



A SINGLE-ARM CLINICAL TRIAL TO EVALUATE THE EFFECTIVENESS OF INDIVIDUALIZED HOMOEOPATHIC MEDICINES IN MANAGEMENT OF INSOMNIA IN DEPRESSIVE DISORDERS – STUDY PROTOCOL

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ABSTRACT

OBJECTIVE:

Insomnia is a condition of unsatisfactory quantity and/or quality of sleep, persisting for a considerable period of time. Among insomniacs, difficulty falling asleep is the most common complaint, followed by difficulty staying asleep and early final awakening. It generally occurs during times of increased life stress and is more common in women, older individuals, and socioeconomically disadvantaged individuals. Homoeopathy could play a greater role for the effective treatment of symptoms of insomnia in depressive disorder, with the fact that it is a holistic treatment approach and has a durable impact. This study is aimed to explore the possibilities of Individualized Homoeopathic medicine in the management of Insomnia in depressive disorders.

MATERIALS AND METHODS:

The study design selected was Interventional Study-Before & After treatment without a control group. The patients who present with symptoms of insomnia in depressive disorders at Outpatient departments, IPDs, peripheral OPDs and medical camps of National Homoeopathy Research Institute in Mental Health Kottayam shall be screened with verbal screening form based on DSM-5 diagnostic criteria. The cases fulfilling inclusion and exclusion criteria's will be enrolled in the study after approval of Psychiatrist and patients consent. The trial sample size is calculated as 33 considering 10% dropouts. The period of treatment and follow-up shall be for 1 ½ years which includes 6 months enrollment and 1 year follow up. Cases will be assessed at baseline with the Athens Insomnia Scale to measure and diagnose insomnia and Insomnia severity index to get the severity of the condition. Bergen Insomnia Scale will be used to assess the sleep pattern. Each case will be reviewed at every 4 weeks interval with the Bergen Insomnia Scale. The severity of symptoms will be assessed using Insomnia Severity Index at baseline & end of the treatment. The Assessment of quality of life will be done at baseline, 6 months and 12 months with WHOQOL BREF. The outcome of treatment will be assessed according to Bergen Insomnia Scale, follow-up charts and WHOQOL scale before and after administering individualized Homoeopathic medicine.

DISCUSSION:

There is no doubt that insomnia is a widespread condition associated with impaired daytime functioning, reduced quality of life, increased risk of morbidity, as well as substantial societal costs. Hence Homeopathy the best practiced medicine in the world, has its proven potential in treatment of the symptoms of insomnia in depressive patients. The Homeopathic treatments should be tailored to each patient's unique characteristics to attain the desirable effects.

KEY WORDS:

Insomnia in depressive disorders, Single arm clinical trial, Interventional study, Homoeopathy

INTRODUCTION:

BACKGROUND AND RATIONALE:

Insomnia is a condition of unsatisfactory quantity and/or quality of sleep, persisting for a considerable period of time¹. Among insomniacs, difficulty falling asleep is the most common complaint, followed by difficulty staying asleep and early final awakening². It generally occurs during times of increased life stress and is more common in women, older individuals, and socioeconomically disadvantaged individuals. In ICD 10, insomnia is coded as F51. Nearly one-fifth of the apparently healthy, productive age group of Indian population, the reported prevalence of insomnia is 9% in the general population. About 30% suffer from occasional insomnia³.

Nearly 30% to 40% of adults in United States report symptoms of insomnia at some point in a given year⁴. In the United States, short-term insomnia is estimated to be 9.5% prevalent, but about one in five cases progress to chronic insomnia, which lasts for years⁵. According to the data from National Health Interview Survey, the prevalence of insomnia or trouble sleeping increased by 8% over a decade, from 17.5% (37.5 million adults) in 2002 to 19.2% (46.2 million adults) in 2012⁶.

