefulness during sleep were monitored and graded accordingly.
- ❖ Pittsburgh Sleep Quality Index Scale was graded.

Laboratory Investigations

- In the subjects with the history of Diabetes Mellitus RBS, FBS and PPBS was noted before, during and after treatment.

C. Intervention

TABLE NO.03: Intervention

CRITERIA	Group 1	Group 2
Sample size	30	30
Medicine	<i>Ashwagandha</i> , <i>Draksha</i> and <i>Sita</i> <i>Choorna</i>	Placebo
<i>Anupana</i>	<i>Ksheera</i> -150ml(Luke warm)	<i>Ksheera</i> -150ml(Luke warm)
Dose	1 <i>Karsha</i> (12 grams =All 3 drugs in equal quantity, that is 4 grams each)	1 <i>Karsha</i>
Duration	21 days	21 days
Time of intake	<i>Nishi</i> (night)	<i>Nishi</i> (night)
Follow up	21 days	21 days

- Group 1- *Choorna*'s in combination -12 grams to be consumed by the subject's, along with the Milk 150ml (Warm) at night daily, after 1 hour of dinner and half an hour before going to bed.
- Group 2- Placebo (Starch powder) -12 grams to be consumed by the subject's, along with the Milk 150ml (Warm) at night daily, after 1 hour of dinner and half an hour before going to bed.

Pathyapathya

TABLE NO.04: Pathya

<p>PATHYA: Ahara</p> <ol style="list-style-type: none">1. Consuming Milk, Ghee daily.2. Consuming Rice, Wheat, Sugarcane and its derivatives, Food prepared using flour, Sugar, Sugar candy, Grapes, Meat of Cock and Goat.3. Avoiding caffeine, alcohol, nicotine before going to bed. <p>Vihara</p> <ol style="list-style-type: none">1. Going to bed and getting up at the same time every day.2. Listen to soothing stories, music at bedtime.3. Keeping bedroom in a relaxing and comfortable environment.4. Avoiding sleep during day time.5. Performing Abhyanga (Oil massage) daily <p>Manasika</p> <ol style="list-style-type: none">1. Cultivating positive thinking attitudes.2. Minimising excessive and over thinking, worry and anger.
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TABLE NO.05: Apathya

<p>APATHYA:</p> <p>Ahara: Excessive consumption of Barley, Green gram, Bengal gram, Kodo millet, dried meat, Meat of Pigeon</p> <p>Vihara:</p> <ol style="list-style-type: none">1. Suppression of Natural urges2. Forceful initiation of natural urges3. Night awakening4. Excessive physical exertion5. Sleeping in un comfort position, beddings <p>Manasika</p> <p>Excessive worry, grief, angry.</p>

D. Adverse effects

No adverse effects were noted during the study

E. Assessment of Outcome

Subjective Parameters:

- *Jrumbha* (yawning),
- *Angamarda* (discomfort due to pains in the body),
- *Anga shiro akshi jadyam* (feel of heaviness in the body, head and eyes along with decreased performance and alertness in daily routine),
- *Tandra* (fatigue)

Objective Parameters:

- Duration of sleep per day.
- Grades of Parameters of sleep deprivation.
- Pittsburgh Sleep Quality Index Scale.

Assessment Criteria

TABLE NO.06: Criteria of Assessment

	SUBJECTIVE PARAMETERS	CRITERIA	SCORES
1.	Yawning	No complaint	00
		Yawns 2 to 3 times which does not hamper daily routine	01
		Yawns frequently which does not hamper daily routine	02
		Yawns frequently which hampers daily routine	03
2.	Discomfort	No complaint	00
		Discomfort, which does not hampers daily routine	01
		Discomfort which slightly hampers daily routine	02
		Discomfort to such as extent which severely hampers daily routine	03
3.	Decreased performance and alertness in daily routine	No complaint	00
		Decreased performance and alertness ,can carry out daily routine	01
		Can carry out daily routine with difficulty, less alertness	02
		Cannot carry out any daily routine, Very less alertness	03
4.	Fatigue	No complaint	00
		Fatigue ,can perform daily routine	01
		Fatigue, can perform daily routine with difficulty	02
		Fatigue due to which daily routine cannot be performed	03
5.	Sleeplessness	No complaint	00
		Disturbed Sleep during night.	01
		Sleep after 2 to 3 hours of bedtime.	02
		Doesn't sleep at all.	03
6.	Sleep quality	Enjoyable sleep	00
		Anxious or agitated before and during sleep	01
		Feeling un fresh and unrest after sleep	02
		Sleep experience negative and not enjoyable	03

