

Effect of Alprazolam Versus Pregabalin on Sleep Quality in Patients of Chronic Kidney Disease

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ABSTRACT

Objective: To assess sleep quality in patients of Chronic Kidney Disease using Pittsburgh Sleep Quality Index score and to compare the effects of Alprazolam and Pregabalin in patients having poor sleep quality.

Study Design: Quasi-experimental study.

Place and Duration of Study: Nephrology Department of Combined Military Hospital, Karachi Pakistan, from Oct 2021 to Mar 2022.

Methodology: A total of 127 individuals coming to Nephrology Department diagnosed with chronic kidney disease were included. Sleep quality was assessed using Pittsburgh Sleep Quality Index score. Age, gender, duration of Chronic Kidney Disease and history of Diabetes, Hypertension and Cardiovascular disease were recorded. Those individuals having poor sleep quality were started randomly on either Alprazolam 0.5 mg and Pregabalin 75 mg daily. Effects of these drugs were assessed by determining Pittsburgh Sleep Quality Index two months after administration of these drugs.

Results: Out of 127 individuals, 82(64.5%) had poor quality sleep characterized by Pittsburgh Sleep Quality Index ≥ 5 at the time of presentation. Among them, 40(48.7%) were male and 42(51.3%) were female, 46(56.1%) had history of Diabetes Mellitus, 48(58.5%) had history of Hypertension and 31(37.8%) had history of Cardiovascular disease. Forty-one were started on Alprazolam and 41 on Pregabalin. No statistically significant difference was found in the sleep quality between groups at the end of two months of regular treatment (p -value =0.088).

Conclusion: Sleep disturbances are present in majority of the patients of Chronic Kidney Disease. Both Alprazolam and Pregabalin can be used to treat sleep related disorders in these patients.

Keywords: Chronic kidney disease, Hemodialysis, Sleep quality.

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INTRODUCTION

Chronic Kidney Disease (CKD) is among the most common chronic illnesses globally, with sleep disturbance being a relatively more common complication of CKD.¹ The high incidence of sleep disturbance with CKD has been confirmed both in adults as well as in young children, with an estimated prevalence of 40 to 80%.²

The pathogenesis and progression of sleep disturbance in patients of CKD has long been studied and attributed to different factors, including pruritic, elevated systolic blood pressure and C-reactive protein, Vitamin D deficiency and deranged parathyroid hormone levels.^{3,4}

Sleep disturbance is well known to frequently compromise quality of life in our patients of CKD.⁵

The relationship between sleep disturbance and other complications of CKD like deterioration in the course of Ischemic Heart Disease (IHD) has also been studied extensively.^{6,7} Although not very clearly elaborated in literature, poor sleep can lead to accelerated course of CKD as well.⁸ Apart from these major health implications, poor sleep quality is also associated with some less severe complications like feeling of excessive fatigue and poor exercise tolerance.⁹ Various screening tools have been devised to determine sleep quality. Among them Pittsburgh Sleep Quality Index (PSQI) is one of the most widely used questionnaire for determining sleep quality. In a study done in a tertiary care hospital in Rawalpindi it was found that 68.6% of patients of chronic kidney disease who are on hemodialysis have poor sleep quality.¹⁰

Due to a paucity of similar studies in our setup, we aimed to determine the PSQI in patients of chronic kidney disease in both who are dialysis dependent and non-dialysis dependent, and also compared the

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effects in improving the sleep quality by Alprazolam and Pregabalin in those patients who had poor sleep quality.

METHODOLOGY

The quasi-experimental study was conducted in Nephrology Department of Combined Military Hospital (CMH), Karachi Pakistan, from October 2021 to March 2022 after approval from Hospital Ethical Review Committee (letter no. 83/2021/Trg/ERC). Sample size was calculated as per World Health Organization (WHO) sample size calculator, with previous prevalence of CKD patients having poor sleep quality being 68.6%.¹⁰ Non-probability, consecutive sampling technique was utilized.

Inclusion Criteria: Patients of either gender over the age of 12 years presenting to Nephrology department having CKD defined as having estimated Glomerular Filtration Rate (eGFR) <60 ml/min/1.73 m² for 3 or more months, were considered for study.

Exclusion Criteria: All those patients with cognitive impairment, permanent physical disability, active psychosis and major depressive illness, already on sleep medications, malignancy and those not giving consent to be included in the study were excluded.

Informed consent was taken from all patients. Detailed history was taken from all the patients in the study. Age of the patient, gender, duration of CKD, history of hypertension, diabetes mellitus and cardiovascular disease (CVD) and whether on maintenance hemodialysis or not, were noted.

