Original Research Article

Study of correlation between perceived sleep disturbances in depressed patients with objective changes in sleep architecture using polysomnography before and after antidepressant therapy

Ganesh Ingole¹, Harpreet S. Dhillon²*, Bhupendra Yadav³

¹Department of Psychiatry, Regional Mental Hospital, Yerwada, Pune, Maharashtra, India
²Department of Psychiatry, 166 Military Hospital, Jammu, Jammu and Kashmir, India
³Department of Psychiatry, 5 Air Force Hospital, Jorhat, Assam, India

Received: 09 May 2020
Accepted: 01 June 2020

*Correspondence:
Dr. Harpreet S. Dhillon,
E-mail: harpreet5467@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: A prospective cohort study to correlate perceived sleep disturbances in depressed patients with objective changes in sleep architecture using polysomnography (PSG) before and after antidepressant therapy.

Methods: Patients were recruited into the study after applying strict inclusion and exclusion criterion to rule out other comorbidities which could influence sleep. A diagnosis of Depressive episode was made based on ICD-10 DCR. Psychometry, in the form of Beck Depressive inventory (BDI) and HAMD (Hamilton depression rating scale) insomnia subscale was applied on Day 1 of admission. Patients were subjected to sleep study on Day 03 of admission with Polysomnography. Patients were started on antidepressant treatment post Polysomnography. An adequate trial of antidepressants for 08 weeks was administered and BDI score ≤09 was taken as remission. Polysomnography was repeated post remission. Statistical analysis was performed using Kruskal Wallis test and Pearson correlation coefficient.

Results: The results showed positive (improvement) polysomnographic findings in terms of total sleep time, sleep efficiency, wake after sleep onset, percentage wake time and these findings were statistically significant. HAM-D Insomnia subscale was found to correlate with total sleep time, sleep efficiency, wake after sleep onset, total wake time and N2 Stage percentage.

Conclusions: Antidepressant treatment effectively improves sleep architecture in Depressive disorder and HAM-D Insomnia subscale correlates with objective findings of total sleep time, sleep efficiency, wake after sleep onset, total wake time and duration of N2 stage of NREM.

Keywords: Depression, Perceived sleep quality, Polysomnography, Sleep architecture

INTRODUCTION

Sleep is a complex behaviour which continues to be an evolutionary enigma. Every animal engages in some form of sleep or sleep-like behavior.¹ Carskado and Dement defined sleep as: Sleep is a recurring, reversible neuro-behavioral state of relative perceptual disengagement from and unresponsiveness to the environment. Sleep is typically accompanied (in humans) by postural recumbence, behavioural quiescence, and closed eyes.² Sleep repairs the physical body to improve and maintain general health, consolidate learning and memory, and recharge the psychological batteries to maintain emotional balance and well-being. Lack of sleep leads to...
various mental and physical illnesses including an increased risk of hypertension, diabetes, obesity, heart attack, stroke and depression. Sleep disturbances are widespread in psychiatric disorders and hence have been integrated in the official diagnostic criteria for many Psychiatric disorders, such as major Depression, Generalized Anxiety Disorder, Post-Traumatic Stress Disorder and Substance Related Disorder. Depression and sleep disturbances have a very complex interaction with sleep disturbances presenting as the most commonly observed physical complaint in depressed patients with roughly 80% complaining of insomnia and the remaining 20% of hypersomnia.

Furthermore, the prevalence of depressive symptoms has been shown to be high in patients with insomnia and breathing related sleep disorders. A study in the general population revealed that 40% of subjects with insomnia presented with a mental illness within 6 months versus 16% of subjects without insomnia. Taken collectively, these results suggest an increased incidence of major depression in those with sleep disturbances. Therefore, diagnosis and treatment of sleep disorders is very important for clinicians. Diagnosis of insomnia is based on the patient’s perception of sleep quality while diagnosis of many other sleep related disorders eg. Restless legs syndrome (RLS), periodic limb movements (PLMs), REM sleep behavior disorder (RBD), obstructive sleep apnea (OSA), and excessive daytime sleepiness (EDS) are defined by polysomnographic (PSG) data. However, these laboratory tests are highly demanding in terms of cost, human resources, and other logistics required; therefore, questionnaires and scales have been developed for screening patients. This study was planned with the objective of testing the utility of a quick, cost-effective and practical psychometry tool (HAM-D insomnia subscale) as an alternative to expensive and time consuming tests such as PSG to assess and monitor the sleep disturbances in depressed patients especially in OPD settings in a resource constraint country.

