



An interventional trial to evaluate efficacy of *Nutool* Therapy in control of Primary insomnia among elderly using Structured Insomnia schedule

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Abstract

Insomnia is a unique and complex problem in geriatric population. As many as half of the elderly population between 60 to 79 years of age complain of disturbed sleep, which includes increased sleep latency, decreased quality of sleep, awaking symptoms, excessive daytime sleepiness, mental stress/ depression which may result in disturbed intellect, impaired cognition, confusion, psychomotor retardation the whole syndrome of complaints can compromise patient's quality of life and create social and economic burden for caregiver. Considering the wide spread prevalence of insomnia in geriatrics, compounded with lack of wholesome drugs in the treatment, an interventional study was carried out with the objectives to evaluate the efficacy and safety of Nutool therapy in control of geriatric insomnia. A total of 30 elderly primary insomniacs, diagnosed for primary insomnia by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, were randomly assigned to test and control groups, comprising 15 patients in each group, respectively. In the test group, Nutool was performed with Roghan e Banafsha (500ml) and Roghan e Gul (500ml), both mixed in equal ratio while Nutool was done with liquid paraffin in control group. The therapy was scheduled on alternate days for one month. Various insomnia related parameters was evaluated by Structured Insomnia schedule. Statistical analysis was done using student t-test (paired) for comparison in intra group and t-test (unpaired) for inter-group comparison. Nutool therapy showed statistically significant improvement in all the parameters of Structured Insomnia schedule, when pre and post interventional values of the parameters were assessed in intra as well as inter group comparisons. This intervention proves the efficacy and safety of Nutool therapy in control of insomnia among elderly.

Key words: Insomnia, geriatrics, Nutool therapy, structured insomnia schedule.

Introduction

Insomnia is a common complaint throughout the world, and is characterized by difficulty in initiating or maintaining sleep or non-restorative sleep, associated with significant morbidity¹. Insomnia in the geriatric patients is commonest among sleep complaints reported by population more than 60 years of age. It is consistently associated with significant reduction in the quality of life, higher risk of depression, and increased use of health care services². An epidemiological study reports that individuals with insomnia have a 4.5 folds higher probability of presenting with depression compared with those with normal sleep pattern. In addition, primary insomniacs have an elevated risk of manifesting depression within 3.5 years after onset, even in absence of psychological disturbances³.

Primary insomnia is a specific disorder, defined in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) as a condition of at least 1 month's duration, not caused by a medical or psychiatric disorder. In addition, a

symptom of insomnia (disturbed sleep initiation or sleep maintenance, or early morning awaking) must present and be associated with complaints of daytime dysfunction.

Pharmacological treatment is the most practical approach to insomnia management; however, adverse events most commonly perceived by the insomniacs include alteration in cognitive function, memory and psychomotor activity, with negative effect on routine daily activities, the so-called hangover is a common manifestation. Moreover, rebound insomnia can occur after abrupt withdrawal of hypnotic therapy. National Institute of Health and Clinical Excellence recommends that doctor should consider using non-drug therapy before starting hypnotic drugs⁴, as side effects and risks associated with long-term use of the drugs are often major reasons for abetting the patients to discontinue their use despite their perception of continued efficacy³. With these limitations in pharmacotherapy there is a growing interest in non-pharmacological interventions for older adults⁵. Considering this unconvincing scenario regarding the use of drugs and their

side effects, researchers are turning to the nature and the traditional pathies. Unani medicine axiomatically comes to the fore as *Seher* (Insomnia) has successfully been treated since ancient times without considerable obnoxious side effects on the body.

Material and Methods

The study was designed as Single blind, randomized, placebo-controlled, concurrent parallel group interventional trial, conducted at National Institute of Unani Medicine Hospital, Bangalore. Ethical clearance was obtained from the Institutional Ethical Committee, NIUM, Bangalore. The study spanned from March 2009 to February 2010. Thirty eligible cases of either sex, above 60 years of age, with primary insomnia and ISI higher than 7, were selected and randomly assigned to Group A (Control Group) and Group B (Test Group), each comprising 15 patients. Group A had been administered liquid paraffin, a placebo drug, under identical conditions as that for test group. Group B was treated with *Roghan Banafshan* and *Roghan gul*, mixed in equal quantity of 500 ml each. Efficacy of the drug was evaluated with a Score of structured insomnia schedule. *Nutool* therapy was performed on every alternate day for one month divided in fifteen sittings. Pre and post treatment values of the parameter were assessed statistically.

