Drug Corner

Effect of Zolpidem Tartrate on Sleep Quality and Health-Related Quality of Life in Indian Patients with Insomnia and Hypertension

Rajiv D Karnik[1], Neha Haris[2]

Objectives : Insomnia and hypertension often coexist. The objective of this study was to assessthe effectiveness and safety of zolpidem tartrate onsleep quality and overall quality of life (QoL) in Indian patients with insomnia and hypertension.

Material and Methods: Patients experiencing sleep disturbances for at least 3 nights/week, having insomnia severity index (ISI) score of ≥8 at screening, and a clinical diagnosis of hypertension were enrolled. The main outcome measuresweremean change in the severity of insomnia symptoms (ISI) and RAND 36-Item Health Survey scores (RAND-SF36) on Day-21compared to baseline. Adverse events (AEs) were recorded for safety assessment.

Results: A total of 41 (91.2%)out of 45enrolled patients completed the study. 21-days of treatment with zolpidem tartrate significantly reduced the ISI score by -10.07 (p<0.0001) compared to the baseline mean (SD) score of 14.73 (4.33). Significant improvement in RAND-SF36mean scores were also evident. Role limitation due to physical and emotional health score increased significantly(p<0.0001) by 51.22 and 55.28, respectively, energy score by 20.49 (p<0.0001), emotional well-being score by 7.41 (p<0.01), social function score by 22.26 (p<0.0001), pain score by 22.62 (p<0.0001), and general health score by 4.88 (p<0.01); physical function scoreincreased marginally by 3.29(p>0.05)over the 21-daysstudy period. The commonly reported AEs were fatigue (4.44%), somnolence (4.44%), and headache (2.2%), which were mild and resolved subsequently.

Conclusion :The study demonstrated that zolpidem tartrate improved sleep quality, health-related QoL, and was found to be well-tolerated in Indian insomniac patients with hypertension (CTRI/2018/12/016688).

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Key words **: Zolpidem, insomnia,hypertension, sleep, quality of life.**

Characterized as a disturbance in sleep initiation or maintenance, insomnia is one of the most commonly encountered sleep disorder in medical practice.[1] Insomnia is often undiagnosed and neglected due to lack of consultation in primary care settings.[2] Disorderaffects 30% to50% of the general adult population[3].In India, the prevalence of insomnia varies between 14 to 18.7% in general population.[4] Etiology of insomnia is not clearly understood, and involves many factors including environmental, genetic, psychological, and behavioral, leading to a state of hyperarousal.[5] Insomniais a risk factor for impaired daytime function, the development of other medical and mental disorders, and increased health care costs.[5]

Dr Karnik's Cardiac Clinic, Mumbai 400078
[1]MD, DM (Card), FESC, FSCAI, Cardiologist and Corresponding Author
[2]Cardiac Perfusionist
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Editor's Comment :

- **Zolpidem at the recommended dose is effective in improving sleep quality and consequently QOL and day-to-day functioning in insomniac patients with hypertension. Drug is well-toleratedand may help in BP control in new-onset hypertension.**

Although long-term sleep loss is often secondary to somatic or psychiatric illness[6], it appears that insomnia may also play a central role in the pathogenesis of somatic illness and metabolic dysregulation[7].Insomnia has been particularly associated with cardiovascular diseases and its precursors such as hypertension and non-dipping blood pressure (BP).[8] Blood pressure physiologically decreases during sleep, a process known as dipping.[9,10] Studies have shown that day-to-night and nighttime regulation of BP appears to be closely linked with autonomic changes happening during the wake-sleep cycle.[11,12] This suggests that BP is especially sensitive to sleep disturbances.[10] Hypersecretion of adrenocorticotropic hormone, cortisol and

catecholamine has been reported in patients with insomnia symptoms, suggesting the over activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system (SNS); which provides a biological basis for the co morbidity of insomnia and hypertension.[13]

The recent evidence suggests that the increasing prevalence of hypertension might be related both to an increased prevalence of insomnia and to the poor sleep quality/ duration.[14-16] Additionally, anxiety that often accompanies sleep disorders is associated with increased BP, a known risk factor for cardiovascular events.[16,17] This indicates that the pharmacotherapy for sleep disorders and insomnia may have beneficial effects on BP.[16,18,19] Furthermore, several experimental studies have suggested that certain sleeping pills may decrease BP or SNS activity.[16] However, only a few researchers have studied the association between hypertension and insomnia treatment, and the impact of this treatment on BP.[18,19]