	OBJECTIVE PARAMETERS	CRITERIA	SCORES
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1	Total sleep time (in hours)	Adequate sleep (6-8 hours)	00
		Inadequate sleep(6-4 hours)	01
		Sleep less than 4 hours	02
		No sleep at night	03
2	Wakefulness during sleep	No wakefulness	00
		One or two times wakefulness	01
		3 to 4 times wakefulness	02
		More than 4 times wakefulness	03

PITTSBURGH SLEEP QUALITY INDEX

- a. Usual Bed time -.....
- b. Number of minutes or hours taken to fall asleep-.....
- c. Usual getting up time-.....
- d. Hours of sleep per night-.....

Hours of sleep during day time-.....

TABLE NO.07: Pittsburgh Sleep Quality Index Assessment

NO	COMPLAINTS	GRADE
01.	Cannot get sleep soon after goes to bed	
02.	Cannot get sleep within 30 minutes or more	
03.	Wake up in the middle of the night or early morning	
04.	Wakes up too early in the morning	
05.	Trouble staying awake while driving, eating meals or engaging in social activity	
06.	Facing problem to keep up enough enthusiasm to get things done	
07.	Any restlessness noticed during sleep	

00: Not at all bothered:

01: Slightly bothered

02: Moderately bothered

03: Severely bothered

F. Statistical Analysis

1. Based on the information gathered by means of observation before and after treatment, various parameters were subjected to Statistical analysis.
2. The Mean, Standard Deviation, Standard Error, 95% Confidence interval of mean, p value and t value were calculated.
3. Student's t test was carried out and the obtained results were interpreted.