Patients were advised to observe abstinence from all sorts of hypnotic drugs or measures one week prior to starting of the therapy, and no concomitant treatment for insomnia was allowed during the treatment.

Patients were selected on the basis of DSM-IV-TR- Diagnostic criteria for primary insomnia which includes the predominant complaint of difficulty in initiating or maintaining sleep, or non restorative sleep, for at least one month and this sleep disturbance is associated with day time fatigue and may cause clinically significant distress or impairment in social, occupational or other important area of functioning.

Insomniacs associated with secondary medical problems such as Acute fevers or painful conditions, known cases of chronic obstructive pulmonary disease, patients with Obstructive sleep apnea syndrome, Central sleep apnea syndrome, known cases of Restless leg syndrome, Periodic Limb Movement Disorders, Idiopathic Insomnias or lifelong insomnia, known cases of narcolepsy, sleep disorders associated with diagnosed mental, neurologic and other medical disorders, history of glucocorticoids consumption, known cases of Parkinson, chorea, epilepsy, dementia, Huntington disease, poor mental health, alcohol or drug abuse with in past six months, patients who do not agree to give consent and adhere to protocol were excluded from the study.

Criteria for Selection of test drugs and placebo: Ancient Unani physicians used *Nutool* as an efficient regimen in the treatment of insomnia, as *Nutool* produces *Tarteeb* (moistness) in the organ⁶.

The test drugs, *Roghan e banafshan* (oil of *Viola odorata*) and *Roghan e gul* (oil of *Rosa centifolia*), used for the *Nutool* possess properties like *Munnawim*, *Murattib* and *Muqavvi* etc.

The purpose of test drug in one group and liquid paraffin in other group is to assess the efficacy of procedure of *Nutool* therapy, otherwise *Roghan banafsha*, being sedative, may relieve insomnia and with liquid paraffin, it would not have relieved the symptom and their outcome. This is because the present study is the first in evaluating the efficacy of *Nutool* therapy; no convincing data are available to suggest the procedure of *Nutool* therapy as an effective management in insomnia.

Nutool therapy: oil or other liquids such as *Joshanda* (decoction of herbs)⁷, *Khaisanda*^{6,7}, milk or warm water⁶, plain water, cold water is poured continuously in a rhythmic flow onto the forehead or other specific organ^{6,8} from a specific height, for a specific period, allowing oil to run through the scalp and into the hair.

Nutool therapy is one of the important components of various procedures of systematic purification techniques of *Ilaj bit Tadbeer*. Ancient physicians had tried it with good results due to its *Murattib*, *Munavvim* (which induces sleep), *Muqavvi* (which strengthens the organ) and *Khuwab awar* (which produces sleep) properties.

Administration of oil: Before starting the therapy, clean gauze was tied just behind the eye brows to avoid spilling of oil over the face. Eyes were protected by keeping a cotton swab soaked in plain water over the closed eye lids. Oil was sterilized and cooled to luke warm to start the therapy. The oil was continuously poured in a rhythmic stream from a distance of half feet⁶ over the fore head of a patient lying in supine position. The oil flowing down the head was collected in a container placed beneath the outlet of the *Nutool* table. The collected oil was reused to maintain an uninterrupted flow of oil over head for duration of 30 minutes.

Efficacy assessment: The assessment of the efficacy in the test and control groups was based on; Structured Insomnia schedule (SIS).

Criteria for construction of Structured Insomnia Schedule (SIS): This schedule instrument is based on the criteria proposed by “Medical Outcome Trust Scientific Advisory Committee” for the development of instruments for assessing severity or ailment and especially to measure sleep-related domains for the research purpose which measure all the required entities to evaluate primary insomnia in elderly, which covers the following six major domains.

Six major domain of structured insomnia schedule (SIS): Sleep latency, Quality of sleep, Awakening symptoms, Day time somnolence, Mental stress and depression, Suicidal tendencies:

Scoring criteria for the evaluation of major outcome domains: Sleep latency, Quality of sleep, Awakening symptoms and Suicidal tendencies equally based on three component or questions, however Day time somnolence and Mental stress has four components as four questions that evaluate the said entity (domains). Each component was evaluated separately as scoring ranged from 0(normal or no difficulty) to 3(severe difficulty).After scoring each component are summed up to evaluate the severity of each major outcome domain separately.