Sleep disturbances are most frequently seen in patients with episodes of mood disorders. In particular, patients with depression often complain of difficulty getting to sleep, frequent awakenings during the night, early morning awakening, or non restorative sleep⁷. Epidemiological studies show that patients with mood disorders exhibit higher rates of sleep disturbance than the general population, and sleep disturbance can continue even during periods of remission. On the other hand, patients with insomnia are up to 10 times more likely to have depression than normal sleepers, and individuals with persistent insomnia have a significantly higher risk of developing new-onset depression than those who have no sleep complaints. A pilot study conducted by Chen et al, on Efficacy on sleep quality in working women mentioned that sleep disturbance can impact significantly upon employee behavior, mental alertness, physical appearance, daytime physiology, emotional condition, and health⁸.

Treatments of insomnia disorder with empirical support are hypnotic medications and cognitive behavioral therapy for insomnia (CBTI). CBTI is an effective non-pharmacological treatment for primary insomnia and insomnia co morbid with medical or psychiatric conditions. Comparing CBTI with sleep medications, CBTI has comparable efficacy and long-term benefits and also help the individual to control or eliminate negative thoughts and actions that keep awake and is generally recommended as the first line of treatment⁹.

Some of the commonly prescribed homoeopathic medicines for sleeplessness are Coffea Cruda, Nux-Vomica, Passiflora Incarnata, Kali Phosphoricum, Phosphorus, Silicea, Sulphur, Ignatia, Staphysagria etc. G Ram Mohan conducted a prospective, non-comparative, open-label observational study on evaluation of Homoeopathic treatment in the approach of depressive disorders and found that remedies such as Ignatia, Nat Mur, Nux Vomica, Staphysagria, Arsenicum Album, and Lycopodium were found to have a positive role¹⁰.

Katy L Cooper et al states for Homoeopathy in insomnia, "Homoeopaths often treat insomnia. However, there are currently lacks of high-quality studies assessing the effectiveness of in treating this condition. Based on the limited evidence available, Homeopathic medicines do not appear to be statistically significant for treating insomnia. Existing RCTs were of poor quality and likely underpowered. Through well-conducted studies using Homoeopathic medicines and treatment by a Homoeopath, the clinical and cost-effectiveness of Homoeopathy must be evaluated."¹¹

A double-blind, randomized, placebo-controlled clinical trial on efficacy of individualized Homoeopathic treatment of insomnia by Michael James et al, concluded that, "there was statistically significant difference measured in sleep efficiency, total sleep time, time in bed, and ISI score in favor of Homeopathy over placebo with moderate to large effect sizes. For the rest of the outcomes, group differences were not significant (i.e. latency to fall asleep, minutes awake in middle of night and minutes awake too early). Individualized Homeopathy seemed to produce significantly better effect than placebo"¹².

This study is aimed to explore the possibilities of Individualized Homoeopathy in the management of Insomnia in depressive disorders.

MATERIALS AND METHODS:

It is an Interventional Study-Before & after treatment without a control group and planned to conduct at OPD and other peripheral centers of National Homoeopathy Research Institute in Mental Health, Kottayam, Kerala, India. The sample size has been calculated as 33 considering 10% dropouts. This clinical trial adheres to the latest revision of the Helsinki Declaration on human experimentation and Good Clinical Practices of India. The protocol has been drafted according to the guidelines provided by the Institutional Review Board. The finalized protocol has been subjected to Institutional Ethical Committee approval. Further review of the protocol and final approval from the university has been obtained. The CTRI registration number is CTRI/2022/04/041635.

METHODOLOGY:

The patients who present with symptoms of insomnia in depressive disorders at Outpatient departments, IPDs, peripheral OPDs and medical camps of National Homoeopathy Research Institute in Mental Health Kottayam shall be screened with DSM-5 diagnostic criteria. After screening, the cases fulfilling inclusion criteria will be enrolled in the study, after approval from the Psychiatrist. After explaining the details of the study, the patient will receive a copy of the patient information sheet. Patients will be required to sign the informed consent form. Cases will be taken in the standard Homoeopathic case record format prepared for the study.

