Original Article

Therapeutic efficacy of oscillating positive expiratory pressure therapy in stable chronic obstructive pulmonary disease

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airway and the lung to noxious particles or gases. Sputum production is a cardinal feature in COPD. Airway clearance techniques have been the mainstay of management. Oscillating positive expiratory pressure (OPEP) devices are handheld devices that provide a combination of positive expiratory pressure (PEP) with high frequency oscillations which involve exhaling against a resistance that is fluctuating. It encourages airflow within secretions, whereas oscillations induce vibrations within airway wall to displace secretions into airway lumen and help in expectoration. **Methods:** A randomized control trial was conducted at the department of pulmonary medicine, Government Medical College & Hospital, Chandigarh, in which 50 patients with stable COPD were enrolled for one- and- half years. After taking proper history, they were subjected to spirometry, six- minute walk test, and were asked to fill the St. George's Respiratory Questionnaire (SGRQ) and COPD Assessment Test (CAT). These patients were randomized into group A (intervention group) and group B (control group), where group A was prescribed Aerobika OPEP device for daily use for a period of three months. After three months of use of device, the patients were again subjected to assessment parameters and inquired about any exacerbation within the three- month period. **Results:** At the end of three months were compared with baseline results. The median change in FEV1, FVC, 6MWD from baseline in group A was significantly more as compared to group B (FEV1: $P < 0.001$; FVC: $P < 0.001$; 6MWD: $P = 0.08$), whereas SGRQ score showed a significant improvement in both the intervention and control groups ($P < 0.001$) and CAT score showed significant improvement in comparison to the control group ($P < 0.001$). The median change in 6MWD and CAT from baseline in group A was significantly more as compared to group B (SGRQ: $P < 0.001$; CAT: $P < 0.001$), whereas it was not significant in case of SGRQ ($P = 0.233$). There was no significant difference in the incidence of exacerbation in the two groups ($P = 0.19$). The device did not help in controlling the rate of exacerbation in the present study at three months. **Conclusion:** Stable COPD patients who were given OPEP therapy as an adjunct to the standard drug therapy showed improvement in the spirometry parameters, exercise capacity and symptom burden in comparison to the drug only group.

KEY WORDS: Obstructive, oscillating, pressure

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airway and the lung to noxious particles or gases.[1] The chronic airflow limitation is caused by a combination of small airway disease with or without destruction of lung parenchyma. Due to increasing prevalence of smoking, the incidence of COPD is expected to increase over the next 20 years, and it is reported that there may be around 4.5 million annual deaths associated with COPD by 2030. The cardinal symptoms are dyspnea, and chronic cough with or without sputum production.[1] Spirometry confirms the diagnosis (post bronchodilator $FEV_1/FVC < 0.70$) as well as classifies degree of airflow limitation.[2]

Global Initiative for Chronic Lung Disease (GOLD) guidelines combined the impact of COPD on the individual patient as per symptomatic assessment, spirometry classification and/or risk of exacerbations in "ABCD assessment tool". GOLD defined exacerbation as an acute event characterized by a worsening of the patients' symptoms, that is, beyond day-to-day variation and leads to a change in medication.[1] Acute exacerbation of COPD is associated with significant morbidity, hospital admission rates and mortality. Hospitalizations due to exacerbation of COPD negatively impact the symptom control of patients and adversely affect the length and quality of life. Preventing exacerbations is an important goal of treatment, and therefore, there is a need to understand the risk factors, clinical features and prognostic factors of exacerbations in patients with COPD. Pharmacological management of COPD include bronchodilators, antimuscarinic agents, methylxanthines and combined bronchodilator therapy.[3] On one hand, mucus production and cough are important for airway defence and protection of lower respiratory tract against inhaled irritants. One the other hand, excessive mucus obstructs the airways and excessive cough has been associated with a number of complications.

Pharmacological management of COPD include bronchodilators, antimuscarinic agents, methylxanthines and combined bronchodilator therapy.[4] Available airway clearance techniques like active breathing techniques like high frequency chest wall oscillation (HFCWO) therapy, cuffing and huffing, oscillating positive expiratory pressure (OPEP), manual chest physiotherapy and autogenic drainage have shown strong evidence.[5] Oscillating positive expiratory pressure (OPEP) therapy was first developed and described in Switzerland, as an adjunct and supplement to traditional airway clearance techniques.[6] The OPEP devices are handheld devices that provide a combination of positive expiratory pressure (PEP) with high frequency oscillations which involve exhaling against a resistance that is fluctuating. The PEP component encourages airflow within secretions, whereas oscillations induce vibrations within airway wall to displace secretions into airway lumen and decrease viscosity of tenacious secretions. It is hypothesized that OPEP therapy aids in improvement in internal airflow distribution through collateral channels during inspiration which improves ventilation distribution; hence more air can enter into spaces behind the secretions. This creates a pressure gradient across the area where sputum is logged; this forces the secretions to move towards large airways and help in its expectoration. Thus, this device is said to alter both sputum rheology (mucus flow) and viscoelasticity (thickness).