Sleep latency= ++=
 Quality of sleep = +.....+.....=
 Awakening symptom =.... +.....+.... =
 Day time somnolence =...+.... +.... +...=
 Mental stress = +.....+.....+.....=
 Suicidal tendencies = ...+.... +.....=

If the summed total of each major outcome domain of Sleep latency, Quality of sleep, Awakening symptoms and suicidal tendencies falls as 0 then it is considered normal or no difficulty, as the normal values are incorporated in it as these domain contain three component, if the total score falls in between 1 to 3 then it is considered as mild problem, and from 4 to 6 considered as moderate problem and if scores fall in between 7 to 9 then it is considered as severe problem. For Day time somnolence and Mental stress, as these domain contain four component, if total scores is equal to 0 then it is normal, and in between 1 to 4 it is considered as mild problem and in between 5 to 8 then considered as moderate problem and in between 9 to 12 then severe problem.

Results and Discussion

Statistical analysis: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance, unpaired Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups(Inter group) analysis) and paired Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group.

In some places like sleep latency where the parameters can be compared with other relevant studies, effect size had been compared as this trail had also been studied in a manner of psychological/behavioral studies, multimodal therapies like CBT(cognitive and behavioral studies), where studies had been evaluated the pre and post changes and thus p values were observed within group (intra group comparison as opposed to between groups) , for this if difference in effect size was more than 1.20(d>1.20) it was considered as very large effect compared if we compare p value of two groups we can also evaluate the variation of therapy in those groups, further more if inter group comparison showed any significant improvement in outcome, this can be considered as the superiority of the test oil over pharmacological inert liquid in improving the variable, sleep latency, mental depression and day time somnolence. Hence pre and post interventional changes within the both the groups are evaluated to prove the efficacy of *Nutool* therapy.

Table- 1
Evaluation of Scores of six major domains studied for geriatric insomnia in group A and group B

Major Domains for geriatric insomnia	Group A(control)				Group B(Test)			
	Before intervention	After intervention	P value	Effect size	Before intervention	After intervention	P value	Effect size
Sleep Latency	5.20±1.66	2.00±1.07	<0.001**	1.93	7.00±1.73	2.13±0.92	<0.001**	2.81
Quality of Sleep	6.20±1.32	3.13±0.92	<0.001**	2.32	6.60±1.45	2.67±1.11	<0.001**	2.71
Awaking Symptom	7.67±1.59	2.67±1.04	<0.001**	3.15	8.07±1.34	2.20±1.01	<0.001**	4.39
Day time Somnolence	9.93±1.90	3.13±1.25	<0.001**	3.56	11.13±1.36	2.27±1.22	<0.001**	6.53
Mental Stress	8.53±2.69	2.80±1.57	<0.001**	2.13	9.80±1.94	1.93±1.44	<0.001**	4.06
Suicidal Tendency	2.60±3.83	0.60±1.12	0.023*	0.52	4.00±4.02	0.53±1.06	<0.002**	0.86

Table-2
Comparison score of six major domains studied for geriatric insomnia in Group A and Group B.

Major Domains Studied For Geriatric Insomnia	Group A (Control)	Group A (Control)	p value	Effect size
Sleep latency	3.20±1.21	4.87±2.00	0.010**	0.98
Quality of sleep	3.07±1.16	3.93±1.71	0.118	0.118
Awaking symptoms	5.00±1.56	5.87±1.25	0.103	0.60
Day time Somnolence	6.80±2.34	8.87±2.23	0.019*	0.80
Mental stress	5.73±2.74	7.87±2.17	0.025*	0.84
Suicidal tendency score	2.00±3.02	3.47±3.64	0.239	0.43

