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TO STUDY THE SLEEP ARCHITECTURE IN TREATMENT NAÏVE DEPRESSED PATIENTS WITH THE HELP OF POLYSOMNOGRAPHY BEFORE AND AFTER TREATMENT

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ABSTRACT

Background: A prospective cohort study to analyze the sleep architecture in treatment naïve depressed patients with the help of polysomnography before and after treatment. **Methods**: Patients were diagnosed for Depressive episode based on ICD-10 DCR. Psychometry, Beck Depressive inventory (BDI) was applied on Day 1 of admission. Polysomnography was conducted on Day 03 of admission after allowing patient to get accustomed to ward environment. Antidepressant treatment was started post Polysomnography. Post remission as indicated by adequate trial of antidepressants for 08 weeks and BDI score ≤09, Polysomnography was repeated. Statistical analysis was performed using Shapiro Wilk test, Kruskal Wallis test, Pearson correlation coefficient. **Results**: This study has shown positive findings (improvement) in terms of Total Sleep Time, Sleep Efficiency, Wake After Sleep Onset, Percentage Wake Time and these findings are statistically significant. **Conclusion**: Antidepressant treatment effectively improves sleep architecture in Depressive disorder and Polysomnography can become a useful tool to understand the course of illness and assess response.

KEYWORDS: Antidepressants, Sleep Architecture, Depression, Polysomnography.

INTRODUCTION

Sleep plays an important role in human body, allowing it to relax, restore and revitalize body, mind, and emotions. Quality sleep is as important as nutrition or exercise in maintaining overall health.[1] Sleep disturbances are widespread in psychiatric disorders, and the interaction is complex. Hence, sleep disturbances 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.[2] These sleep disturbances cause significant distress and many depressed individuals report that sleep problems are the sole most debilitating feature of their disorder.[3] Polysomnography (PSG) research has recognized that besides disturbances of sleep continuity, depression is interrelated with multiple other sleep distortions. Increased REM density, shortened REM latency and increased REM sleep duration are well-known to be likely biological markers of depression which might help us to foresee relapse and recurrence.[4,5] Currently, REM sleep disturbances are considered to be markers or "true" endophenotypes of Depression.[5] Effective pharmacologic management of the mood disorders does not always dissipate insomnia; in fact, less than 20% of full responders to antidepressants are free of every symptom and nearly half the responders have persistent sleep disturbances and changes in sleep architecture.[6]

There is scarcity of studies on impairment of sleep architecture in depression and the relative importance of improvement in the same with respect to overall improvement in depression and hence this study was planned.

MATERIALS AND METHODS

Inclusion criterion

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

Exclusion criterion

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

METHODOLOGY

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.[7]

On day 1 of admission, The Beck Depression Inventory-II (1996) (BDI)[8] which is a self-administered design was applied. The inventory rates symptoms of depression in terms of severity on a scale from 0 to 3 based on the 21 specific items. Patients were kept drug free till 3rd day of admission. Polysomnography was conducted on day 3 after allowing patients to get accustomed to ward environment. All patients who completed study were followed up till 8 weeks post treatment. Polysomnography was conducted after achieving full remission as indicated by BDI score of 9 or less. The sleep parametres[9] studied were as follows-

a. **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.

b. **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.

c. **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.