Age group between fifteen to sixty years of both sexes fulfilling DSM-5 criteria for insomnia with depressive disorders. Patients with mild to moderate depressive disorders taking allopathic medications for long period will be enrolled after a washout period of minimum of two weeks.

In the case record format prepared for the study, detailed case taking will be done. In analyzing and evaluating the complete case, the individual totality is obtained, and repertorization is done with Synthesis Repertory using the RADAROPUS software. Final selection of remedy will be done by consulting with Homoeopathic Materia Medica. The indicated medicine will be administered in 30C potency. Will wait and observe if there is any progress in the patient. If improvement stops at a period, the next higher potency will be given. If any acute complaints arise, acute totality will be taken and the appropriate remedy will be administered. During the Homoeopathic management part, strict operative procedures will be followed based on Homoeopathic Principles. Each month, Homoeopathic assessments will be conducted using the Homoeopathic intervention format prepared for the study.

Every month, the enrolled patients will be closely monitored by a follow-up chart. At the time of enrollment, the patient will receive a follow-up calendar with a one-year date of visit. Details of follow-up dates, times, and other measures are included in the follow-up chart. A social worker will make regular phone calls and other available communications via mail, telephonic calls to ensure a high degree of compliance.

OUTCOME MEASURES:

The outcome of treatment will be assessed according to Bergen Insomnia Scale, follow-up charts and WHOQOL scale before and after administering individualized Homoeopathic medicine. Each case will be reviewed at every 4 weeks interval with the Bergen Insomnia Scale and severity of symptoms of insomnia assessment will be done with Insomnia Severity Index at baseline & end of the treatment. The Assessment of quality of life will be done at baseline, 6 months and 12 months with WHOQOL BREF.

Primary outcome:

- Improvement of symptoms in Bergen Insomnia Scale and Insomnia Severity Index Scale.

Secondary outcome:

- Analyze the improvement in the overall sleep quality through initiation and continuation of sleep patterns in patients with depressive disorders.
- Find out the changes in the quality of life of patients with respect to the Homoeopathic intervention.

DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS FIFTH EDITION (DSM-5) CRITERIA

Insomnia Disorder

A. A predominant complaint of poor sleep quantity or quality, associated with one or more of the following symptoms:

1. Inability to get to sleep.
2. Frequent waking or trouble getting back to sleep after being awakened, characterized by difficulty maintaining sleep.
3. Awakening early in the morning with difficulty returning to sleep.

B. Disturbances in sleep cause clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning.

C. At least three nights per week, the sleep problem occurs.

D. Sleep difficulty has been present for at least 3 months.

E. Sleep difficulty persists despite adequate sleep opportunities.

F. The insomnia is not better explained by and does not occur exclusively during the course of another sleep-wake disorder (e.g., narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep-wake disorder, a parasomnia).

G. Sleep deprivation is not due to the physiological effects of a substance (e.g., a drug of abuse, a medication).

H. Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia.

Major Depressive Disorder

A. At least five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous behavior.

1. Feeling depressed most of the day, nearly every day, according to either objective or subjective measures (e.g., feels sad, empty, hopeless, appears tearful)

2. A marked decrease in interest or pleasure in almost all activities most of the day, nearly every day (as indicated by either subjective account or observation).

3. Without dieting or gaining weight, significant weight loss occurs (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.

4. Insomnia or hypersomnia mostly for every day.

5. Psychomotor agitation or retardation almost every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

6. Fatigue or loss of energy almost every day.

7. A feeling of worthlessness or excessive or inappropriate guilt nearly every day.

8. Difficulty to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).

9. Repeated thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. A significant impairment in social, occupational, or other important aspects of functioning is caused by the symptoms.

C. It is not attributable to the physiological effects of a substance or to another medical condition.

D. The major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusion disorder, or any other specific or unspecified schizophrenia spectrum or other psychotic disorders.