Discussion: Sleep latency: i. Mean and SD of Sleep latency before and after the intervention are 5.20+1.66 and 2.00+1.07 respectively in Group A(control) and 7.00+1.73 and 2.13+0.92 in the group B(Test) respectively. The Intra group comparison was made using paired student t- test (dependent/two tailed); the findings were significant in both the groups with p value<0.001 of the control group as well as in test group. This shows that *Nutool therapy* is efficacious irrespective of the type of liquid used. The effect size of group A and group were B 1.93 and 2.81 respectively with $d > 1.20$. Both the value showed very large effect statistically (table 2). ii. These finding are in consonance with the study conducted by Erman et al.⁹ in DSM-IV diagnosis of primary insomnia in elderly, where Eszopiclo 2 mg showed significant improvement in sleep latency with $P < 0.001$, Another study done by Scharf et al¹⁰ shows significant improvement in sleep latency with $P < 0.004$, but as stated earlier, both the drug being nonbenzodiazepine sedative-Hypnotic agents has common side effects which includes unpleasant taste, dry mouth, headache, dizziness, nausea and somnolence, in addition to this non-benzodiazepine sedative-hypnotic agents have been known to produce negative effects on balance, gait and equilibrium. However, these side effects are not reported with the current intervention; hence, it is inferred that *Nutool therapy* is safe and can be administered in lieu of Sedative Hypnotics. iii. In a study conducted by Stephen et al,¹¹ using classical benzodiazepine hypnotics, evaluating the effect on sleep latency, found an effect size of 0.56; where as in the present study the effect size for the same parameter were 1.93 and 2.81 in group A and group B respectively; $d > 1.20$ is considered a very large effect this shows that the present intervention of *Nutool therapy* has better efficacy than the conventional measures in management of insomnia w.r.t. Sleep latency. In addition it is emphasized that, the use of classical benzodiazepine hypnotics significantly increases the risk of hip fracture by 50%¹². iv. According to the study conducted by Morin and colleagues¹³ using psychological and behavioral treatment, the effect size of sleep latency was 0.88, as compared to the present study, which has the effect sizes of 1.93 and 2.81 in test and control groups respectively. The present study, showing better efficacy, may be considered as an alternate to the CBT. v. The Inter group comparisons were considered significant statistically when assessed by student t- test (Independent), $P < 0.05$. This may be attributed to the effect of test drug, possessing the qualities such as *Munavvim, Murattib and Muqwwi e dimagh*. Furthermore, intergroup findings in the present study, together with the supporting studies, showed significant advantage ($P < 0.05$) of medicated oil (Test) over the pharmacologically inert liquid in group A (control).

Quality of sleep: The Mean and SD of Quality of sleep before and after the intervention are 6.20+1.32 and 3.13+0.92 respectively in Group A(Control) and 6.60+1.45 and 2.67+1.11 in group B(Test group) respectively. The Intra group comparison was made using paired student t- test (dependent/two tailed); the findings were significant in both the groups with p value<0.001. The improvement from the baseline

data for the subjective variables of quality of sleep indicate significant improvement in quality of sleep with $P < 0.001$, signifying the effect of *Nutool therapy* (table 2).

In the study by P.D.Nowell, S.Mazumdar, D.J.Buysse et al, the effect size relative to placebo of the same variable is 0.53¹⁶ when classical benzodiazepines were used; while, effect size is 0.57 in the present study, considered as moderate effect. It is thus inferred that *Nutool therapy* can be opted in place of benzodiazepines, which are associated with adverse effects such as daytime drowsiness, dizziness or light headedness, which were not reported in the present study. In the study conducted by Krystal et al,¹⁴ using classical benzodiazepines, there was a significant improvement in quality of sleep with $p < 0.001$, which is same as the present study. It is inferred that *Nutool therapy* may be opted in place of benzodiazepines which is associated with the adverse effect such as daytime drowsiness, dizziness or light headedness, which were not reported in the present study. Hence, *Nutool therapy* can be considered as a safe alternative to improve the quality of sleep. The Intergroup comparison were made using student t- test (Independent), $P = 0.118$, considered non-significant statistically (table 3).

Awaking symptoms: The Mean and SD of Awaking symptoms before and after the intervention are 7.67+1.59 and 2.67+1.04 respectively in Group A(Control) and 8.07+1.34 and 2.20+1.01 in group B(Test group) respectively. The Intra group comparison were made using paired student t- test (dependent/two tailed); the finding were significant in both the groups with p value<0.001. The comparison showed that the efficacy of *Nutool therapy* as a whole. Effect size of group A and group B are 3.15 and 4.39, respectively which were more than $d > 1.20$ and considered very large effect statistically (table 2).

The same can be compared with the study conducted by Vaughn, Rosenberg R, et al¹⁵ using eszopiclone in elderly. The same variable measuring morning sleepiness has the $p = 0.07$ which is suggestive of less significance than the present study, moreover the adverse effect included unpleasant taste, dry mouth, somnolence and dizziness in eszopiclone group. However, in the present study these effects are not reported.

This signifies that effects within the groups are statistically significant which shows that efficacy of *Nutool therapy*. The Inter group comparison were made using student t- test (Independent), $P = 0.103$, considered non-significant statistically).

