International Journal of Community Medicine and Public Health
Singh S et al. Int J Community Med Public Health. 2026 Jan;13(1):224-229
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20254429

Original Research Article

Long duration treatment of chronic insomnia in elderly shows poor cognition

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Received: 21 August 2025
Revised: 09 December 2025
Accepted: 10 December 2025

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ABSTRACT

Background: Chronic insomnia is a common, underlined condition during old age. Long duration therapy for chronic insomnia leads to show symptoms of difficulty in day time functioning and other risk factors among geriatric population.
Methods: An observational, cross-section study was conducted in the out patient department of geriatric medicine, Sir Sunderlal Hospital, BHU, Varanasi, to see the association of cognitive functions on old age chronic insomnia patients under long duration drug therapy. The chronic insomnia patients (age >60 years) under long duration therapy (not less than twelve months) were screened for sleep quality and cognitive performance simultaneously with Pittsburgh sleep quotient index (PSQI) and Addenbrooke's cognitive examination test, both in Hindi version.
Results: Chronic insomnia was seen in high prevalence of 26% among old age population. Cognitive performance was significantly decreased in working memory in chronic insomnia subjects compared to their healthy counterparts (0.85±0.55, 1.71±0.53), other domains like orientation and coordination also showed symptoms of mild cognitive impairment, difficulty in day time functioning and other co morbidities among geriatric population. Chronic insomnia was significantly associated with concomitant diseases which include diabetes, hypertension, and arthritis. Based in a clinically significant study, 23% of patients with chronic insomnia did not perceive the ailment, and 32% more elderly women had insomnia than men of the same age.
Conclusions: The study suggested the elderly population should be evaluated routinely for long-term use of hypnotic medications for chronic insomnia. The non pharmacological therapies may be included during treatment of geriatric population like maintenance of sleep hygiene; melatonin and bright light therapy.

Keywords: Cognition, Drug therapy, Insomnia, Long duration, Memory, Old age

INTRODUCTION

The disturbance in sleep is common problem with advancing age. By the definition chronic insomnia is stated as difficulty in getting to sleep, staying asleep or having non-restorative sleep despite having adequate opportunity for sleep, together with associated impairment of daytime functioning, with symptoms being present for at least >3 weeks.[1] The person feels difficulty in initiating and maintaining sleep is a wide problem, which includes many subtypes of case-based classification of insomnia.[2] The difficulty in sleep initiation, frequent night awaking goes unnoticed many times due to possible changes in sleep architecture at later stages of ageing.[3] The sleep disturbance involves decrease in delta waves and sleep fragmentation, which is affected by circadian rhythm alterations and uncoupling of neurological metabolic activity in lactate metabolism. This favors increased amyloid plaque and tau tangle deposition changing the sleep wake cycle. This type of

