Original Article

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Internal Medicine Section

Effect of CPAP Therapy in Improving Daytime Sleepiness in Indian Patients with Moderate and Severe OSA

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ABSTRACT

Introduction: Obstructive Sleep Apnoea (OSA) is a highly prevalent disease and a major public health issue in India. Excessive daytime sleepiness is an almost ubiquitous symptom of OSA. Epworth Sleepiness Scale (ESS) score is a validated objective score to measure the degree of daytime sleepiness. Continuous Positive Airway Pressure (CPAP) therapy has been established as the gold standard treatment modality for OSA patients. A few Indian studies have reported the effectiveness of CPAP therapy in improving ESS scores after 1st month of CPAP use.

Aim: To observe both, short-term (one month) and long-term (Three month) effects of CPAP therapy on ESS scores in moderate to severe OSA patients.

Materials and Methods: The patients complaining of excessive day-time sleepiness, snoring and choking episodes during sleep, consecutively presenting to medicine OPD over a period of 2 years, were subjected to Polysomnography (PSG). Seventy-three patients with apnoea-hypopnea index (AHI) ≥15 were categorised as having moderate to severe forms of OSA (moderate OSA with AHI=15-30 and severe OSA with AHI >30), and were scheduled for an initial trial of CPAP therapy. Forty-seven patients reported good tolerance to CPAP therapy after a trial period of 2 weeks and comprised the final study group. ESS scores in these patients were recorded at the baseline, and after 1st and 3rd month of CPAP therapy, and statistically analysed for significance.

Results: Mean ESS score at the baseline among moderate and severe OSA patients were 13.67±2.29 and 16.56 ±1.87, respectively. ESS score in both these subgroups improved significantly to 11.63±3.79, p=0.022, CI (0.3293-4.0106)} and 14.13 ±3.74, p < 0.001, CI (1.2991-4.5408), respectively after one month of CPAP therapy. Likewise, mean ESS scores among moderate and severe OSA patients improved significantly to 9.84 ±2.97, p = 0.022, CI (0.3293-4.0106) and 12.29 ±3.97, p <0.001, CI (2.9414-6.1385), respectively after three months of CPAP therapy.

Conclusion: The result of the present study shows that CPAP therapy is significantly effective in improving ESS scores in Indian patients having moderate to severe OSA. Benefits in daytime sleepiness were observed after short-term as well as long-term use of CPAP therapy.

Keywords: Epworth sleepiness scale, Hypopnea, Polysomnography

INTRODUCTION

The Obstructive Sleep Apnoea (OSA) is a chronic respiratory disorder. OSA and Obstructive Sleep Apnoea - Hypopnea Syndrome (OSAHS), both are part of the same disease spectrum which is characterised by repetitive narrowing or collapse of the upper airway during sleep when complete and partial obstruction of the airway causes apnoea and hypopnea, respectively. The epidemiological significance of the disease in Indian perspective can be estimated from its high prevalence which approximates 9-13% for OSA and 3-4% for OSAHS in various studies [1,2]. In fact, among the respiratory disorders, the prevalence of OSA is next only to asthma and Chronic Obstructive Pulmonary Disease (COPD), thus making the disease as a major public health issue [3,4]. Epworth Sleepiness Scale (ESS) is a simple questionnaire which is used to indicate the level of daytime sleepiness of individuals [5]. ESS score is a measure of tendency to fall asleep in different situations of routine life and is used as a screening tool for OSA [6]. In other words, ESS score is a measurement of behavioural morbidity associated with OSA. Continuous Positive Airways Pressure (CPAP) therapy is the treatment of choice for OSA. A Cochrane systematic review has shown that CPAP therapy is effective in reducing sleepiness and improving quality of life in cases of moderate and severe OSA [7]. Respecting Indian patients, Goel et al., studied the effects of short-term nasal CPAP therapy in patients of OSAHS and documented significant improvement in exercise capacity and ESS scores after a short follow-up period of 4 weeks [8]. However, whether improvement in ESS scores persist after an extended duration of CPAP therapy needs to be studied. Effects of CPAP therapy on ESS scores after a longer follow-up period have not been adequately studied in Indian population. The present study enrolled OSA cases to observe the change in ESS scores after 1st month and 3rd month of starting CPAP therapy, and thus to determine whether short-term effectiveness of CPAP therapy in improving ESS scores, as already reported in Indian studies, remains sustained after long-term CPAP use or not.