Day time somnolence: The Mean and SD of Day time somnolence before and after the intervention are 9.93+1.90 and 3.13+1.25 respectively in Group A (Control) and 11.13+1.36 and 2.27+1.22 in the Group B (Test) respectively. The Intra group comparison were made using paired student t- test (dependent/two tailed); the findings were significant in both the groups with p value<0.001. The effect size of group A and group

B are 3.56 and 6.53 respectively which is even more than $d > 1.20$ which has very large effect statistically. (Table No.2) this signifies efficacy of *Nutool* therapy These findings are in accordance with the observations noted by Krystal et al¹⁴ and Scharf et al,¹⁰ using eszopiclone, a non benzodiazepine hypnotic, significance level were $p < 0.001$ and $p < 0.05$ respectively. The drug being non-benzodiazepine sedative-Hypnotic agent has common side effects which includes headache, dizziness, nausea and somnolence, in addition to this non-benzodiazepine sedative-Hypnotic agents have been known to produce negative effects on balance, gait and equilibrium. However these side effects are not reported with the current intervention hence it is inferred that *Nutool therapy* is safe and can be administered in place of Sedative Hypnotics. The Inter group comparison were made using student t- test (Independent), $P < 0.05$, (Table No. 3) considered significant statistically, this can be attributed to the effect of test drug, possessing the qualities viz *Munavvim, murattib and muqawwi dimagh*, giving additional relief from the Day time somnolence.

Mental stress and depression: The Mean and SD of Mental stress and depression before and after the interventions are 8.53 ± 2.69 and 2.80 ± 1.57 respectively in Group A and 9.80 ± 1.94 and 1.93 ± 1.44 in the Group B respectively. (Table No. 2) The Intragroup comparisons were made using paired student t- test (dependent/two tailed); the finding were significant in both the groups with $p \text{ value} < 0.001$, Signifying the efficacy of *Nutool* therapy The effect size of group A and group B are more than $d > 1.20$, which is very large effect statistically The Inter group comparison were made using unpaired student t- test (Independent) with ($P < 0.05$), (Table No. 3) considered significant statistically; pre and post changes having $p < 0.001$, signifies the efficacy of *Nutool* therapy, however, in the test drug dominance as an additional relief is attributed to *Munnawim* effects of *Roghan e Banafsha* and *Roghan e Gul* in group B.

Suicidal tendencies: The Mean and SD of Suicidal tendencies before and after the intervention are 2.60 ± 3.83 and 0.60 ± 1.12 respectively in Group A. This finding was significant with $P < 0.05$; similarly Mean and SD in the group B are 4.00 ± 4.02 and 0.53 ± 1.06 . This finding was statistically significant with $P < 0.01$ within groups. (Table No.2) The Intergroup comparisons were made using student t- test (Independent), $P = 0.271$, considered non-significant statistically, signifying the effect of *Nutool* in both the groups.

Conclusion

Efficacy of *Nutool* therapy was analyzed statistically and significant improvement $p < 0.001$ was found in all the parameters. *Nutool* therapy showed comparable effect in both test and control group after analysis of post interventional values of various parameters of SIS such as sleep latency, quality of sleep, awaking symptom, day time somnolence, mental stress and depression, suicidal tendencies and insomnia

severity index, it suggests that *Nutool* therapy irrespective of use of any kind liquid exerts its own effect by the virtue of its sheer streaming effect on the forehead. In addition to the inherent effect of *Nutool* therapy the efficacy was further enhanced by using *Roghan e Banafsha* and *Roghan e Gul*. It is evidenced by improvement in sleep latency, day time somnolence/dysfunctioning and mental stress/Depression in Test group in comparison with the control group. The benefits of *Nutool* therapy outweighed the risk involved with the use of pharmacological treatment in elderly insomniacs. It is the maiden research work towards the validation of *Nutool* therapy as a potential treatment strategy in the control of insomnia in elderly. Further research is vital to clarify the full clinical and economical implications of *Nutool* therapy and to determine the true potential of this age old reliable regimetal therapy of Unani system of medicine. The present study is first of its kind in evaluating the age old therapy with significant results, confirming the efficacy of the therapy. *Nutool* therapy has certain limitations mainly that it is little known, is not widely available, and is more time-consuming than pharmacological interventions. Nevertheless, *Nutool* therapy can be used as more widely and to a greater effectiveness in the clinical settings to reduce severities and manifestations of various types of insomnia without side effects that are associated with other pharmacological treatments. Studies can be conducted in a manner of psychological/behavioral studies, multimodal therapies like CBT (cognitive and behavioral studies) as open studies with or without placebo in insomnia associated with different psychological disorders including anxiety, mood disorders and painful conditions, where pre and post treatment values are assessed. Sleep latency, Day somnolence/dysfunctioning and mental stress and depression are very common complaints of geriatric insomnia and test oil had proven its dominance in curing these major domains hence the trial with same oil should be conducted on larger sample size. Present study evaluated the efficacy and safety (during intervention) of *Nutool* therapy in primary insomnia; the same can be evaluated for other types of insomnia described in Unani literature using various medicated oils as supportive for the underlying disease.

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