PSQI was used to assess the sleep quality of the patients undergoing hemodialysis. PSQI is a self-rated questionnaire which is used to assess quality of sleep and associated disturbances during sleep. Nineteen individual items are assessed which combine to generate seven “component” scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. These scores are then combined to produce one combined score which ranges from zero to 21. A score of 5 or greater was considered as “poor” sleep quality.^{11,12} Those patients who had poor sleep quality were started on either tablet Alprazolam 0.5 mg daily at bedtime or tablet Pregabalin 75 mg daily at bedtime on random basis (Figure). Patients were continued on these medications and change in PSQI was noted following 2 months of treatment upon follow-up visits.

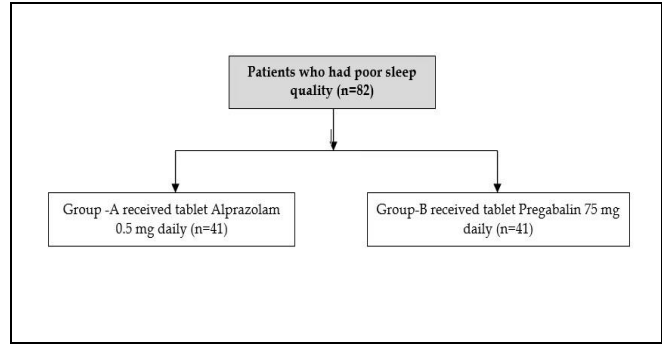


Figure: Patient Flow Diagram

Data was analysed using Statistical Package for Social Sciences (SPSS) version 23. Quantitative variables, including age, PSQI and change in PSQI following intervention, were presented as mean and standard deviation. Frequencies and percentages were calculated for variables like gender, previous history of hypertension, diabetes and CVD. Sleep Quality among different groups was assessed using Paired Sample t-test. Comparison between outcomes of two groups was made using Chi-Square test. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 127 individuals were included in the study out of which 68(53.5%) were male and 59(46.5%) were female. Overall, 70(55.1%) individuals had history of Diabetes Mellitus, 74(58.3%) individuals had history of Hypertension and 53(41.7%) individuals had history of CVD. The mean age of the individuals included in the study was 59.18±13.207 years, mean total years of being diagnosed as CKD were 2.05±1.096 and mean PSQI at the time of presentation was 6.33±3.392. A total of 82(64.5%) individuals had poor quality sleep characterized by PSQI ≥5 at the time of presentation (Table-I). Among these 82 individuals, 40(48.7%) were male and 42(51.3%) were female (*p*-value =0.094), 46(56.1%) had history of Diabetes Mellitus (*p*-value =0.122), 48(58.5%) had history of Hypertension (*p*-value =0.304) and 31(37.8%) had history of CVD (*p*-value =0.001) (Table-II).

Among 82 individuals who had poor sleep quality on initial presentation, 41(50%) were started on tablet Alprazolam and 41(50%) were started on tablet Pregabalin. Mean PSQI in these individuals before start of medications was 8.13±2.702, whereas mean PSQI after two months of these medications was 5.59±2.572. Mean PSQI pre-medication in Alprazolam group was 8.02±2.761 whereas mean PSQI post medication in this group was 5.32±2.444. Mean PSQI

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pre-medication in Pregabalin group was 8.24 ± 2.672 whereas mean PSQI post medication in this group was 5.85 ± 2.698 . In the Alprazolam group, 20(48.7%) individuals had normal sleep quality at two months of treatment and in the Pregabalin group, 13(31.7%) individuals had normal sleep quality after two months of regular treatment (Table-III). However, the difference between improvement of sleep quality between two groups was not significant (p -value =0.088).

Table-I: Baseline Characteristics of Patients (n=127)

Characteristics		n(%)
Gender	Male	68(53.5%)
	Female	59(46.5%)
Previous history of Diabetes Mellitus	Yes	70(55.1%)
	No	57(44.9%)
Previous history of Hypertension	Yes	74(58.3%)
	No	53(41.7%)
Previous history of CVD	Yes	53(41.7%)
	No	74(58.3%)
Sleep Quality	Poor (PSQI ≥ 5)	82(64.5%)
	Good (PSQI < 5)	45(35.5%)
Age (Mean \pm SD)		59.18 \pm 13.21
Years since diagnosed as CKD (Mean \pm SD)		2.05 \pm 1.10
PSQI on Initial Presentation (Mean \pm SD)		6.33 \pm 3.39

Table-II: Effects of Baseline Features on Sleep Quality (n=127)