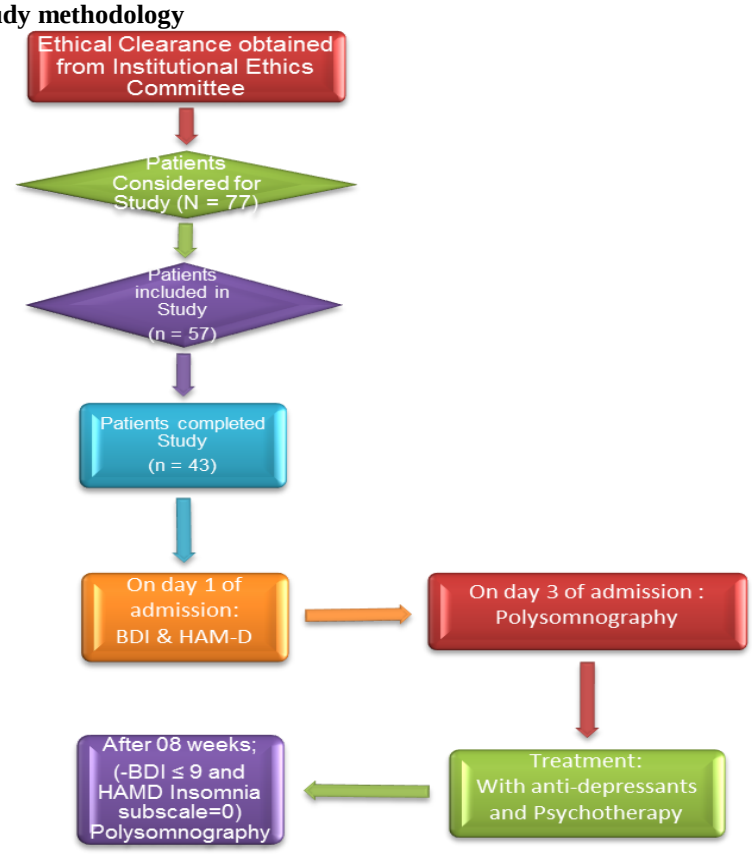
d. **Wake After Sleep Onset** (WASO)- The total time scored as awake occurring after the sleep onset. Typically WASO should not exceed 30 min.

e. **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.

f. **REM % -** Total duration in minutes and as percentage relative to total sleep time of sleep stage REM. Normal values are 20–25%.

g. **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

Flow Chart-1 study methodology



Statistical Analysis

Data analysis was done with the help of SPSS Software version 21. Considering 90% prevalence[10] of sleep disturbances in Depression and 10% variation, sample size[11] 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 and Sleep architecture parameters was done with the help of Kruskal Wallis test. 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.

Table 1 - Comparison of Severity of Depression based on ICD 10 DCR Criteria and BDI Score.

Severity	ICD-10 DCR	BDI
Mild	07 (16.3%)	0 (0%)
Moderate	27 (62.8%)	33 (76.74%)
Severe	09 (20.9%)	10 (23.26%)
Total	100%	100%

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.

Table 2- Treatment given.

Medicines	Frequency	Percentage
Escitalopram	4	9.3%
Fluoxetine	11	25.6%
Mirtazapine	5	11.6%
Paroxetine	5	11.6%
Sertraline	18	41.9%
Total	43	100.0%

Sertraline was the most commonly prescribed medicine (41.9%) and Escitalopram was least commonly prescribed antidepressant (9.3%).

Table 3- BDI score before and after treatment.

	N=43	Minimum	Maximum	Median	Mean	SD
BDI before treatment	43	18	43	**24**	26.07	7.33
BDI after treatment	43	0	8	**5**	4.98	2.44

Median value for BDI score before treatment was 24 and after treatment was 5. This was statistically significant with a p value <0.001.

Table 4 - Sleep Architecture changes before and after treatment.

	Before Treatment			After Treatment			Z	p value
	Mean	Median	SD	Mean	Median	SD		
Total Sleep Time	263.08	**279.00**	93.93	325.65	**320.00**	43.12	-4.372	<0.001
Sleep Efficiency	60.94	**67.90**	20.34	76.19	**76.50**	9.18	-4.735	<0.001
Sleep Latency	28.51	**26.50**	25.34	21.33	**20.00**	14.13	-0.991	0.322
Wake After Sleep Onset	143.89	**114.50**	93.18	80.79	**89.00**	48.28	-4.215	<0.001
Total Wake Time	169.53	**130.00**	94.08	99.05	**100.00**	46.26	-4.553	<0.001
% Wake Time	38.72	**32.10**	20.52	24.09	**27.27**	9.60	-4.662	<0.001
N1 %	12.88	**6.40**	14.91	7.93	**6.00**	6.05	-1.740	0.082
N2 %	36.56	**31.90**	16.48	31.46	**28.50**	10.59	-0.870	0.385
N3 %	32.65	**39.00**	19.97	40.04	**42.50**	12.96	-0.906	0.365
REM %	18.54	**15.20**	11.57	24.53	**23.00**	14.74	-2.731	0.006
N1 Latency	12.57	**1.00**	28.10	1.42	**1.00**	1.52	-2.633	0.008
N2 Latency	9.94	**2.00**	32.51	4.10	**3.00**	4.19	-1.006	0.314
N3 Latency	27.87	**9.50**	45.41	16.44	**16.50**	10.43	-0.036	0.971

REM Latency	118.80	**82.00**	86.13	111.67	**120.00**	50.67	-0.072	0.942

Median value for Total Sleep time before treatment was 279 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 114.5 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 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.