The drugs primarily used for insomnia treatment include benzodiazepines, non-benzodiazepines hypnotics, ramelteon, and antidepressants such as doxepin.[2] Benzodiazepines formed the mainline therapy for insomnia for many years. However, associated side-effects and addiction potential has restricted the use of benzodiazepines.[20]Among non-benzodiazepines, zolpidemtartrate is the highly prescribed drug for the short term treatment of insomnia globally.[2,21]Huang *et al*., demonstrated that zolpidemtartrate, through improvements in sleep quality, stress status, and activation of the SNS, could significantly help the conversion of non dippers to dippers.[18] However, there is no data regarding the use of zolpidemtartrate in Indian patients suffering from co-morbid insomnia and hypertension. The present studywas designed with the objective to obtain insights on the effectiveness and safety of zolpidemtartrate in Indian patients with insomnia and hypertension over a period of 21-days.

Study Design and Population :

This was a prospective, single-center, open-label, non-comparative study (CTRI/2018/12/016688) conducted between May 2019 and September 2019at Dr. Karnik's Cardiac Clinic, Mumbai, India. Outpatients of both sexes, between 18-65 years of age, experiencing sleep disturbances (difficulty in sleep initiation or middle of the night awakening or early morning awakening or poor quality of sleep) for at least 3 nights/week, insomnia severity index (ISI) score of $\geq$8 at screening, with a clinical diagnosis of hypertension, and willing to sign informed consent for study participation were enrolled in this study.

Patients on prescription and non-prescription sedative drugs for more than 2 days for sleep disturbances or to relieve jet lag and/or patients with regular change in sleep schedule by at least six hours within the last 28 days preceding to enrolment, evidence of any medical condition as revealed by history, physical examination or laboratory assessment which may interfere with administration or assessment of study medication, current alcohol or drug abuse, patients having history of obstructive sleep apnea, restless leg syndrome, myasthenia gravis, hepatic insufficiency, respiratory depression, other sleep disorders, patients having presence of any untreated or uncompensated clinically significant renal, endocrine, gastrointestinal, hepatic, respiratory, cardiovascular, neurologic, hematologic, oncologic, immunologic, cerebrovascular disease or malignancy, cognitive impairment, symptoms of chronic/ incapacitating pain, patients having history of severe cardiac, hepatic, neurological and renal diseases within 6 months prior of screening, bipolar disorder, psychosis, major depression, unstable anxiety disorders/panic attacks, patients viewed by the investigator as not being able to complete the study, and/or patients on other CNS depressants drugs like antipsychotics (neuroleptics), hypnotics, anxiolytics/ sedatives, antidepressant agents, narcotic analgesics, antiepileptic drugs, anesthetics and sedative antihistamines or CYP 3A4 or CYP 1A2 inducers or inhibitors were excluded from the study. Pregnant or breastfeeding women, elderly patients having symptoms of urinary obstructions, patients having participated in a clinical trial in the last one month, and/or with any other serious disease or condition at the screening that might affect the normal sleep pattern were also not included in the study.

The total duration of the study was 21 days. Patients enrolled were prescribed with zolpidem tartrate10mg. (Zolfresh®, Abbott India Limited)at the baseline, for a period of 21 days. Progress made by the patient was reviewed on Day 21.

The study was conducted as per the good clinical practices (GCP) and the applicable national regulations to assure that the rights, safety, and wellbeing of all the participants were protected, consistent with the ethical principles that have their origin in the Declaration of Helsinki. Written informed consent was obtained from all study participants before being examined for eligibility criteria. The study protocol and the informed consent form were reviewed and approved by the relevant institutional review board before initiation of the study.

Scales used in the Study :

ISI: Increasingly being used as a yardstick of treatment response in clinical research, ISI is a brief instrument designed to measure the severity of nighttime and daytime components of insomnia.[22] Designed as a brief screening tool for insomnia, the seven-item self-report instrument rates the nature and symptoms of patients' sleep problems, and is intended both for screening purpose and for assessing the efficacy of treatment.[23]

RAND 36-Item health survey (RAND-SF36) : A set of comprehensible, easy to administer, patient-reported quality-of-life (QoL) assessment tool, RAND-SF36 is commonly used for routine monitoring and assessment of treatment outcomes in adult patients.[24]

Study Endpoints :

The primary effectiveness endpoint of the study was the mean change in the severity of insomnia symptoms, as measured by the ISI, from baseline to Day 21 post-zolpidem tartratetreatment. The secondary effectiveness endpoints included mean change in Health-Related QoL(HRQoL), as measured by RAND-SF36scores, from baseline to Day 21, post-zolpidem tartrate treatment. The safety of zolpidem tartrate was assessed throughout the treatment period of 21-days.