E. No manic or hypomanic episode has ever occurred.

Severity is based on the number of criterion symptoms, severity of criterion symptoms, and the degree of functional disability.

Mild: Presence of few symptoms need for diagnosis and with manageable distress along with minimal social impairment or occupational functioning.

Moderate: The severity, intensity and number of symptoms, with functional impairment falls between those specified for "mild" and "severe."

Severe: Presence of excessive number of symptoms, the intensity of the symptoms is distressing and unmanageable, and marked interference in social and occupational functioning.

CRITERIA FOR BASELINE AND FOLLOW – UP ASSESSMENT:

Cases will be assessed at baseline with the Athens insomnia scale to measure and diagnose insomnia and Insomnia severity index to get the severity of the condition. Each case will be reviewed at every 4 weeks interval with the Bergen insomnia scale and severity of symptoms of insomnia assessment will be done with Insomnia severity index at baseline & end of the treatment. The Assessment of quality of life will be done at baseline, 6 months and 12 months with WHOQOL BREF. Using the Homoeopathic intervention format prepared for the study, Homoeopathic assessments will be done every month.

DATA COLLECTION:

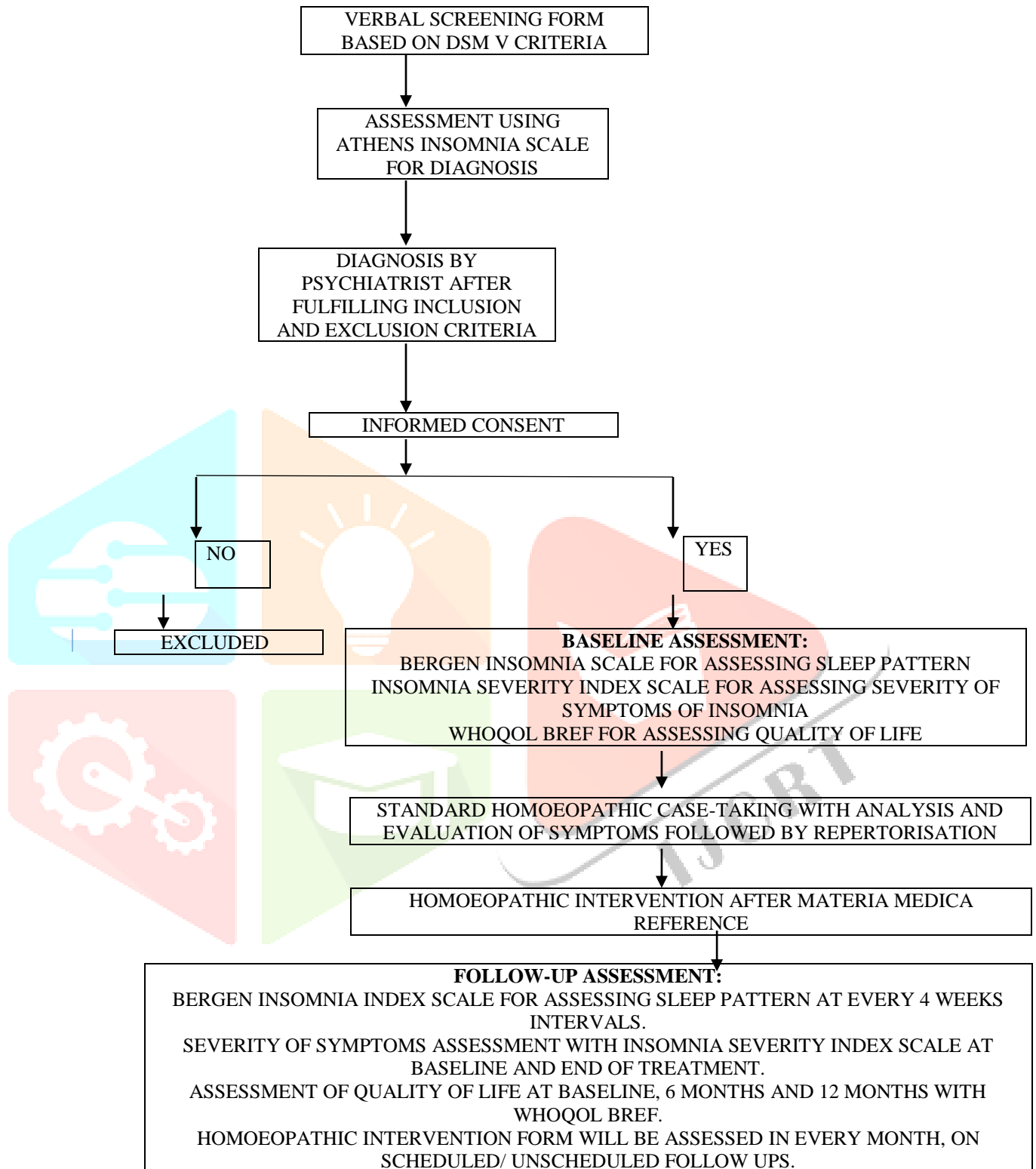
The data capture shall be done using a standard case recording format and pre-designed excel sheet. The diagnostic information are gathered through Athens Insomnia Scale and other basic screening for Insomnia will be obtained through Bergens Insomnia Scale and Insomnia Severity Index scale for assessing severity of symptoms of insomnia. The Assessment of quality of life will be done with WHOQOL BREF. The outcome of treatment will be assessed according to Bergen Insomnia Scale, follow-up charts and WHOQOL scale.