Median value for Stage N1 sleep percentage before treatment was 6.4% and after treatment was 6% (p value 0.082). Median value for Stage N2% before treatment was 31.9% and after treatment was 28.5% (p value 0.385). Median value for Stage N3% before treatment was 39% and after treatment was 42.5% (p value 0.365). Median value for REM % before treatment was 15.2% and after treatment was 23%. This was statistically significant as p value was 0.006.

Median value for N1 latency before treatment was 1 minute and after treatment was 1 minute. This was statistically significant as p value 0.008. Median value for N2 latency before treatment was 2 minute and after treatment was 3 minute (p value 0.314). Median value for N3 latency before treatment was 9.5 minute and after treatment was 16.5 minute (p value was 0.971).

Median value for REM latency before treatment was 82 minute and after treatment was 120 minute (p value was 0.942).

DISCUSSION

In table no. 1, out of total 43 patients, 16.2% were classified into mild depression, 62.7% were moderate and remaining i.e. 20.1% were severe depression as based on ICD 10 DCR criteria for depressive episode. However, based on BDI score, 33 were of moderate depression and 10 were having severe depression and none were in mild depression category. This discrepancy in finding could be due to subjective nature of BDI.[12]

Table 2 enumerates medicines prescribed during the study were Escitalopram, Fluoxetine, Paroxetine, Sertraline and Mirtazapine (88.4% of the patients were prescribed SSRIs and 11.6% Mirtazapine). Out of the SSRIs, Sertraline was the most commonly prescribed medicine (41.9%) and Escitalopram was least commonly prescribed antidepressant (9.3%).

In table no. 3, BDI score before treatment had maximum value of 43 and minimum 18 with median 24, mean of 26.07 and SD 7.33. BDI score after treatment had maximum value of 8 and minimum 0 with median 5, mean of 4.98 and SD 2.44. These results were statistically significant (p<0.0001). Improvement in BDI to less than 9 was also a criterion of study, which indicated remission.

Table no. 4 enumerates the sleep architecture before and after treatment. Total sleep time (TST) before treatment had maximum value of 403 minutes and minimum 60.5 with median 279 minutes, mean of 263.08 and SD 93.93. Total sleep time after treatment had maximum value of 402 minutes and minimum 260 with median 320 minutes, mean of 325.65 and SD 43.12. This change in TST before and after was statistically significant with a P value of <0.0001. Pillai[2] et al and Baglioni[5] et al found similar findings with increase in total sleep time after treatment with antidepressants in two different meta-analyses.

Sleep efficiency before treatment had maximum value of 81.8% and minimum 14% with median 67.9%, mean of 60.94 and SD 20.34. Sleep efficiency after treatment had maximum value of 92.4% and minimum 60.2% with median 76.5%, mean of 76.19 and SD 9.18. Change in sleep efficiency was statistically significant (p<0.0001), thus signifying that treatment of depression had significantly improved sleep efficiency. Wichniak and Wierzbicka found similar results with increase in sleep continuity[9] (sleep efficiency and total sleep time) after treatment with antidepressants.

Sleep Latency had improved after the treatment 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. These results were in accordance with 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.[9,13,14,15]

Effective treatment with antidepressants increases REM latency and suppresses REM sleep[13], however in our study, REM% before treatment had median value of 15.2% and after treatment had median value of 23%, (P value= 0.006) which could be attributed to activating effects of predominantly used SSRI's (88.4% of the patients were prescribed SSRIs and 11.6% Mirtazapine) over a short duration of time.

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[5,9,13,16] however results in our study were not statistically significant (p =0.942).

Conflicts of interest

All authors have none to declare.

CONCLUSION

1. Although various means are available for classifying severity of depression and response to treatment like BDI, HAMD; Polysomnography can become a useful objective tool to understand the course of illness and assessing response.
2. Antidepressants treatment effectively improves sleep architecture, however transient initial sleep disturbances[15,17] (Insomnia as well as somnolence) during treatment are generally encountered in clinical practice.

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