METHODS

Inclusion criteria

- Patients admitted in psychiatry ward within the age range of 18 to 50 years.
- Meeting the ICD-10 Diagnostic criteria for research of depressive episode.

Exclusion criterion

- Those not consenting for the study.
- Patients having history of sleep disorder prior to onset of depression.
- Other psychiatric co-morbidities.
- Actively consuming alcohol, other psychoactive substances and psychotropic medications.
- Other co-morbid active medical and surgical illness.

The study was carried out in a tertiary care hospital over a period of 01 year and a total of 77 male patients were recruited, out of which, 09 met the exclusion criterion, 11 were not willing to participate. 57 patients were included in the study out of which 08 were lost to follow up and 06 did not improve with treatment. Remaining 43 patients completed the study. The subjects were evaluated by structured as well as unstructured clinical interview for diagnosis of depressive disorder as per ICD -10 Diagnostic Criteria Research. On day 1 of admission, Psychiatric rating scales - The Beck’s Depression Inventory-II (1996) (BDI) and The Hamilton Rating Scale for Depression (HAM-D) were applied. The Hamilton Rating Scale for Depression (HAM-D) is one of the longest standing, most widely used measures of depression severity in research and clinical practice with good sensitivity and specificity. It is a clinician administered 21 items scale and takes approx. 10 minutes to complete the test. Items 4, 5, and 6 refer specifically to sleep, inquiring about insomnia prior to sleep onset, disturbed sleep in the middle of the night, and trouble falling back asleep in the early morning, respectively. Other items may be peripherally involved with sleep difficulties as they refer to fatigue, retardation, and somatic symptoms in general. Patients were kept drug free till 3rd day of admission. Polysomnography was conducted on day 3 after allowing patient to get accustomed to ward environment. All patients who completed study were followed up till 8 weeks and post treatment. Polysomnography was conducted after achieving full remission as indicated by BDI score of 9 or less and HAMD insomnia subscale score of 0.

The sleep parameters studied were as follows:

- Total sleep time (TST)- The total time spent asleep during the sleep episode. This is equal to the time in bed less the awake time.
- Sleep efficiency (SE)- The ratio of total sleep time to time in bed expressed as a percentage of time spent asleep during the recording period. Normal values are typically above 90% in young and above 85% in elderly patients.
- Sleep Latency - Time from start of the recording (“lights out”) to the onset of sleep. Normal values are typically below 30 min in young and below 45 min in elderly patients.
- Wake After Sleep Onset (WASO)- The total time scored as awake occurring after the sleep onset. Typically WASO should not exceed 30 min.
- N3 Latency- Total duration in minutes and as percentage relative to total sleep time of sleep stage N3. The amount of stage N3 decreases with older age, normal values are around 10% for elderly and 20-25% for young subjects.
- REM%- Total duration in minutes and as percentage relative to total sleep time of sleep stage REM. Normal values are 20-25%.
- REM Latency- The number of minutes from the onset of sleep to the onset of the first REM sleep.
period. Reduced values are typically below 65 min in young and 50 min. in elderly patients.

**Statistical analysis**

Data analysis was done with the help of SPSS Software version 21. Considering 90% prevalence of sleep disturbances in Depression and 10% variation, sample size was calculated to be 43. Application of Shapiro-Wilk test showed that data was not normally distributed. Hence, paired comparison between before and after treatment for BDI score, HAM-D Insomnia subscale and Sleep architecture parameters was done with the help of Kruskal Wallis test. Correlation of HAM-D Insomnia Subscale with Polysomnography was done with Pearson Correlation Coefficient. p value less than 0.05 was taken as significant level.