This OPEP device serves as an adjunct in the management of COPD which has not been much evaluated. To the best of our knowledge, no Indian study available has evaluated the effect of this device on different patient-centred and disease-specific objective parameters. If found effective, this can be a useful addition in the comprehensive management of COPD patients. Hence this study was conducted to evaluate its effect on symptom burden, pulmonary functions, exercise capacity and quality of life in COPD patients.

MATERIAL AND METHODS

The study was conducted in the department of pulmonary medicine, Government Medical College & Hospital (GMCH), Sector-32, Chandigarh. This was a randomized control trial with concurrent parallel study design in which 50 patients of stable COPD were enrolled for one-and-half years. Optimum sample size was calculated by 41% increase in Forced Expiratory Volume in 1 second (FEV1) as the main outcome parameter resulting from OPEP therapy in the available literature.[5] Confidence interval was assumed to be 90% and permissible error was 10% with 10% absolute precision. Under these assumptions, optimum sample size came out to be 50. The subjects of the study were divided into two groups:

Group A: Twenty-five patients of stable COPD who received both drug therapy and OPEP device (intervention group)

Group B: Twenty-five patients of stable COPD who received only drug therapy (control group)

Inclusion criteria were group C and D COPD patients diagnosed as per GOLD guidelines who were clinically stable for the past one month.[1]

Exclusion criteria were COPD patients in group A and B as per GOLD guidelines, Patients with history of exacerbation in the past one month, COPD patients with hemoptysis, rib fracture, pneumothorax, right and left cardiac decompensation and infection at the beginning of trial and patients who did not give consent for the study.

The study was conducted after approval from the institute's ethics committee and after registration in the Clinical Trails Registry-India (CTRI). Informed consent was obtained from all subjects. Detailed history was taken including name, age, gender, address, their current symptoms, previous hospitalizations, smoking index and any co-morbidity present. All patients were subjected to spirometry, six-minute walk test and were asked to fill the St. George's Respiratory Questionnaire (SGRQ) and COPD Assessment Test (CAT).[7,8]

All cases were subjected to spirometry for staging of COPD. Spirometry was performed in the pulmonary function testing laboratory in the department of pulmonary medicine, GMCH, with the RMS Helios 702 and RMS Helios 401 as per the American Thoracic Society Guidelines (ATS).[9] The test included estimation of Forced Vital volume (FVC), Forced Expiratory volume in 1 second (FEV_1) and FEV_1/FVC ratio.

The exercise capacity of the patient was measured using six-minute walk test which measures the distance that a patient can quickly walk on a flat, hard surface in a period of six minutes (6MWD)[10,11]. During this test, distance walked by the patient in six minutes was noted along with pre-test and post-test pulse, blood pressure, SpO_2 using pulse oximetry.

Symptom assessment was done by CAT and quality of life by SGRQ.

These patients were randomized into group A (intervention group) and group B (control group) according to computer generated randomisation sequence. Allocation concealment was maintained using brown envelope which was opened by the study investigator.[12] Patients allocated to group A were prescribed Aerobika OPEP device [Figure 1] for daily use for a period of three months.

After proper resistance settings, the patients were given detailed instructions about the device: Place the mouthpiece in the mouth and close lips around it to make an effective seal; inhale deeply and hold the breath for 2–3 seconds before exhaling; continue deep breaths and long exhalations for 10–20 breathes, do 2–3 huff coughs to clear the airways; continue this cycle for 15 minutes, the device was to be used three times a day for 15 minutes duration each time and in case of any dizziness, light headedness, or any other kind of discomfort the patient was asked to report immediately.

Figure 1: Figure showing OPEP therapy device

After three months of use of device, the patients were again subjected to spirometry, six-minute walk test, SGRQ and CAT assessment. All subjects were enquired about any exacerbation within the three-month period. The results at the end of three months were compared with baseline results. All the parameters were compared within the group as well as cases and controls.

Statistical analysis

The quantitative variables were summarized as mean ± SD or median (IQR) and qualitative variable as proportion (%). Intra-group comparison (before and after therapy) of spirometry values, 6MWT distance, SGRQ score and CAT score was done using paired *t* test. Inter-group comparison (between groups A and B) of the changes in the above-mentioned variable parameters was done using Mann–Whitney *U* test. Qualitative variable was compared between the two groups using Chi-squared test or Fischer's exact test. Data analysis was carried out using SPSS 25.0 software. *P* value of < 0.05 was taken as significant.