SAMPLE SIZE:

The objective of this study is to find out the Effectiveness of Individualized Homoeopathic medicines in the management of Insomnia In Depressive Disorders. The sample size of 30 was selected and considering 10 % drop out, the sample size has fixed to 33.



The Flowchart of complete study (Figure 1):



STATISTICAL ANALYSIS:

Data will be analyzed using STATCRAFT version 2.0.3. Descriptive analysis will be done for demographic variables. The normality of the data will be checked. The changes in Bergen Insomnia Scale and WHO QOL BREF total score at baseline and end will be compared using paired t-test based on normality of data.

GANTT CHART:

Time	Study Period				Close out
	Enrolment	Post allocation in month			
		6	12	Every month	
Eligibility screening	+	-	-	-	-
Informed consent	+	-	-	-	-
Interventions Homoeopathy	+	+	+	+	+
Assessments Athens insomnia scale	+	-	-	-	-
Bergens insomnia scale	+	+	+	+	+
Insomnia severity index	+	-	+	-	+
WHOQOL BREF	+	+	+	-	+

DISCUSSION AND CONCLUSION:

Homoeopathy one among the alternative medicines, relies on subjective patient reports for diagnosis and treatment. There are numerous pharmacological and non-pharmacological therapeutic options available for treatment of insomnia. But, these treatments are not always completely effective and some have marked adverse effects. Since homoeopathy has minimal or no adverse effects, people preferences for this mode of treatment has been considerably increased.

There are few limitations in this study. In this trial the study of Insomnia is conducted only in mild and moderate depressive disorder. No comparison group is included in this study. The limited evidence available does not demonstrate a statistically significant effect of Homoeopathic medicines for insomnia treatment.¹¹ Well-conducted studies of Homoeopathic medicines and treatment by a Homoeopath are required to examine the clinical and cost effectiveness of Homoeopathy for insomnia. While insomnia was originally conceived as a symptom of depression, it is now more commonly categorized as an independent risk factor¹³. This study is aimed to explore the possibilities of Individualized Homoeopathy in the management of Insomnia in depressive disorders. Moreover this study will give a strong basement and provides a new idea to understand the effectiveness of homoeopathic medicine through symptom based approach in a particular diagnosis. It also enhances new research methods in future, considering symptom based psychopathological understanding during prescription.

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