MATERIALS AND METHODS

This prospective cohort study was conducted at 'Department of Medicine' in collaboration with the 'Department of Physiology', at King George's Medical University, Lucknow. All the patients consecutively presenting to the Outpatient Department (OPD), over a period of 2 years (from December 2013 to November 2015), diagnosed as moderate or severe Obstructive Sleep Apnoea (OSA) were included in the study. The institutional ethics committee approved the protocol and informed consent was obtained from the participants.

Patient selection and study group: All the patients complaining of excessive day-time sleepiness, snoring and choking episodes during sleep were subjected to Polysomnography (PSG). Patients with apnoea-hypopnea index (AHI) ≥15 to 30 were categorised as having moderate OSA and those with AHI >30 were categorised as severe OSA. Moderate and severe OSA patients were scheduled for an initial trial of CPAP therapy. The subjects with medical conditions that could interfere with the study procedure or the therapy, including congestive heart failure, renal failure, pulmonary disease, cancer and neuromuscular diseases were excluded from the study. Pregnant women and those having a history of alcoholism also met the exclusion criteria. Seventy-three patients underwent a

CPAP titration study and were put up on a CPAP trial for 2 weeks. Subsequently after two weeks, 47 patients reported to have used the CPAP machine for ≥6 hours per night and rest of the 26 patients reported intolerance. So, these 47 patients comprised the final study group, out of which 24 patients had moderate OSA and 23 had severe OSA. These subjects were assessed at baseline and after a follow-up period of one and three months of CPAP therapy. Each patient's Epworth Sleepiness Scale (ESS) score was noted during the baseline and follow-up visits. The statistical analysis was done using statistical software SPSS for windows (16.0). 'Two sample paired t-test' was used to statistically compare the ESS scores at the baseline and after one and three months of CPAP use. The p-value <0.05 was stated as statistically significant.

RESULTS

Minimum age of a subject in the study group was 27 and maximum was 75 (Mean Age: 50.20). Baseline characteristics of the moderate and severe OSA patients in the study group are shown in [Table/Fig-1].

Epworth Sleepiness Scale (ESS) Score: Mean ESS score at the baseline among moderate and severe OSA patients were 13.67±2.29 and 16.56 ±1.87, respectively. ESS score in both these subgroups improved significantly to 11.63±3.79, p = 0.022, CI (0.3293-4.0106) and 14.13 ±3.74, p < 0.001, CI (1.2991-4.5408), respectively after 1 month of CPAP therapy. Mean ESS score when observed for the combined group of moderate and severe OSA patients was 15.83±3.67 at the baseline, which improved significantly to 13.67 ±3.93, p = 0.002, CI (0.5616-3.5183) after 1 month of CPAP therapy.

On similar lines, mean ESS scores among moderate and severe OSA patients improved significantly to 9.84 ±2.97, p = 0.022, CI (0.3293-4.0106) and 12.29 ±3.97, p < 0.001, CI (2.9414-6.1385), respectively after 3 months of CPAP therapy. Likewise, mean ESS score for the combined group of moderate and severe OSA patients, improved significantly to 11.01 ±3.64, p < 0.001,CI (3.3781-6.0218) after 3 months of CPAP therapy. ESS scores of the patients in moderate and OSA subgroups after 1st and 3rd month of CPAP therapy are shown in [Table/Fig-2].

