ORIGINAL ARTICLE

Positive Expiratory Pressure Oxygen Therapy for Respiratory Distress: A Single-arm Feasibility Trial

Nitin Dhochak[1], Animesh Ray[2], Manish Soneja[3], Naveet Wig[4], Sushil K Kabra[5], Rakesh Lodha[6]

Received on: 10 June 2022; *Accepted on:* 07 October 2022; *Published on:* 31 October 2022

Abstract

Background: Oxygen delivery devices with positive end-expiratory pressure (PEEP) valves have been described, but high inspiratory flows may lead to poor tolerance in tachypneic patients. Positive expiratory pressure oxygen therapy (PEP-OT) using an occlusive face mask, oxygen reservoir, and PEEP valve has not been evaluated in clinical settings.

Materials and methods: In a single-arm intervention trial, patients aged 19–55 years admitted with acute respiratory illness with oxygen support were enrolled. PEP-OT trial was given with PEEP of 5 and 7 cm of water over 45 minutes. Feasibility was assessed as uninterrupted completion of the PEP-OT trial. The effects of PEP-OT on cardiopulmonary physiology and adverse effects of therapy were recorded.

Results: Fifteen patients (6 males) were enrolled. Fourteen patients had pneumonia and one patient had pulmonary edema. Twelve patients (80%) completed the PEP-OT trial. There was significant improvement in respiratory rate (RR) and heart rate (HR) at the end of the 45-minute PEP-OT trial (*p*-values 0.048 and 0.003, respectively). There was a trend toward improved SpO_2 and perceived dyspnea. None of the patients developed desaturation, shock, or air leaks. Positive expiratory pressure oxygen therapy is a feasible oxygen therapy in patients with acute hypoxia.

Conclusion: Positive expiratory pressure oxygen therapy seems to be safe and has a positive impact on respiratory mechanics in parenchymal respiratory pathology.

Keywords: Acute respiratory distress, Oxygen therapy, Positive end-expiratory pressure valve, Positive expiratory pressure oxygen therapy, Positive expiratory pressure.

Indian Journal of Critical Care Medicine (2022): 10.5005/jp-journals-10071-24348

Highlights

- A novel PEP-OT has been shown to be feasible and safe in patients with acute respiratory distress.
- Positive expiratory pressure oxygen therapy use is associated with improvement in parameters of respiratory distress.

Introduction

The most important mechanism of hypoxemia in acutely ill patients is shunting of blood due to nonparticipation of diseased alveoli in gaseous exchange. The affected alveoli are collapsed or flooded with secretions (dense consolidation and collapse) and do not open during respiration. These alveolar changes also lead to impaired compliance and hence, increased work of breathing. Persistently increased work of breathing leads to highly negative intrapleural pressure, which can further accentuate the established lung injury by lung strain, also known as patient self-inflicted lung injury (P-SILI).[1,2] Respiratory support devices with end-expiratory pressure, such as high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP), and bilevel positive airway pressure (BIPAP), help in recruitment of alveoli, hence decreasing shunting and improving work of breathing. A recent meta-analysis demonstrated lower mortality with face mask and helmet noninvasive ventilation (NIV) compared with standard oxygen therapy (SOT) in patients with acute respiratory failure.[3] But all these therapies require special equipment or ventilators, which are expensive and may not be available in peripheral hospitals of resource poor countries. These equipment run on electricity (some with power backup), limiting their use in transport and remote areas. Unprecedented need for respiratory support devices during coronavirus disease-2019 (COVID-19) pandemic has further strained the demand–supply for such equipment.[4]

Positive expiratory pressure therapy is an established chest physiotherapy technique that is commonly used in patients with lung diseases such as bronchiectasis, lung collapse, and prevention of lung atelectasis in postoperative patients.[5] Positive expiratory pressure therapy helps in distending airways and preventing collapse of alveoli during expiration, and hence improving functional residual capacity (FRC). Positive expiratory pressure therapy has been seen to improve FRC and tidal volume in healthy subjects as well as patients with cystic fibrosis.[6]