RESULTS

In this study, a majority patients were elderly patients (age >60 years). Males were more prevalent in the study. Patients in the intervention arm had higher mean grade of breathlessness (measured by mMRC scale) as compared to controls ($P = 0.012$).

History of sputum production was seen in 13 patients (52%) in intervention group as compared to 10 (40%) in the control group. There were more smokers in the intervention group (52%) as compared to the control group 40% ($P = 0.57$). However, the pack years were more in the control group in comparison to the intervention group (26.6 ± 11.1 vs 32.6 ± 8.8; $P = 0.052$).

All COPD patients were taking either of four classes of drug treatments: Long Acting Muscarinic Antagonist (LAMA) only, combination of LAMA with Long Acting Beta-2 Agonist (LABA), combination of LABA with ICS or triple combination of LABA with LAMA with ICS. [Table 1]

The present study used FEV_1 and FVC as parameters to assess the effect of OPEP therapy on lung function parameters. Both the groups were comparable at baseline in terms of FEV_1 and FVC (FEV1: *P* value = 0.6 and FVC: *P* value = 0.8). In the present study, there were 84% patients ($n = 24$) in group A which showed improvement in FEV_1 more than 100 ml as compared to

only 20% patients ($n = 5$) in group B ($P < 0.01$). Similar improvements were also seen in FVC in the trial arm in the study ($P < 0.001$).

Exercise capacity was assessed using six-minute walk distance (6MWD) in all of the patients. The two groups were not comparable in terms of 6MWD at baseline ($P = 0.06$). After three months, there was a borderline improvement in 6MWD in the OPEP group ($P = 0.08$). The mean improvement in the OPEP group was 14 ± 25 meters in comparison to the non-OPEP group which was only 2 ± 23 meters. The median improvement in 6MWD was statistically better in the OPEP group as compared to control group ($P \leq 0.001$). Health-related quality of life was assessed in the study using SGRQ score. The two groups were not comparable in terms of SGRQ at baseline ($P < 0.001$). Both of the groups showed significant improvement in SGRQ score (changes in SGRQ score in group A and B was: 11.1 ± 10.9 and 9.6 ± 13.2, respectively). However, the median improvement in SGRQ score in group A was not statistically different from group B ($P = 0.233$).

In the present study, symptom assessment was done using CAT score. The mean baseline score for patients in group A and group B was 12.3 ± 5.6 and 11.8 ± 5.2, respectively. The patients at the time of recruitment were in medium impact range. It was seen that there was significant improvement in the CAT score in group A (OPEP group) (CAT change 1.2 ± 1.0; $P < 0.001$) as compared to no significant improvement in group B. 26% out of 50 patients of stable COPD developed exacerbation in the follow-up period of three months. It was seen that 16% of patients in group A had exacerbation as compared to 36% in group B ($P = 0.19$) [Table 2].

DISCUSSION

Basic demographic data and clinical details of the patients were collected and found to be in accordance with the existing literature.[13,14] Smoking is considered to be an important risk factor in association with COPD. The current study showed a low prevalence of smoking among the study population (46%). This is supported by existing literature.[15]

Previous history of exacerbation is an important risk factor for predicting the future risk of exacerbation. There was no statistical difference between the two groups ($P > 0.05$).

Table 1: Comparison of baseline characteristics of the study population and of the two groups

Parameter	Study Population (*n*=50)	Group A	Group B	*P*
Age±SD (Years)	65.3±11.9	69±11.1	61.6±11.1	0.11
Gender		18 (43%)	23 (56%)	0.138
Male	41 (82%)			
Female	9 (18%)	19 (43%)	2 (22%)	
MMRC (Mean±SD)	2.5±1.2	2.1±0.9	2.9±1.3	0.012
Sputum Production (Present In)		13 (52%)	10 (40%)	0.29
Smoking Status	23 (46%)	13 (52%)	10 (40%)	0.57
Pack Years (Mean±SD)	29.6±10.3	26.6±11.1	32.6±8.8	0.052
Exacerbation History In One Year	27 (54%)	14 (56%)	13 (52%)	1
Baseline FEV1 (In Liters) (Mean±SD)		1.1±0.4	1.1±0.5	0.6
Baseline FVC (In Liters) (Mean±SD)		2.0±0.8	2.0±0.7	0.8
Baseline 6MWD (In Meters) (Mean±SD)		343±82	313±104	0.06
Baseline SGRQ Score (Mean±SD)		35.5±16.8	62.6±23.0	< 0.001
Baseline CAT Score (Mean±SD)		12.3±5.6	11.8±5.2	0.8

Table 2: Comparison of change and median change in parameters in the two groups after three months