Duration of nightly use of CPAP machine and ESS scores: Further, moderate and severe OSA patients were each divided into two subgroups on the basis of nightly use of CPAP machine, those having a nightly use of 6-7 hours and those with >7 hours of use. A 18 out of 24 patients of moderate OSA reported to have used CPAP machine for >7 hours per night and 6 patients used the same for

Variable	Moderate OSA	Severe OSA
Number of total subjects	24 M=16,F=8	23 M=15,F=8
Mean age (Years)	48.65	53.50
Mean weight(kg)	68.04	76.65
Mean BMI(kg/m^2)	30.66	31.26
Loud Snoring	17(70.8%)	20(86.9%)
Choking in sleep	17(70.8%)	20(86.9%)
EDS#	18(75%)	23(100.0%)
ESS* score	13.67±2.29	16.56±1.87

[Table/Fig-1]: Baseline characterstics of moderate and severe OSA subjects.
Excessive daytime sleepiness , * Epworth sleepiness scale.

Follow-up	Variable	ESS* (Mean+/-SD)	p-value# (ESS at baseline vs ESS at 1st and 3rd months)	Confidence Interval (CI)
1st month	Moderate OSA	11.63±3.79	0.022	0.3293-4.0106
	Severe OSA	14.13±3.74	<0.001	1.2991-4.5408
3rd month	Moderate OSA	9.84±2.97	0.022	0.3293-4.0106
	Severe OSA	12.29±3.97	<0.001	2.9414-6.1385

[Table/Fig-2]: ESS of moderate and severe OSA subjects at 1st and 3rd months of follow-up., #- Two sample paired t-test *- Epworth sleepiness scale.

Number of hours of overnight CPAP use	Number of patients	p-value# & CI at 1st month	p-value & CI at 3rd month
Moderate OSA			
6-7 hours	6	0.28 (-1.4867-6.6067)	0.25 (-1.1361-6.9038)
>7 hours	18	0.04(0.4290-4.6909)	0.01(0.3215-4.6701)
Severe OSA			
6-7 hours	10	0.009(0.2474-5.5525)	0.004(1.4571-6.6628)
>7 hours	13	<0.001(1.008-5.152)	<0.001(1.1221-6.4989)

[Table/Fig-3]: Nightly use of CPAP machine and ESS scores.
#- Two sample paired t-test

6-7 hours per night, throughout the duration of clinical follow-up. Likewise, 13 out of 23 patients of severe OSA used the CPAP for >7 hours and rest of the 10 patients used it for 6-7 hours. Analysis of ESS scores in these subgroups revealed that moderate OSA patients who used the CPAP machine for 6-7 hours did not show a significant improvement in ESS score, throughout the period of follow-up. On the other hand, moderate OSA patients who used CPAP for more than 7 hours, showed a significant improvement both at 1st (p = 0.04) and 3rd (p = 0.01) month of follow-up. Contrary to the moderate OSA group, severe OSA patients showed a significant improvement in ESS scores in both the subgroups, however, with those using CPAP machine for more than 7 hours overnight showing a better improvement than those using it for 6-7 hours, at both 1st (p < 0.001 vs p = 0.009) and 3rd month(p < 0.001 vs p = 0.004), respectively. ESS scores analysis in these subgroups have been summarized in [Table/Fig-3].

DISCUSSION

Excessive daytime somnolence is a chief symptom in OSA patients. The ESS is a validated scoring method, which was introduced by Murray John which measures the possibility of falling asleep in different situations. It consists of 8 questions, each scored with a degree of severity ranging from 0-3. Sum of the total score is 0-24 [5]. It is easy to administer and currently the most widely used subjective test for sleepiness [9,10].

CPAP therapy has been shown to have significant reduction in daytime sleepiness in OSA patients and thus, has been established as the most effective treatment of OSA [11,12]. In a meta-analysis, Patel et al., revealed that CPAP therapy reduced the ESS score on a mean of 2.9 points more as compared with placebo (p < 0.001). Patients with moderate to severe OSA were shown to have a greater fall in ESS than mild OSA [13]. Among Indian studies, Goel et al., had reported a significant improvement (p < 0.001) in ESS scores in a study group of 15 patients of moderate and severe OSA at 1 month follow-up period on CPAP therapy [8]. On similar lines, in the present study, moderate and severe OSA patients showed a significant improvement in ESS scores after 1st and 3rd month of CPAP therapy. Further, ESS scores in severe OSA subgroup showed a better improvement as compared to moderate OSA subgroup with mean reduction of 2.43 (p < 0.001) points in ESS score vs 2.04 (p = 0.022) in moderate OSA after 1st month and mean reduction of 4.27 (p < 0.001) points in ESS score vs 3.83 (p = 0.022) in moderate OSA after 3rd month of being put on CPAP. However, the fact worth mentioning is that despite significant improvement, ESS scores did not normalize after CPAP therapy. Mean ESS score of both moderate and severe OSA subgroup patients remained above 10 points, after first month of CPAP therapy despite statistically significant improvement. Following the same trend, mean ESS score of severe OSA patients remained above 10 even after 3 months of CPAP therapy, however, the average score of the moderate OSA patients barely managed to be on the normal side, being borderline at 9.92. Thus, it appears that CPAP despite being the gold standard therapy for OSA does not completely reverse the symptoms of excessive daytime sleepiness, at least in