**RESULTS**

The results of the study are discussed with the help of tables below. The range of the age group was 22 - 46 years with mean age of 31.28 years and standard deviation of 5.56.

As per ICD-10 DCR, 16.3% patients were of mild depression, 62.8% moderate and remaining i.e. 20.09% were of severe depression. Severity classification as per BDI score revealed, 76.74% moderate and remaining 23.26% falling in severe depression category. Median value for BDI score before treatment was 24 and after treatment was 5. This was statistically significant with a p value <0.001. Median value for HAM-D insomnia subscale score before treatment was 3 and after treatment was 0 (Table 1). This also was statistically significant with a p value <0.001.

Table 2 illustrates the median value for Total Sleep time before treatment was 278 minutes and after treatment was 320 minutes. This was statistically significant with a p value <0.001. Median value for Sleep Efficiency before treatment was 67.9% and after treatment was 76.5%. This was statistically significant with a p value <0.001. Median value for Sleep Latency before treatment was 26.5 minutes and after treatment was 20.0 minutes. This was statistically not significant as p value was 0.322. Median value for Wake After Sleep Onset before treatment was 114.25 minutes and after treatment was 89 minutes. This was statistically significant as p value <0.001. Median value for Total Wake Time before treatment was 130 minutes and after treatment was 100.50 minutes. This was statistically significant as p value <0.001. Median value for Percentage Wake Time before treatment was 32.1% and after treatment was 27.3%. This was statistically significant as p value <0.001.

| Table 1: BDI and HAM-D Insomnia subscale Score. |
|-------------------------------------------------|
| **Before treatment** | **After treatment** | **Z** | **p value** |
|----------------------|--------------------|-------|-------------|
| **BDI** | Mean | Median | SD | Mean | Median | SD | -5.716 | <0.001 |
| 26.08 | 24.00 | 7.33 | 4.98 | 5.00 | 2.44 | | |
| **HAM-D Insomnia Subscale** | 3.40 | 3.00 | 1.12 | 0.00 | 0.00 | 0.00 | -5.768 | <0.001 |

| Table 2: Sleep Architecture changes before and after treatment. |
|-------------------------------------------------|
| **Before treatment** | **After treatment** | **Z** | **p value** |
|----------------------|--------------------|-------|-------------|
| **Total Sleep Time** | Median | SD | Median | SD | -4.372 | <0.001 |
| 278.00 | 93.93 | 320.00 | 43.12 | | |
| **Sleep Efficiency** | 67.90 | 20.34 | 76.50 | 9.18 | -4.735 | <0.001 |
| **Sleep Latency** | 26.50 | 25.34 | 20.00 | 14.13 | -0.991 | 0.322 |
| **Wake After Sleep Onset** | 114.25 | 93.18 | 89.00 | 48.28 | -4.215 | <0.001 |
| **Total Wake Time** | 130.00 | 94.08 | 100.50 | 46.26 | -4.553 | <0.001 |
| **% Wake Time** | 32.10 | 20.52 | 27.27 | 9.60 | -4.662 | <0.001 |
| **N1 %** | 6.40 | 14.91 | 6.00 | 6.05 | -1.740 | 0.082 |
| **N2 %** | 31.90 | 16.48 | 28.50 | 10.59 | -0.870 | 0.385 |
| **REM %** | 39.00 | 19.97 | 42.50 | 12.96 | -0.906 | 0.365 |
| **N1 Latency** | 15.20 | 11.57 | 23.00 | 14.74 | -2.731 | 0.006 |
| **N2 Latency** | 1.00 | 28.10 | 1.00 | 1.52 | -2.633 | 0.008 |
| **N3 Latency** | 2.00 | 32.51 | 3.00 | 4.19 | -1.006 | 0.314 |
| **REM Latency** | 9.50 | 45.41 | 16.50 | 10.43 | -0.036 | 0.971 |
| **Total Sleep Time** | 82.00 | 86.13 | 120.00 | 50.67 | -0.072 | 0.942 |
The antidepressant medicines prescribed during our study were Escitalopram, Fluoxetine, Paroxetine, Sertraline and Mirtazapine (88.4% of the patients were prescribed SSRIs and 11.6% Mirtazapine). This prescription pattern was consistent with a recent multicentric study in India in which, 194 (62.2%) out of 312 patients were prescribed selective serotonin reuptake inhibitors (SSRIs).\textsuperscript{21}