changes in circadian rhythm on addition of different lifestyle disorders and lack of attention deteriorates the overall health in older adults. The chronic insomnia sufferers show additional medical condition like hypoxemia and dyspnea, gastro esophageal reflux disease, pain conditions, and dementia.[4] The subjective complaint of insomnia is based on sleep disruption and sleep duration, sleep disruption is classified into sleep onset, sleep maintenance, sleep offset insomnia, and lack of non-restorative sleep, while duration of sleep is categorized into transient, short-term, and long-term/chronic insomnia.[5] The insomnia complaint lasting more than three weeks is said to be chronic. The annual incidence of 10-15% of chronic insomnia is seen among elderly and increasing gradually, the chronic insomnia older adults may face challenges in daytime sleepiness, risk of fall, fractures, accidents, reduced daytime functioning and poor cognition.[6] The studies based on insomnia in elderly reported prevalence of 32% among north India, the other similar study in south and central India have 35.95% prevalence reports, showing an increase in chronic insomnia among older age population.[7] The treatment of chronic insomnia involves pharmacological support with major consumption of benzodiazepine (BDZ) and Z drugs (zopiclone zolpidem and zaleplon) during treatment. The Z drugs are wide range of hypnotics which induce GABA-chloride channel, and type I-BDZ (BZ1) receptors in the central nervous system, also referred as GABAA receptor agonists.[8] The site for regulation of sleep cycle and cognition are common basal forebrain which affects the memory and orientation during long term treatment with Benzodiazepine and Z drugs therapy due to deposition of (Aβ) amyloid beta.[9] The studies based on long term drug effect are important in reference to geriatric population. The pharmacokinetic properties of drugs mainly benzodiazepine and Z drug used in subjects with chronic insomnia complaints during specific dose therapy depends on the half-life and metabolite clearance and accumulation in body which is specific for individuals during treatment. The elderly population encounters poor biotransformation of these drugs and leads to accumulation of metabolites. The metabolites of long lasting drug induce decline in brain functions and result in cognitive impairment. The long term usage of drug without clinical consultation leads to rebound anxiety, insomnia and other issues, at withdrawal of the drug similar clinical problems are seen in old age adults. Many times, prolonged drug usages develop a sedative use disorder, which remains undiagnosed in iatrogenic elderly population. The loss of cognitive functions comprises loss in working memory, attention, logical and critical thinking, executive functions required in day to day life.[10] The loss of cognition has been associated with sleep loss in previous studies; cognitive decline affects the lack of attention, mood swings and anxiety disorders, daytime tiredness, frailty, muscle weakness and poor locomotion in elderly population.[11] The changes in cognitive decline depends on changes occurring in the sleep cycle in older people and has many variables and not one single factor is responsible for sleep disturbance, the objective of the study was to understand the effects of long term drug therapy on cognitive performance among elderly population and risk factors associated with it.

METHODS

The study was approved by ethical committee of the institute and consent of subjects was taken prior to start the data collection. An observation based cross sectional study was conducted from (March, 2018 till September, 2022) in OPD, Geriatrics Medicine, Institute of Medical Sciences, Banaras Hindu University; the subjects were divided in two groups, chronic insomnia drug users and healthy control subjects. The drugs users included in the study were older adults under the treatment of benzodiazepines, zolpidem IR, zolpidem ER, zopiclone, eszopiclone and zaleplon. According to the previous report, sample sizes was calculated (n=200) subjects. The inclusion criteria for the study were as follows: Under insomnia treatment >six month or above, age (>60) male or female with subjective complaints of distress and dysfunction. Pittsburgh sleep quality index (PSQI) score >7, meeting DSM-V criteria for insomnia. The exclusion criteria were as follows: Past history of drugs or alcohol abuse, medication which affects cognition (antidepressant or psycho stimulants), clinically diagnosed for psychiatric disease, dementia or other brain disorder, low score of ACE.[12]

The sleep variable diagnosis was made under the guidance of expert geriatrician with standard measure by PSQI, drug dose level, and other demographic parameters (Table 1).[13] Participants were screened with psycho-metrically cognitive measures with the help of clinical psychologist from department of psychiatry, IMS, BHU, and Varanasi. Addenbrooke's cognitive examination- the study analyzed cognitive performance based on neuropsychological tests questionnaire, ACE- Hindi as global measure and other sub components for cognitive domain specific test for working memory, executive function and attention. The ACE-III for Hindi literate is available with seventeen questions, each section with domain specific test, seven sections for attention and memory; seven for language and fluency and three for visuospatial domain. The psychological battery test was conducted on all the subjects. Trail, A and B for the psychomotor speed, attention Digit span test were included in the study.[14] The statistical analyses were conducted using the SPSS (version19.0, Chicago, IL).[15] Pearson's correlations were used to assess the direction and strength between variables. T-tests was used to test for differences between groups, and where significant.