some patients. Similar observations have been reported earlier in a multicentric randomized controlled open label clinical trial in Australia [14]. In our study, the reasons for the same could be several. Firstly, the already high baseline severity of the disease in severe OSA patients, could have led to the failure to achieve normalization of ESS scores, despite significant improvement. Secondly, there is a possibility that despite the patients reporting good compliance, their nightly CPAP use was inadequate. Further, some of the researchers have postulated that hypoxic damage to the brain structures like locus coeruleus, median raphe and forebrain, may result in residual excessive sleepiness despite CPAP therapy [15,16]. Some of the authors have also mentioned about the emergence of central sleep apnoea in patients who are diagnosed as OSA, thus resulting in an inadequate response to CPAP therapy [17]. This mixed picture of OSA and central sleep apnoea has been termed as 'complex sleep apnoea'[17]. However, in our study, emergence of complex sleep apnoea appears to be unlikely, the reason being, we observed a significant improvement in ESS scores in severe OSA patients and it is the same group of patients in which ESS did not normalize. The already high baseline ESS scores in these patients could well explain the failure to achieve normalization in ESS despite significant improvement, considering the fact that if it would have been a complex sleep apnoea pattern, we would probably have not found significant improvement in ESS scores.

Further, in the present study we observed a CPAP dose dependent improvement in moderate OSA patients as patients who used CPAP for >7 hours overnight showed significant improvement in ESS scores which was sustained throughout the duration of therapy. However, patients who used CPAP for 6-7 hours per night did not show significant improvement in ESS scores. However, this observation is limited by the fact that the number of patients using CPAP for 6-7 hours was very small. Unlike the moderate OSA group, all the patients having severe OSA showed a significant improvement in ESS scores throughout the period of therapy. Moreover, those using CPAP for >7 hours were observed to have a more significant improvement in ESS as compared to those using the same for 6-7 hours. This CPAP dose dependent improvement in ESS scores is in agreement with several previous studies [14].

To summarize, the present study reveals that CPAP therapy, which is considered to be the gold standard treatment modality for OSA worldwide, brings significant improvement in daytime sleepiness and ESS scores in Indian patients as well. We observed the improvement in ESS scores after short-term (1st month) and long- term (3rd month) use of CPAP therapy, while the previous Indian studies have studied the same only after short-term use of therapy. Further, the sample size of OSA patients in the current study is significantly larger as compared to the existing Indian studies.

LIMITATION

We acknowledge a few limitations of our study. Firstly, the spectrum of duration of CPAP therapy per night was quite narrow to actually judge the dose-dependent effectiveness of CPAP therapy. We had just two range brackets (6-7 hours and >7 hours) for CPAP use per night, while according to several studies more than 6 hours is adequate duration for CPAP therapy to be effective [18]. So, there is fair amount of possibility, that our results for the dose-dependent CPAP effectiveness may not hold true for a wider range of nightly use of CPAP machine. Also, number of patients using the CPAP therapy for 6-7 hours in moderate OSA group was very small, and its statistical inference may not apply to a larger group size.

CONCLUSION

The results of the present study recapitulate the fact that CPAP therapy is significantly effective in OSA and the benefits are sustained with long-term use of therapy as well. However, it is premature to say that the results of this single study actually reflect a true long-term clinical improvement in the wider epidemiological perspective of the disease and hence, further studies are warranted to study the same.

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