In table 1, BDI score before treatment had a median score of 24, which reduced to a median score of 5 post treatment (p<0.0001). Improvement in BDI to less than 9 was also a criterion of study, which indicated remission. Similarly, HAMD Insomnia subscale score before treatment had maximum value of 6 and minimum 2 with median 3, mean of 3.40, and SD 1.12. (Table 1). After treatment, all the values were 0 as it was one of the criteria for assessing sleep improvement after treatment (Table 1). This also was statistically significant with a p value <0.001. This statistically significant improvement in HAMD Insomnia subscale after treatment with antidepressants was consistent with multiple other studies on effect of antidepressants on sleep.\textsuperscript{22,24}

Table 2 enumerates the sleep architecture before and after treatment. The median value of Total sleep time (TST) before treatment was 278 minutes, which increased to a median value of 320 minutes (p value of <0.0001). Pillai et al and Baglioni et al found similar findings with increase in total sleep time after treatment with antidepressants in two different meta-analyses.\textsuperscript{2,25}

The median value of Sleep efficiency before treatment was 67.9 %, which after treatment improved to a median value of 76.5% (p<0.0001), thus signifying that treatment of depression had significantly improved sleep efficiency (Table 2). Wichniak and Wierzbicka found similar results with increase in sleep continuity (sleep efficiency and total sleep time) after treatment with antidepressants.\textsuperscript{17}

Sleep Latency had improved after the treatment (Table 2), however the results were not statistically significant (p=0.322). Statistically significant improvement post treatment was found in Wake After Sleep Onset (p value <0.001), Total Wake Time (p value <0.001) and Percentage Wake Time (p value <0.001). Our study also observed reduction in N1 and N2 stages of sleep and increase in N3 stage of sleep, although these findings
were statistically not significant (Table 2). These findings were consistent with multiple other studies, which have shown that all antidepressants improve sleep parameters over long term despite the fact that some of them may impair sleep initially due to the activating effects.17,26

Effective treatment with antidepressants increases REM latency and suppresses REM sleep, however in our study, REM% before treatment had median value of 15.2% (Table 2) and after treatment had median value of 23%, (p value= 0.006) which could be attributed to activating effects of predominantly used SSRIs’s (88.4% of the patients were prescribed SSRIs and 11.6% Mirtazapine) over a short duration of time.26 Median value for REM latency before treatment was 82 minute and after treatment was 120 minute. This finding of increased REM Latency was similar to most other sleep studies, however results in this study were not statistically significant (p =0.942).17,25,26

In table 3, objective findings of sleep disturbances are correlated with perceived sleep disturbances assessed by HAMD Insomnia subscale using Pearson correlation coefficient. A strong correlation was noted between perceived sleep disturbances and Total sleep time (Table 3). A moderately strong correlation between the two was seen with Sleep efficiency, Wake after sleep onset, Total wake time and N2%. A weak correlation was noted between perceived sleep disturbances and Percentage Wake Time, N3% and N1 Latency (Table 3). In a study by Vitiello and Larsen consisting of large group of healthy men (150) and women (95), to understand the relationship between self-reported subjective and objectively measured sleep quality, results showed a considerable correspondence between subjective and objective sleep quality for men but not for women, despite women more frequently endorsing the presence of significant sleep disturbance.27 This finding coincides with our study, which could be attributed to all male patients in our study group. However, Some studies have reported significant differences between subjective and objective measures. A pilot study conducted by Farahani DM et al did not find any significant correlation between perceived sleep disturbances and PSG findings in depression patients.28 In another study by Hebert and Fullum, it was found that self-reported sleep disturbances in a group of chronic tinnitus patients, complaints did not correlate with objective polysomnographic assessments of their sleep.29 Majer et al, in a cohort of patients with chronic fatigue syndrome, reported sleep problems significantly more often than control subjects.30 Yet, when measured objectively, these parameters and sleep architecture did not differ between the two groups.