Statistical Analysis :

Qualitative and quantitative variables are presented using descriptive statistics. Quantitative variables were evaluated using paired t-test at a 5% level of significance and the corresponding p-value is presented. Data were analyzed using RStudio version 4.0.0.

Results :

A total of 45 (Male: Female—22:23) patients with mean (SD) age of 47.18 (13.25) years were enrolled in the study, out of which 41 (91.2%) patients completed the study. The demographic and baseline characteristics of patients are summarized in Table 1.Data of patients completing the study (n=41) was considered for effectiveness analysis and full data set (N=45) for safety analysis.

Mean change in effectiveness parameters in 41 patients at Day 21 post zolpidem tartratetreatmentare presented in Table 2.Compared to the baseline, there was a statistically significant reduction in the mean ISI scores (-10.07 [95%CI: -11.80 to -8.34, p<0.0001]) at 21-days. The improvement in HRQoL in the study cohort was evaluated by RAND-SF36.Compared to the baseline there was no statistically significant improvement in the mean physical function score from baseline to Day 21 visit (3.29 [95%CI: -0.89 to 7.48, p>0.05]). However, there was a statistically significant improvement in score of role limitation due to physical health (51.22 [95%CI: 36.57 to 65.87, p<0.0001]), and emotional health (55.28 [95%CI: 40.86 to 69.71, p<0.0001]), on Day 21compared to the baseline.

Table 1 — *Patient characteristics at baseline (N=45)*

Parameter	Overall (N=45)
Sex, n (%)	
Male	22(48.89%)
Females	23(51.11%)
Age (Years), mean±SD	47.18±13.25
Height (Cms), mean±SD	163.49±7.07
Weight (Kgs), mean±SD	74.50±15.74
BMI (kg/mt²), mean±SD	27.82±5.55
Insomnia Severity Index Score, mean±SD	14.91±4.18
RAND 36-Item Health Survey score, (mean±SD)	
Physical Functioning	80.33±20.49
Role Limitations-Physical health	32.22±38.30
Role Limitations-Emotional Problem	30.37±37.49
Energy/fatigue	66.52±22.36
Emotional Well Being	65.24±15.23
Social Functioning	53.06±14.88
Quality of life due to Pain	62.11±19.27
General Health	59.67±19.44
Vitals, (mean ± SD)	
Pulse (beats/min)	79.49±15.02
Respiratory Rate (breaths per minute)	20.20±0.69
Systolic BP (mmHg)	149.53±7.77
Diastolic BP (mmHg)	81.71±9.65
Patients completing study	
Patients completed the study as per protocol	41 (91.2%)
Reason for withdrawal	
Adverse Events	04 (8.8%)

The mean energy score also increased significantly (20.49 [95%CI: 12.67 to 28.31, p<0.0001]) from baseline to Day 21 visit. Likewise, compared to the baseline there was a statistically significant improvement in mean emotional well-being score (7.41 [95%CI: 3.17 to 11.66, p<0.01]) at 21-days.Compared to the baseline there was a statistically significant improvement in the social function score from baseline to Day 21 visit (22.26 (95%CI: 14.54 to 29.97, p<0.0001]). The mean pain score also improved significantly (22.62 [95%CI: 15.10 to 30.14, p<0.0001])at 21-days.Correspondingly, compared to the baseline, general health score also improved significantly (4.88 [95%CI: 1.43 to 8.33, p<0.01]), at 21-days.

Change in Pulse rate and BP of patients with <1-year and >1-yearhistory of hypertension were analyzed and are presented in Table 3.Compared to the baseline, there was no statistically significant reduction in the pulse rate from baseline to Day 21 visit in patients with <1-year of hypertension (-6.39bpm [95%CI: -13.01

to 0.23,p=0.0578]). But in patients with >1-year history of hypertension, pulse rate reduced significantly from baseline to 21-days (-7.33bpm [95%CI: -12.86 to -1.81, p<0.05]).However, compared to the baseline systolic BP reduced significantly at Day 21 in patients with <1-year (-9.26 mmHg [95%CI: -13.54 to -4.98, p<0.001]) and >1-year (-8.56 mmHg [95%CI: -12.44 to -4.67, p<0.001]) history of hypertension. But no statistically significant changes in the diastolic BP were seen from baseline to 21-daysin patients with<1-year (-0.65mmHg [95%CI: -3.69 to 4.99,p=0.7583]) and >1-year (-2.66mm Hg [95%CI: -6.30 to 0.97, p=0.1400]) history of hypertension.