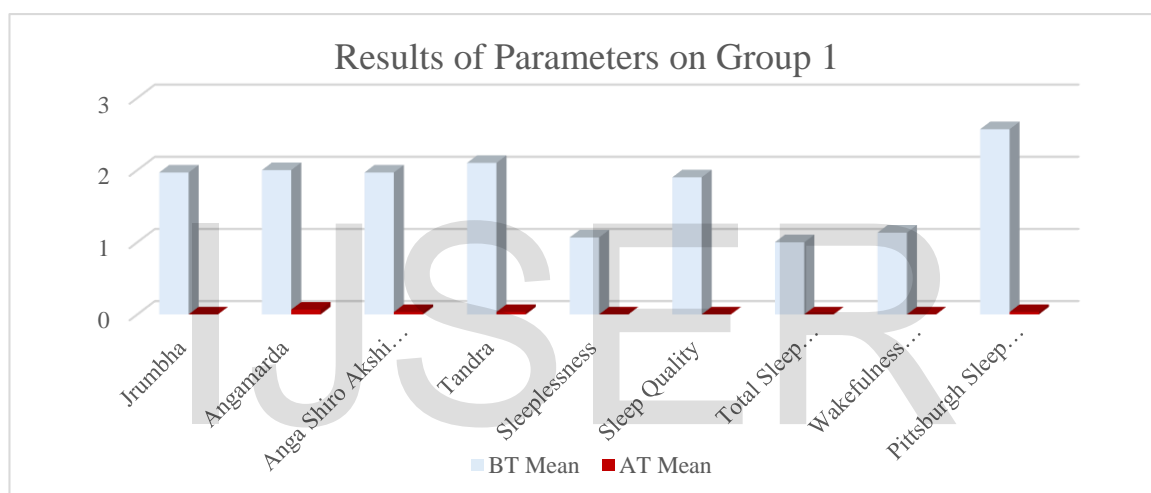
G. Total Assessment of the therapy

TABLE NO.08: Total assessment of therapy

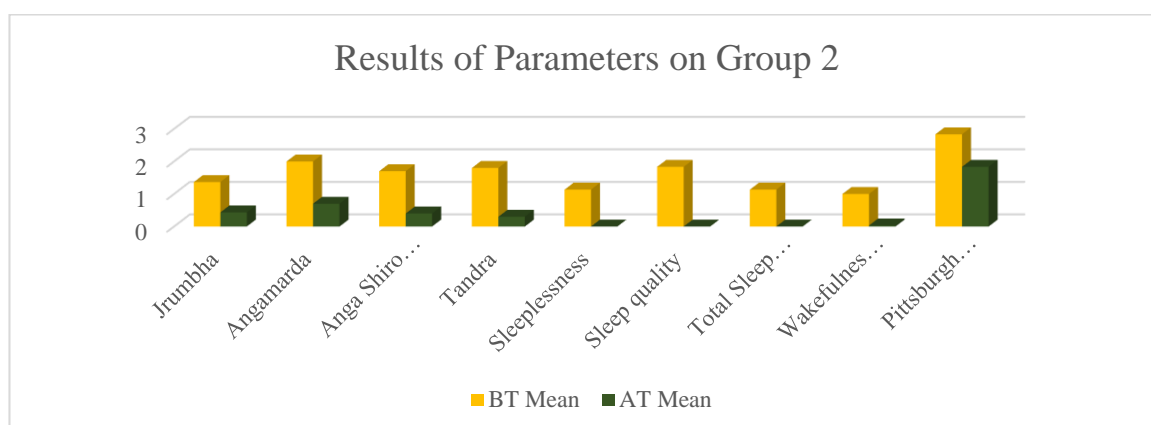
Worsened	
Unchanged	0 % relief
Slightly Improved	1-30 % relief
Moderately Improved	30-60% relief
Markedly Improved	60-99% relief
Completely Cured	100% relief

RESULTS

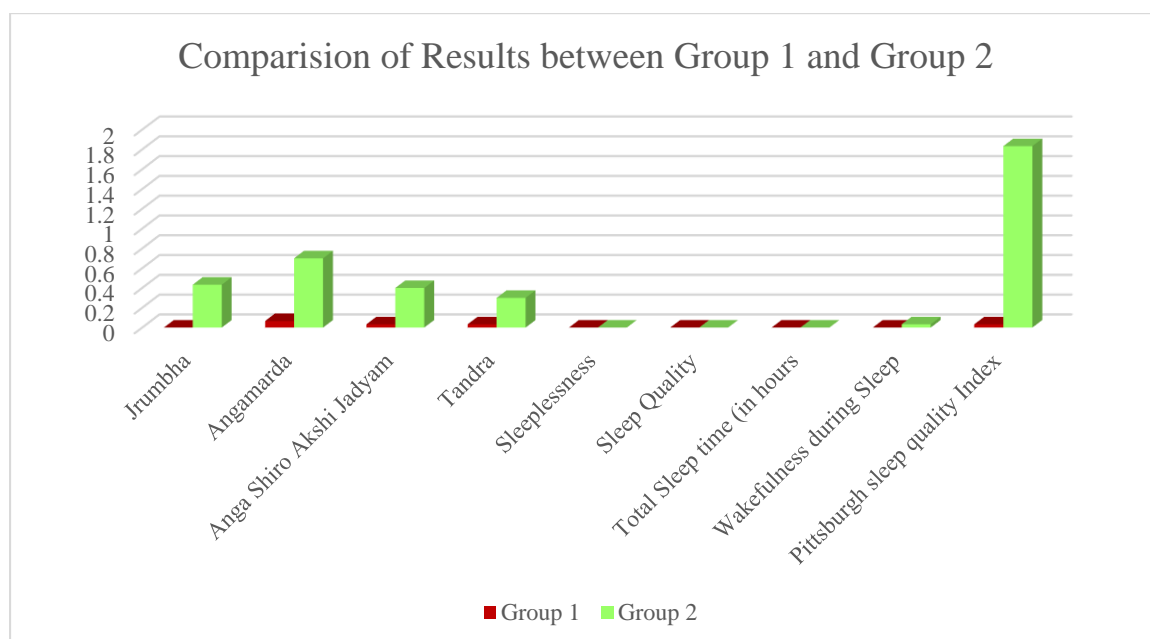
GRAPH NO.01: Results of parameters on Group 1



GRAPH NO.02: Results of parameters on Group 2



GRAPH NO.03: Comparison of results between Group 1 and Group 2



Interpretation

Since Unpaired t test is statistically significant at 0.001%, 0.01% and 0.05 % (that is, $p < 0.0001$, $p < 0.0004$ and $p < 0.005$) in criteria's of *Jrumbha*, *Angamarda*, *Anga Shiro Akshi Jadyam*, *Tandra* and Pittsburgh Sleep Quality Index. Thus, Group 1 is significantly effective than Group 2.

DISCUSSION

“A good laugh and a long sleep are the two best cures for everything”

Nidrajodavarta has become a significant Public Health Crisis in the present world as human being often in the laudable arrogance accompanied by blinding ignorance, has always attempted to exceed the limits of his own nature appearing to be racing to eliminate sleep. Due to the hampered life style, sleep disturbance has been a major concern especially since few decades.