In view of the dissenting findings, present evidence in this area is somewhat inconsistent. Moreover, such resemblances/differences can be largely disparate in various populations; therefore, the research results obtained with specific populations cannot be completely generalized. Hence, in an idealistic scenario, a concurrent use of objective and subjective sleep measures could provide more valid and reliable information of the patient’s sleep health.

CONCLUSION

Antidepressant treatment effectively improves sleep architecture in Depressive disorder and HAM-D Insomnia subscale correlates with objective findings of Total sleep time, Sleep Efficiency, Wake After Sleep Onset, Total Wake Time and duration of N2 stage of NREM. Hence, HAM-D insomnia subscale being a simple and inexpensive tool can be a used as a screening tool, especially in the OPD setting.

ACKNOWLEDGEMENTS

Authors would like to thank all the subjects who consented to participate in this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Allada R, Siegel J. Unearthing the Phylogenetic Roots of Sleep. Current Biol. 2008;18(15):R670-R9.
2. Hirshkowitz M. Normal human sleep: an overview. Med clin North America. 2004;88(3):551-65.
3. Harding K, Feldman M. Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. J Am Acad Child Adolesc Psychiatr. 2008;47(4):473-4.
4. Baglioni C, Novoska S, Regen W, Spiegelhalder K, Feige B, Nissen C, et al. Sleep and mental disorders: a meta-analysis of polysomnographic research. Psychol Bull. 2016;142:969-90.
5. Bixler EO, Vgontzas AN, Lin HM, Calhoun SL, Vela-Bueno A, Kales A. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. J Clin Endocrinol Metab. 2005;90:4510-5.
6. Hohagen F, Rink K, Kappler C, Schramm E, Riemann D, Weyerer S, et al. Prevalence and treatment of insomnia in general practice. A longitudinal study. Eur Arch Psychiatry Clin Neurosci. 1993;242:329-36.
7. Deldin P, Phillips L, Thomas R. A preliminary study of sleep-disordered breathing in major depressive disorder. Sleep Med. 2006;7(2):131-9.
8. Ford D. Epidemiologic Study of Sleep Disturbances and Psychiatric Disorders. JAMA. 1989;262(11):1479-84.
9. Kurtis MM, Balestrino R, Rodriguez-Blazquez C, Forjaz MJ, Martinez-Martin P. A review of scales to evaluate sleep disturbances in movement disorders. Frontiers Neurol. 2018 May 29;9:369.
10. Gutierrez CT, Lomeli HA, Reyes RE, de la Peña FR, Pérez-Olmos I, Benavides CM, et al. Sleep evaluation scales and questionnaires: a review. Actas Españolas de Psiquiatría. 2008;36(1):50-9.

11. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research, World Health Organization; 1993.

12. Joe S, Woolley ME, Brown GK, Ghahramanlou-Holloway M, Beck AT. Psychometric properties of the Beck Depression Inventory–II in low-income, African American suicide attempters. J Personal Assess. 2008 Aug 20;90(5):521-3.

13. Rohan KJ, Rough JN, Evans M, Ho SY, Meyerhoff J, Roberts LM, et al. A protocol for the Hamilton rating scale for depression: item scoring rules, rater training, and outcome accuracy with data on its application in a clinical trial. J Affective Disorders. 2016 Aug 1;200:111-8.