Table 2 — *Mean Change In Effectiveness Endpoints after 21 Days of Treatment Compared to Baseline*

Variables (n=41)	Baseline Mean±SD	Day 21 Mean±SD	Difference (95% CI)	P value[a]
Insomnia Severity Index (ISI)	14.73±4.33	4.66±3.97	-10.07(-11.80, -8.34)	<.0001
RAND-SF36 Parameters				
Physical Functioning	79.27±21.84	82.56±27.11	3.29 (-0.89, 7.48)	0.1196
Role Limitations-Physical health	31.71±38.33	82.93±31.84	51.22 (36.57, 65.87)	<.0001
Role Limitations-Emotional Problem	30.08±37.86	85.37±28.91	55.28 (40.86, 69.71)	<.0001
Energy/fatigue	67.48±16.74	87.97±24.19	20.49 (12.67, 28.31)	<.0001
Emotional Well Being	66.35±14.15	73.76±16.49	7.41(3.17, 11.66)	<.01
Social Functioning	53.65±15.42	75.91±22.25	22.26 (14.54, 29.97)	<.0001
Quality of life due to Pain	62.75±19.19	85.37±18.16	22.62 (15.10, 30.14)	<.0001
General Health	59.27±20.30	64.15±19.13	4.88 (1.43, 8.33)	<.01

CI=confidence interval, SD=standard deviation[a]Analyzed using Paired Sample T-Test

Table 3 — *Change In Pulse Rate And Blood Pressure*

Variables	Baseline Mean±SD	Day 21 Mean±SD	Difference (95% CI)	P value[a]
Patients With >1-Year History of Hypertension (n=18)				
Pulse (beats/min)	78.33±15.39	71.00±10.09	-7.33 (-12.86, -1.81)	<0.05
Systolic BP (mmHg)	151.44±7.66	142.89±9.55	-8.56 (-12.44, -4.67)	<0.001
Diastolic BP (mmHg)	82.83±8.28	80.17±7.33	-2.67(-6.30, 0.97)	0.1400
Patients With <1-Year History of Hypertension (n=23)				
Pulse (beats/min)	79.61±15.25	73.22±8.13	-6.39 (-13.01, 0.23)	0.0578
Systolic BP (mmHg)	147.48±6.77	138.22±10.16	-9.26 (-13.54, -4.98)	<0.001
Diastolic BP (mmHg)	79.39±10.30	80.04±6.44	-0.65 (-3.69, 4.99)	0.7583

CI=confidence interval, SD=standard deviation[a]Analyzed using Paired Sample T-Test

Safety :

About 4(8.89%)patients reported 5(11.11%) incidences of AEs (N=45). The most commonly reported AEs were fatigue (2[4.44%]) and somnolence (2[4.44%]), followed by headache (01 [2.2%]).All the AEs (5 [11.11%])were mild, with unlikely relation with study medication, and were resolved subsequently. No severe or serious AEs were reported.

Discussion :

Sleep plays a key role in the regulation and functioning of the central nervous system and other physiological functions such as regulation of body temperature, metabolism, catabolism, learning, and memory consolidation.[2] Although, one fourth to one-third of the general population reports of the problem in falling or staying asleep, approximately 10% present with chronic complaints and seek medical help for the problem.[25] Untreated insomnia results in clinically significant impairment in social, occupational, or other important areas of subsequent daytime functionality.[26]

The hypothesis that insomnia symptoms increases the risk for hypertension incident over time has been well-established in several studies.[2] But, until a few years ago, the connection between insomnia with hypertension was considered to be inconsistent and discreet.[25] However, in recent years, studies using objective measures of sleep have demonstrated a significant association between the two disorders.[4,25,27-29]