Characteristic	Poor Sleep Quality (PSQI ≥ 5) n(%)	Good Sleep Quality (PSQI < 5) n(%)	p -value
Gender			
Male	40(48.7%)	28(62.2%)	0.094
Female	42(51.3%)	17(37.8%)	
Previous History of Diabetes Mellitus			
Yes	46(56.1%)	24(53.3%)	0.122
No	36(43.9%)	21(46.7%)	
Previous History of Hypertension			
Yes	48(58.5%)	26(57.8%)	0.304
No	34(41.5%)	19(42.2%)	
Previous History of CVD			
Yes	31(37.8%)	22(48.9%)	0.001
No	51(62.2%)	23(51.1%)	

Table-III: Study Outcomes in Study Groups (n=127)

Outcomes		Alprazolam Group (Mean \pm SD)	Pregabalin Group (Mean \pm SD)	p -value
Mean PSQI Pre-medication		8.02 \pm 2.761	8.24 \pm 2.672	<0.001
Mean PSQI Post-medication		5.32 \pm 2.444	5.85 \pm 2.698	<0.001
Sleep Quality	Good	20(48.7%)	13(31.7%)	0.088
	Poor	21(51.3%)	28(68.3%)	

DISCUSSION

CKD has multisystem effects leading to significant psychological, physical and health related issues. A variety of sleep disorders have been associated with CKD, including insomnia, sleep related breathing disorders like central sleep apnoea, daytime hyper-somnolence, hypoventilation, disturbances of sleep-wake rhythm cycle, parasomnias and daytime movement disorder like restless leg syndrome.¹¹ These sleep related issues not only lead to poor quality of life, but they are also associated with increased morbidity and mortality in CKD.¹² In our study, we assessed sleep quality of individuals suffering from CKD and included patients who were either undergoing hemodialysis or were on conservative management. PSQI is a scoring tool used to assess sleep quality worldwide. We also used the same scoring tool in the study. Our study found that 64.5% individuals had poor sleep quality characterized by PSQI ≥ 5 , which was comparable to studies by Shafi *et al.*¹¹ and Grandner *et al.*¹² which showed that 66% and 65.8% individuals respectively had poor sleep quality. In our study mean PSQI at the time of presentation was 6.33 ± 3.39 , which was similar to median PSQI score of 6 in study of Nigam *et al.*¹³ however, mean PSQI in study by Maung *et al.*¹⁴ was 11.4 ± 3.9 which was a little higher than our study. Among comorbid factors presence of CVD was significantly associated with sleep quality of the patients (p -value =0.001) similar to the findings of Mujahid *et al.*¹⁵ The advantage of comparing with these studies is that both of these studies were done in populations group similar to ours.

In our study, we also studied effects of Alprazolam and Pregabalin on sleep outcomes in these patients who have disturbed sleep patterns characterized by a high (≥ 5) PSQI. Alprazolam is an anxiolytic benzodiazepine agonist, widely used world over in various sleep disorders.¹⁶ Pregabalin is a Gamma Amino Butyric Acid (GABA) analog used in treatment of uremic pruritis and neuropathic pain in CKD patients. It is believed that uraemia pruritis is present in around 40% of CKD patients, so effectively treating pruritis also improves sleep quality in hemodialysis dependent CKD patients.¹⁷ Both these drugs can be used to improve sleep quality of the patients in CKD. Although there is no comparable data available, however the effects on quality of life of both Alprazolam and Pregabalin in CKD patients have been studied separately and beneficial outcomes were

found.^{17,18} In our study it was demonstrated that Alprazolam improved PSQI from mean of 8.02±2.761 to 5.32±2.444 post medication with improvement to good sleep quality in 48.7% individuals. Pregabalin also improved mean PSQI from 8.24±2.672 to 5.85±2.698 with improvement to good sleep quality in 31.7% individuals. However, there was no statistically significant difference (*p*-value =0.088) in outcomes of treatment with these two drugs.

We found out that quite high percentage of individuals of CKD have poor sleep quality and thus poor overall quality of life. Both Alprazolam and Pregabalin can be used to improve PSQI and thus sleep quality in these patients. The data is however limited in regards to which drug is preferable in such scenarios so more studies at a larger scale are required to further strengthen our results.

LIMITATION OF STUDY

Data regarding previous use of sleep medications, hemodialysis status and its duration and the socioeconomic status of the patient were not recorded. These factors may also play important role in determining sleep quality of the patients. In the comparison groups, co-morbidities were not considered in determining the effects of those medications.

CONCLUSION:

The study illustrates that sleep disturbances are present in majority of the patients of CKD especially those having long standing disease and CVD. Both Alprazolam and Pregabalin can be used to treat sleep related disorders with variable efficacy and response.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

KM & HWK: Data acquisition, data analysis, critical review, approval of the final version to be published.

UZF & MIK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MZA & GRM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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