The signs and symptoms of *Nidrajodavarta* along with their classical definitions are interpreted as follows:

1. जृम्भा (Yawning)

Definition: The process in which prolonged inhalation of the air through a widely open mouth, subsequent exhalation with the contraction of limbs and tearful eyes is termed as *Jrumbha*. (Su. Sha 04/50) (Peetvaikam Anilochwasam udwestan vivrutananaha. Yanmunchati sa netrasram sa Jrumbha iti sanjnitaha)

Interpretation: Yawning in case of *Nidrajodavarta* can be interpreted as, diminished quality and quantity of sleep alters brain activity and causes increase in cortical temperature, to normalize this yawning process occurs.

2. अङ्गमर्द (Discomfort due to pains in the body)

Definition: Pain or discomfort experienced by an individual is termed as *Angamarda*. (A.Hru.Su 04/12) (Angamardaha angabhangaha)

Interpretation: The disturbed sleep patterns stimulates specialized nerve endings (nociceptors) which leads to hyper excitability of spinal sensory neurons (central sensitization) which causes discomfort or pain.

3. अङ्गशिरोक्षि जाड्यं (Feel of heaviness in the body, head and eyes along with decreased performance and alertness in daily routine)

Definition: Sluggish, decreased or inactive state is termed as *Jadyam*. (Dalhana on su.utt.55/17, A .Hru Su 7/64, Su. Sha 4/55) (Jadyatam apatyam gauravamiti tatparyaha. Jadyatam Jnana bhramshaha. Ardracharmavanaddham hi yo gatram abhimanyate, tatha guru shiroathyartham gauravam tadvinirdishet)

Interpretation: Sleep deprivation impacts effects on frontal and parietal lobes of brain by reducing their activity which in turn causes decrease performance and alertness in daily activities.

4. तन्द्रा (Fatigue)

Definition: The combined state of sense organs unable to perceive their senses properly, heaviness, excessive yawning and sense of fatigue without any physical strain and sensation of sleep is termed as *Tandra*. (Su. Sha 04/49) (Indriyartheshwa sampraptihi gauravam jrumbhanam klamaha. Nidrantasyeva yasyeha tasya tandram vinirdishet)

Interpretation: Due to hampered sleep the c-Fos immunopositive cells gets stimulated in dentate gyrus of ventral hippocampus, cingulate cortex area 2, Ventral part of lateral septum nucleus, Para ventricular hypothalamic nucleus and induces fatigue.

The **probable mode of action** of Indigenous compound and Placebo are as follows:

- *Ashwagandha* with *snigdha guna*, *ushna veerya* and *Nidranashahara properties*, possess the chemical constituents Saponins, Trethylene glycol and Alkanoids which induces Sleep and also has anti-stress, anti-inflammatory, anti-oxidant and neuro protective properties.
- *Draksha* with *madhura rasa*, *guru guna*, and *sheeta veerya*, *madhura vipaka* and *Nidranashahara*, possess the chemical constituents Catechin, Epicatechin, Betasetosterol, Ergosterol which induces Sleep.
- *Sita* possess *madhura rasa*, *guru guna*, *sheeta veerya*, and *madhura vipaka* and it induces sleep by activating the neurons responsible for sleep onset.
- *Ksheera* possessing *Madhura rasa*, *Madhura Vipaka*, *Snigdha guna*, *Jeevaniya*, *Dhatu Vardhaka*, *Ojaswi*, *Balya*, *Shrama Klama hara*, *Vata-Pitta-Shonita-Manasa Vikarahara*, *Udavartahara* , *Shoolahara* as *Anupana*.
- Placebo effect has focussed on the relationship of mind and body and has significant effect in Sleep disorders. One of the most common theories is that the placebo effect is due to a person's expectations. If a person expects a pill to do something, then it's possible that the body's own chemistry can cause effects similar to what a medication might have caused.

CONCLUSION

- *Nidrajodavarta* is mainly caused due to *Nidranashakara* and *Udavartakara* *Nidana Sevana* leading to predominantly *Vata Prakopa* which affects *Hrudaya* and causes impairment of *Tamo guna*.

- The present study was conducted on 60 subjects randomly selected and grouped into two equal group of 30 each. *Choorna*'s were given along with Milk for 21 days with a follow up during and after the study.
- Based on the t value and statistical results, the Group 1 is significantly effective than Group 2 in the management of *Nidrajodavarta*.
- Thus, the subjects treated with Indigenous compound showed comparatively significant effect than those who were treated with Placebo in case of *Nidrajodavarta*.
- The trial drugs Indigenous compound and Placebo were proved to be safe and effective Oral formulations for the management of *Nidrajodavarta*.

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