14. Mottram P, Wilson K, Copeland J. Validation of the Hamilton Depression Rating Scale and Montgomery and Asberg Rating Scales in terms of AGECAT depression cases. Int J Geriatric Psychiatry. 2000 Dec;15(12):1113-9.

15. Todorova KS, Velikova VS. The validity of the Hamilton depression rating scale as a screening and diagnostic instrument for depression in patients with epilepsy. J IMAB—Annual Proceeding Scientific Papers. 2012 Oct 23;18(3):305-7.

16. Shahid A, Wilkinson K, Marcu S, Shapiro CM. Hamilton Rating Scale for Depression (HAM-D). InSTOP, THAT and One Hundred Other Sleep Scales. New York: Springer; 2011:187-190

17. Wichniak A, Wierzbicka A, Walęcka M, Jernajczyk W. Effects of antidepressants on sleep. Current psychiatry reports. 2017 Sep 1;19(9):63.

18. Mccall W, Reboussin B, Cohen W. Subjective measurement of insomnia and quality of life in depressed inpatients. J Sleep Res. 2000;9(1):43-8

19. Charan J, Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research. Indian J Psychiat Med. 2013;35(2):121-6.

20. Wichniak A, Wierzbicka A, Jernajczyk W. Sleep as a biomarker for depression. Int Rev Psychiatry. 2013;25:632-45.

21. Tripathi A, Avasthi A, Desousa A, Bhagabati D, Shah N, Kallivayalil RA, et al. Prescription pattern of antidepressants in five tertiary care psychiatric centres of India. Indian J Med Res. 2016 Apr;143(4):507.

22. Neckelmann D, Bjorvatn B, Bjørkum A, Ursin R. Citalopram: differential sleep/wake and EEG power spectrum effects after single dose and chronic administration. Behavioural Brain Res. 1996;79(1-2):183-92.

23. Vitas V, Appelberg B, Rimón R, Selvaratnam J. The effect of fluoxetine on sleep. International Clinical Psychopharmacology. 1994;9(3):203-6.

24. Oberndorfer S, Saletu-Zyhlarz G, Saletu B. Effects of Selective Serotonin Reuptake Inhibitors on Objective and Subjective Sleep Quality. Neuropsychobiol. 2000;42(2):69-81.

25. Pillai V, Kalmbach D, Ciesla J. A Meta-Analysis of Electroencephalographic Sleep in Depression: Evidence for Genetic Biomarkers. Biol Psychiatry. 2011;70(10):912-9.

26. Wilson S, Argyropoulos S. Antidepressants and sleep: a qualitative review of the literature. Drugs. 2005; 65:927-47.

27. Vitiello MV, Larsen LH, Moe KE. Age-related sleep change: gender and estrogen effects on the subjective–objective sleep quality relationships of healthy, noncomplaining older men and women. J Psychosomatic Res. 2004 May 1;56(5):503-10.

28. Moshkani Farahani D, Tavallaie A, Vahedi E, Rezaie Amaram P, Naderi Z, Talae A. The Relationship between Perceived Sleep Quality, Polysomnographic Measures and Depressive Symptoms in Chemically-Injured Veterans: A Pilot Study. Iran J Psychiatry. 2014;9(3):169-74.

29. Hebert S, Fullum S, Carrier J. Polysomnographic and quantitative electroencephalographic correlates of subjective sleep complaints in chronic tinnitus. J Sleep Res. 2011 Mar; 20(1p1):38-44.

30. Majer M, Jones JF, Unger ER, Youngblood LS, Decker MJ, Gurbaxani B, et al. Perception versus polysomnographic assessment of sleep in CFS and non-fatigued control subjects: results from a population-based study. BMC Neurol. 2007 Dec;7(1):40.

Cite this article as: Ingole G, Dhillon HS, Yadav B. Study of correlation between perceived sleep disturbances in depressed patients with objective changes in sleep architecture using polysomnography before and after antidepressant therapy. Int J Res Med Sci 2020;8:2551-6.