RESULTS

The study enrolled 200 subjects with consent, 20 subjects were screened out due the exclusion criteria, the mean age of the geriatric population was 69 years on average for both insomnia suffers and healthy control. The

prevalence of chronic insomnia was 26% in total population. The gender ratio for disease was determined, female: male sex ratio was higher in insomnia suffers (10:23) compared to healthy control (10:17) group indicated more female among the total population were suffering from insomnia. The chronic insomnia subjects showed more pain perception and depression score compared to healthy subjects. The variables for sleep duration, sleep efficiency and sleep quality were significantly low in chronic insomnia subjects (Table 1) The cognitive decline were analyzed in population at various measures in symbol digit modality test (total score), letter series (total score), word list delayed recall and working memory SOL (minutes) (Table 1).

Table 1: Descriptive data on average sleep parameters and cognitive performance of older adults.

Variables	Insomnia SUFFERERS	Healthy older adults
Age	69.45 (7.82)	69.70 (7.94)
Sex (M:F)	10:23	10:17
Education/ Illiterate n (%)	37	31
Insomnia duration (months)	176.6 (183.20) [12.00-720.00]	Nil
Prescriptions sleep medication use, n (%)	18 (36)	5 (26)
Pain rating*	2.49 (2.18) [0.00-8.50]	1.17 (1.39) [0.00-4.29]
Insomnia drug usage	28.65 (1.05) [26-30]	9.41 (1.53) [25-30]
Depression score	10.93 (9.51) [1.00-46.00]	9.84 (9.71) [1.00-42.00]
Sleep duration measures (minutes)	40.95 (31.74) [3.29-142.31]	48.95 (48.07) [13.21-305.36]
Sleep efficiency (%)	44.08 (12.26) [44.88-91.16]	71.50 (12.29) [26.17-86.91]
Sleep quality	0.95 (0.43) [0.90-3.62]	2.70 (0.63) [1.43-3.50]
Cognitive measures		
Symbol Digit Modality Test (total score)	31.62 (11.32) [3.71-70.90]	39.05 (14.76) [0.00-60.29]
Letter Series (total score)	11.02 (4.45) [2.36-18.42]	13.03 (5.68) [3.64-24.21]
Word List Delayed Recall (# recalled)	9.45 (3.54) [2.77-14.43]	8.98 (2.91) [4.36-14.86]
Working memory SOL (minutes)	0.85 (0.55) [0.00-1.30]	1.71 (0.53) [1.70-2.00]
Short term memory (minutes)	31.06 (16.41) [22.36-104.08]	40.86 (16.63) [22.67-74.43]
PSQI n (%)	22 (79)	10 (76)

(Sample size n=200).

Table 2: Correlation of chronic insomnia and other co morbidities.

Variables	Control	Chronic Insomnia	Total	P value
Diabetes	30	48	78	0.001
Hypertension	24	37	64	0.393
Heart disease	10	17	27	0.374
Thyroid disease	18	25	43	0.182
Asthma	9	22	31	0.873
Kidney disease	24	31	71	0.741
Arthritis	11	34	65	0.927

The working (short term) memory test was significant; the total PSQI score was 22% in chronic insomnia subjects (Table 1). The correlation of chronic insomnia with other co morbidities showed significant outcome (Table 2). High number of subjects suffering from chronic insomnia were from diabetics, hypertension, heart disease which was statically significant, other co morbidities thyroid, asthma and arthritis were also associated with insomnia suffers. The diabetes showed strong association with chronic insomnia, long duration treatment for older adults needs frequent monitoring due changes in conditions. The demographic data like educational background, monthly income, rural or urban resident showed no correlation with chronic insomnia (insignificant variables). The perception of insomnia was poor among female subjects compared to their male counterparts; twenty-five percent subjects had no complained for poor sleep in total population having high PSQI scores which is important for their total health. The employability had no significant role when associated with insomnia in older adults 28% were re-employed, 33% were unskilled and homemakers, 45% were retired. Despite the warnings and consultation, 24.6% subjects were taking the BZDs and Z drugs beyond the recommendation period, at the risk of health, 12% subjects had extended consuming drugs without any consultation. The data was further analyzed for adjusted model, stepwise method to find the significant variables

for the study. The analysis of variance (ANOVA) indicated the adjusted variables were significant for sleep duration and working memory which is significant result for cognitive decline. The analysis did not find multi-co linearity and the model was not rejected by statistical analysis.