Parameters	Follow up (3 months)	Change	*P*	Median change (25th percentile-75th percentile)	*P*
FEV1 (in liters) (mean±SD)					
Group A	1.2±0.4	0.1±0.0	< 0.001	30 (20-50)	< 0.001
Group B	1.1±0.5	0.001±0.04	0.83	−10 (−20-5)	
FVC In Liters (Mean±SD)					
Group A	2.1±0.8	2.0±0.7	0.004	20 (20-40)	< 0.001
Group B	2.0±0.7	0.02±0.04	0.01	10 (−50-0)	
6 MWD in meters (mean±SD)					
Group A	358±74	14±25	0.08	12 (5.5-27.5)	< 0.001
Group B	311±103	2±23	0.69	0.0 (−10.5-6)	
SGRQ Score (Mean±SD)					
Group A	24.4±17.0	11.1±10.9	< 0.001	−9.92 [−13.7-(−7.82)]	0.233
Group B	52.9±22.8	9.6±13.2	< 0.001	−8.69 [−14.4-(−2.99)]	
CAT score (mean±SD)					
Group A	11.2±4.8	1.2±1.0	< 0.001	−2.0 [−2.0-(0.0)]	0.001
Group B	11.8±5.1	0.0±1.1	1	0.01 (0.01-0.0)	
Number Of Exacerbations (Percentage)	Yes	No			
Group A	4 (16%)	21 (84%)	0.19		
Group B	9 (36%)	16 (64%)			

In this study, both the intervention group (60%) and the control group (52%) had more patients in stage 2 of COPD. As per exclusion criteria, patients of grade A and B were excluded from this study. In the present study, all COPD patients were taking either of four classes of drug treatments: LAMA only, combination of LAMA with LABA, combination of LABA with ICS or triple combination of LABA with LAMA with ICS.

The present study used FEV_1 and FVC as parameters to assess the effect of OPEP therapy on lung function parameters. Both the groups were comparable at baseline in terms of FEV_1 and FVC (FEV1: $P = 0.6$ and FVC: $P = 0.8$). After three months, 84% of patients ($n = 24$) in group A showed improvement in FEV_1 more than 100 ml as compared to only 20% patients ($n = 5$) in group B ($P < 0.01$). Similar improvements were also in FVC in the trial arm in the study ($P < 0.001$). This finding was in consensus with existing literature.[16]

Exercise capacity was assessed using 6MWD in all of the patients. The median improvement in 6MWD was statistically better in the OPEP group as compared to control group ($P \leq 0.001$).

Health-related quality of life was assessed in the study using SGRQ score. The two groups were not comparable in terms of SGRQ at baseline ($P < 0.001$). Both of the groups showed significant improvement in SGRQ score (changes in SGRQ score in group A and B were 11.1 ± 10.9 and 9.6 ± 13.2, respectively). However, the median improvement in SGRQ score in group A was not statistically different from group B ($P = 0.233$). The lack of significant improvement over and above the control showed that OPEP therapy did not have any added advantage in improving the quality of life of COPD patients. The reason could be responder analysis, in which the result is treated as only dichotomous variables, that is, either improved or not improved because in the whole group there could be some patients with clinically relevant deterioration too and here, the study analyzed only the net change. In the present study, symptom assessment was done using the CAT score. The mean baseline scores for patients in group A and group B were 12.3 ± 5.6 and 11.8 ± 5.2, respectively. The patients at the time of recruitment were in medium impact range. It was seen that there was significant improvement in the CAT score in group A (OPEP group) (CAT change 1.2 ± 1.0; $P < 0.001$) as compared to no significant improvement in group B. This finding was similar to existing literature.[17]

In the present study, 26% of the patients of stable COPD developed exacerbation in the follow-up period of three months. It was seen that 16% of patients in group A had exacerbation as compared to 36% subjects in group B ($P = 0.19$). Shorter period of follow up in the present study might be the reason for the difference in the results. The present study did a comprehensive analysis of the role of OPEP device as an addon therapy with standard drug therapy in bringing improvement to six respiratory parameters/scores in stable COPD patients.

Limitation

The study's small sample size was a major limitation that might have affected the results. A longer follow up might have given a more authentic picture about the long-term efficacy of OPEP device in stable COPD patients. The present study did not compare the efficacy of device in COPD patients in comparison to drug treatment but as an addon therapy only. Lastly, the effect of this device was limited to stable COPD patients and didn't evaluate those in acute exacerbation.

CONCLUSION

The present study showed a beneficial effect of OPEP in the management of COPD patients. The results suggest incorporation of OPEP device as an add-on intervention along with standard drug treatment in patients of COPD patients. However, more prospective data with larger sample size may help to validate the results and consolidate its role in COPD management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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