Positive end-expiratory pressure valve has been used to deliver PEEP during bag and mask ventilation in intubated neonates.[7] Positive end-expiratory pressure valves have been used to add CPAP in few oronasal devices with venturi-based high flow, but

[1,5,6]Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

[2–4]Department of Medicine, All India Institute of Medical Sciences, New Delhi, India

Corresponding Author: Rakesh Lodha, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India, Phone: +91 01126593621, e-mail: rlodha1661@gmail.com

How to cite this article: Dhochak N, Ray A, Soneja M, Wig N, Kabra SK, Lodha R. Positive Expiratory Pressure Oxygen Therapy for Respiratory Distress: A Single-arm Feasibility Trial. Indian J Crit Care Med 2022;26(11):1169–1174.

Source of support: Nil

Conflict of interest: None

© The Author(s). 2022 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

the clinical data of such devices is scant.[8,9] We have developed a novel PEP-OT using occlusive face mask, PEEP valve and oxygen reservoir.[10] In this study, we investigated the feasibility of use of PEP-OT in patients requiring oxygen therapy.

Materials and Methods

Study Design and Setting

In a single-arm, open-label intervention feasibility clinical trial, patients aged 19–55 years admitted to medical wards of a tertiary care hospital in North India from 1st May 2021 to 31st January 2022 with acute respiratory illness requiring oxygen support were included. Patients with features of respiratory distress [either one of these: respiratory rate ≥24/minute, SpO_2 <94%, or features of accessory muscle use (intercostal retractions and nasal flaring)], with stability on current support for at least 1 hour were included. Patients with any of these were excluded: acute exacerbation of asthma or chronic obstructive pulmonary disease, impending respiratory failure (features of exhaustion, or SpO_2 <90% on current respiratory support), poor respiratory efforts (muscular weakness or reduced central drive), chronic or acute hypercapnia ($PaCO_2$ >45 mm Hg), hemodynamical instability (hypotension or requirement of inotropic support), or altered sensorium (Glasgow Coma Scale <15). Eligible patients were enrolled after obtaining written informed consent. The trial was approved by the Institute Ethics Committee and registered at Clinical Trial Registry – India (CTRI/2020/12/029679).

Objectives and Outcome Measures

The primary objective of the study was to assess the feasibility of using PEP-OT in hospitalized patients requiring oxygen support. The secondary objectives were to assess the physiological effects of PEP-OT on respiratory system and cardiovascular system, and the adverse effects of PEP-OT.

Feasibility was assessed as the proportion of patients completing a 45-minute trial of PEP-OT. Change in perceived difficulty in breathing was assessed by dyspnea visual analog scale (DVAS) from baseline. Dyspnea visual analog was rated from 0 to 10 (10 being worst dyspnea).[11] Physiological effects on respiratory and cardiovascular system were assessed by change in RR, SpO_2, HR, capillary refill time (CRT), peripheral pulse volume, and blood pressure (BP). Patients were monitored for adverse effects – desaturations (SpO_2 <90%), hypotension (systolic BP <90 mm Hg), and any clinical features suggestive of air leaks.