Taylor *et al.* reported a 43.1% prevalence of hypertension in patients with insomnia as compared to 18.7% in individuals without insomnia.[27] Zhanet al. reported the prevalence of hypertension in patients with occasional and frequent insomnia as 43.0% and 48.0%, respectively.[28] Uchimura et al. investigated 5747 workers regarding insomnia and hypertension and reported that insomniac workers reporteda significantly higher incidence of hypertension compared to non-insomniac workers, suggesting a close relationship between insomnia and hypertension.[29]A recent study in India reported 47.2% prevalence of insomnia in adults (≥18 years) with newly diagnosed or known history of hypertension.[4]

It is proposed that the therapy aiding in satisfactory/adequate sleep is directly and/or indirectly effective in treating hypertension.[29]The two most widely used treatment strategies for insomnia are pharmacotherapy

(hypnotic medications) and cognitive behavioral therapy, though pharmacotherapy remains the primary treatment for insomnia.[30] Zolpidemtartrate was the first non-benzodiazepines drug developed to address safety concerns associated with benzodiazepines use.[31]The most widely prescribed drug for the treatment of insomnia worldwide,[2] zolpidemtartrateis characterized by a rapid onset of action as well as minimal residual and rebound effects.[32] The approved doses of zolpidem tartrate (10mg for adults, 5mg for the elderly) are found to be effective in reducing sleep latency and consequently increasing duration of sleep in insomniac patients.[33] The present study evaluated the effectiveness and safety of zolpidem tartrate in patients of insomnia with hypertension, over a medium-term observation period of 21-days.

The assessment of insomnia is multidimensional, though a clinical evaluation remains the gold standard for making a valid insomnia diagnosis; a brief and valid questionnaire can facilitate the initial screening and formal evaluation of insomnia.[34] The ISI is a brief instrument that was designed to assess the severity of both nighttime and daytime components of insomnia and is a reliable and valid instrument with good psychometric properties to detect cases of insomnia.[34] Achange in the score by $\geq$9 corresponds to a marked improvement in the ISI score rating.[34] In our study, compared to baseline, the mean ISI score was reduced by -10.07 ($p<0.0001$), suggesting that that zolpidem tartrate improved sleep quality in insomniac patients with hypertension.

The results reported in our study are consistent with published literature. In a randomized, double-blind, placebo-controlled, parallel-group multicenter trial, zolpidem10mg had a significant effect on latency to persistent sleep and sleep efficiency. The effectiveness of the drug was maintained all through the 35 nights of administration.[35] Another study assessing clinical effectiveness and safety of 4-weeks of treatment with zolpidem 10mgin perimenopausal and postmenopausal women, reported a considerable increase in total sleep time, along with a significant reduction in wake time after sleep onset and number of awakenings.[36] In a double-blind, placebo-controlled study, 12-weeks of non-nightly administration of zolpidem significantly improved sleep continuity in patients with primary insomnia. Moreover, these clinical gains were sustained over time, with no evidence of insomnia reversion.[37]

In a double-blind, placebo-controlled randomized polysomnography trial, eight months of nightly zolpidem treatment in primary chronic insomniacs significantly increased total sleep time and sleep efficiency, decreased latency to persistent sleep and wake after sleep onset, when assessed at month-1 and 8, relative to baseline and placebo.[38] A recent randomized controlled study in patients of total hip arthroplasty reported that the zolpidem 10 mg improved sleep quality effectively, and reduced perioperative anxiety and depression. Moreover, patients taking zolpidem achieved greater satisfaction and improvement in the QoL.[39]

The RAND-SF36 questionnaire can assess eight aspects of health ranging from physical to emotional well-being, social functioning, common perceptions of vitality, and role limitations because of physical or emotional problems.[24] The questionnaire has the advantage of describing the impact of the disease from a patient's point of view, instead of biological or disease-centered outcomes perceived by clinicians.[24] Sleep disorders have a considerable negative effect on the QOL of hypertensive patients, especially in the physical domain of the QOL questionnaire.[40] The result from our study also confirms this, as the mean physical function score in our study increased marginally ($p>0.05$) at 21-days.

It's known that individuals with insomnia have more health concerns that limit their physical activity, cause more body pain, and emotional difficulties, compared togood sleepers.[41] The results from our study show that 21-days zolpidemtartratetreatment improved physical and emotional health, resulting in significant improvement ($p<0.0001$) in role limitations due to physical health and emotional problem, and QoL due to painscores, at the Day-21. Mental status and emotional state are worse in insomniac patients compared to the good sleepers.[41]Twenty-one days of treatment with zolpidemtartrate in our study resulted in significant improvement in emotional wellbeing scores ($p<0.01$), resulting in an overall improvement in social functioning ($p<0.0001$), energy/fatigue ($p<0.0001$), and general health($p<0.01$) domains. In our study, improvement in sleep quality post-21-days of treatment with zolpidemtartrate contributed to the improved QOL and day-to-day functioning in insomniac patients with hypertension.