DISCUSSION

The results of the study showed high prevalence of chronic insomnia which was consistent with previous reported studies between prevalence ranged between 10.9% to 28.1% in different part of the country.[16] The gender ratio for older females suffering from chronic insomnia and poor sleep quality was observed which has similar pattern with previous studies on insomnia.[17] This type of observation for drug effect on gender ratio is an important factor in pharmacokinetics of medicines and therapeutic strategies for clinical conditions and the changes occurring in physical condition.[18] The difference in gender ratio also relates to the postmenopausal issues and nutrition deficiency among the aged females.[19] The chronic insomnia subjects showed more pain perception and geriatric depression score compared to healthy subjects, pain perception may be the reason behind frequent night awakenings and sleep fragmentation.[20] Other factor for higher depression score may be associated with daytime nap, lack of physical movements like exercise, yoga and morning walks, the change in sleep quality or any type of sleep disturbance is the most frequent compliant in different reports.[21,22] Most of the parameters of sleep disorders remain unnoticed and self-perception for sleep problems remain neglected due to ageing.[23] The sleep variables scoring were low in chronic insomnia sufferers.[24] This observation is consistent with other studies conducted on older adults.[25] The usage of Benzodiazepines has reported to be risk factor for dementia, the use of Z drugs is safer option for adults suffering from chronic insomnia, and still long duration of therapeutics beyond treatment affects the cognition.[26,27] The related risk factors associated with sleep problems are significant to determine the course of treatment in chronic insomnia.[28] The studies in geriatric population has shown reduced cognitive abilities compared to healthy adults under long usage of therapy for chronic illness, however the effect of drugs in chronic insomnia alone cannot be deciding factor for cognitive decline and several other factors, life skills, burden of other diseases, poor finances and other conditions must be taken under consideration.[29,30] This type of result is consistent with other previous reports.[31] The overall population lack knowledge of sleep hygiene, physical exercise and cognitive behavioral therapy for insomnia, which shows lack of knowledge and health awareness and its consequences among the geriatric population of the region. The ignorance of sleep complaints and mild forgetfulness and attention deficiency was not considered important for older adults and aging is compounded by the burden of cognitive decline in older population. The various social, behavioral and cultural factors are crucial while considering health of older subjects.[32]

CONCLUSION

The study evaluated defined associations between measures of sleep and cognition performance using large representative samples of older adults in order to understand the role of cognitive decline under long term sedative therapy. The pharamcotherapeutic agents used in treatment for chronic insomnia within geriatric population without any vigilant consultations can be added risk factor of cognitive decline. The pharmoco-genomic association of cognitive impairment, insomnia and other symptoms makes a composite network and more variables needs to be included to get the exact role of drugs in cognitive impairment. The study was significant attempt for medical awareness towards the cognitive decline in older population suffering from insomnia and its management from prolonged drug intervention and its side effects. The development of predictors of susceptibility to drug induced cognitive decline in elderly population can be significant for further research in geriatric population in India. The association of risk factors such as onset of dementia, cardiovascular and other lifestyle diseases needs intervention for future research in older adults.

ACKNOWLEDGEMENTS

The work was performed and supported by Department of Geriatric Medicine, Institute of Medical Sciences; Banaras Hindu University under DST PDF (CSRI) scheme.

Funding: Department of Science & Technology (Cognitive Science Research Initiative Scheme), DST/CSRI/065/19-20, and INDIA
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee Institute of Medical Sciences, BHU, on sanction project no. DST/CSRI/065/19-20

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Cite this article as: Singh S, Kumar A. Long duration treatment of chronic insomnia in elderly shows poor cognition. Int J Community Med Public Health 2026;13:224-9.