Stages 3 and 4 (N3, the third stage) of non-rapid eye movement (NREM) sleep are often referred to as deep sleep or slow-wave sleep (SWS) and are considered "restorative" period of sleep.[2] In healthy adults, approximately 20% of sleep time is spent in SWS, which is characterized by the increased vagal tone and reduced sympathetic activity which decreases heart rate, BP, and cardiac workload.[2] On an average,

BP declines by 10 mmHg or more during sleep and those not experiencing this are "non-dippers".[2] Sleep deprivation excites SNS during the night, resulting in increased BP persisting during the daytime.[2]

In a cross-sectional analysis of sleeping pill use among hypertensive (n = 5099) and normotensive (n = 6126) subjects by Sasaki *et al.*, authors observed a negative dose-response relationship between the frequency of sleeping intake and systolic or diastolic BP, in subjects not taking any antihypertensive medication.[16]This suggests that the improvement in sleep quality and duration with sleeping pill use results in decreased BP, since both poor sleep quality and shorter sleep duration are involved in the activation of SNS and the elevation of BP;[16] and also, that the use of a sleeping pill may reduce BP, independent of its effects on sleep.[16]

In our study, compared to the baseline, pulse rate reduces significantly by -7.33 bpm(p<.0001)in patients with >1-year history of hypertension and non-significantly by-6.39bpm (p>0.05) in patients with <1-year history of hypertension, post 21-days of treatment with zolpidemtartrate. However, 21-days of treatment with zolpidemtartrate, resulted in a significant reduction (p<.0001)in the systolic BP by -8.56 mmHg and -9.26mmHg, in patients with >1-year and <1-yearhistory of hypertension, respectively. The diastolic BP reduced marginally by -2.67mmHg and -0.65mmHg, respectively, in both the groups. This indicates that the improvement in sleep quality post zolpidemtartrate treatment may have a potential role in BP control in insomniac hypertensive patients.

Another randomized, placebo-controlled study has also shown that zolpidemtartratecan reduce SNS activity and nocturnal BP in hypertensive patients.[18]In a study by Huang *et al.*, poor sleepers treated with zolpidem tartrate for 30 days showed significant improvements in sleep quality and stress levels (p<0.01). Epinephrine and norepinephrine levels were also significantly reduced in poor sleepers treated with zolpidem (p<0.05).[18] Another randomized, parallel-group study evaluated the effect of zolpidem tartrate on BP and BP patterns in patients with non-scoop type of hypertension complicated with insomnia.[42]The authors reported that the 4-weeks of treatment with zolpidem tartrate 10mg in combination with levamlodipine besylate 2.5mg significantly lowered night and day time BP when compared with levamlodipine besylate 2.5mg alone (p<0.05). Combination treatment also effectively retrieved the non-scoop type of BP in study cohort.[42]

The general safety of zolpidemtartrate has been studied in data obtained from both adult and elderly population during its clinical development phase and post-marketing experience.[43]The drug has been reported to be well-tolerated when administered as per prescribing information.[38]Also, there is little evidence of tolerance to the hypnotic effects of zolpidemtartrate, or rebound insomnia or withdrawal symptoms after discontinuation of the drug when prescribed atthe recommended dose.[43]In the present study also zolpidem tartrate treatment was well-tolerated. The AEs observed in our study were fewer than compared with AEs reported with the use of zolpidem tartratein other studies.[44-47] No severe or serious AEs were reported. The most commonly reported AEs in our study were fatigue, somnolence, and headache.

In conclusion, the result of this single-center, open-label, prospective study suggests that 21-days treatment with zolpidem tartrate resulted in significant and clinically relevant improvements in insomnia symptoms and QoL, as determined by ISI and RAND-SF36 scale scores, respectively. The results also emphasize the plausibility that improvement in sleep quality may aid in BP control in new-onset hypertension. The drug was effective and well-tolerated in patients with insomnia. However, while interpreting the result of this study some limitations such as small sample size, not statistically powered, and absence of control and/or comparator need to be considered. Further studies on a larger sample size, assessing the 24-hr ambulatory BP monitoring is warranted to substantiate our findings.

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Conflict of interest :

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