Positive Expiratory Pressure Oxygen Therapy

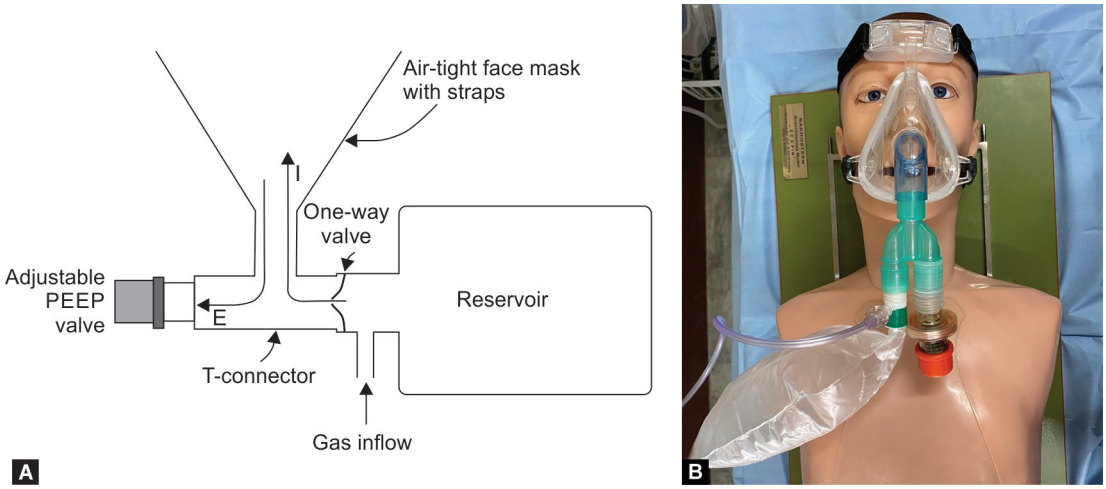
Positive expiratory pressure oxygen therapy device was assembled using a PEEP valve, nonvented NIV oronasal mask, and reservoir from nonrebreathing mask as per Figure 1 (Video 1 and Supplementary Material 1; written informed consent was obtained from the volunteer for publication of video).[10] A reusable PEEP valve (AMBU, Ballerup, Denmark) with spring adjusted valve assembly able to deliver pressure from 0 to 10 cm of water was used.[12] Reservoir with one-way valve assembly from a nonrebreathing mask (Hi mask, Romsons, Agra, India) was used. Noninvasive ventilation oronasal mask was fixed to the patient with straps to create leak-proof seal. During inspiration, oxygen flows to the patient from the reservoir, and the gas flow is adjusted, such that the reservoir is not emptied anytime during inspiration. During expiration, exhaled gases evacuate through the PEEP valve while maintaining the set PEEP, while the one-way valve prevents re-entry of exhaled air to the reservoir. Fresh oxygen fills the reservoir of this device during expiration. The assembly was initially evaluated on a healthy volunteer to check for leaks and expiratory pressure delivery. Expiratory pressure delivery was confirmed by attaching a continuous pressure monitoring line (used for invasive BP monitoring) to a sideport of the NIV mask, and adjusting PEEP valve pressure from 0 to 10 cm of water.

Sample Size

As the study was exploratory and aimed at feasibility of a novel respiratory support, a convenient sample size of 15 patients was decided.

Procedure

For enrolled patients, information on demographic data, diagnosis, underlying comorbidities, current oxygen device and flow, and baseline physiological parameters (HR, RR, CRT, pulse volume, and BP) was recorded. Humidified oxygen flow of 15 L/min was started just before attaching the assembly to the patients. The assembly was attached to the patient's face with straps, and oxygen flow was adjusted, so that the reservoir bag did not completely deflate at any phase of respiration. The patient



Figs 1A and B: PEP-OT assembly. I and E represent direction of inspiratory and expiratory flow

was initially started at PEP-OT support of 5 cm of water for 15 minutes followed by 7 cm of water for 30 minutes. The patients' physiological variables were recorded on a multipara monitor, and monitored continuously bedside by a single investigator (ND). HR and SpO_2 were continuously monitored, while RR (counted manually for full 1 minute), DVAS, peripheral pulse volume, CRT, and BP were recorded at baseline and every 15 minutes for 45 minutes of PEP-OT trial and 15 minutes after the completion of trial. Positive expiratory pressure oxygen therapy was stopped in case of any physiological worsening [increase in HR or RR by 10%, or fall of SpO_2 by 5% from baseline or less than 90%, or hypotension [systolic (BP <90 mm Hg)] or if the patient had asked to stop therapy due to discomfort. The reason for stopping PEP-OT was recorded. After completing 45 minutes of PEP-OT trial, patients were shifted back to their previous oxygen support.

Statistical Analysis

The data were managed in Microsoft Excel and analyzed using STATA Software Version 13.0 (StataCorp, College Station, TX). The continuous parameters were described as median (IQR), and categorical parameters were described as a number (%). Respiratory rate, SpO_2, DVAS, and HR measured at baseline and at 15-, 30-, and 45-minutes were summarized. The direction of change in RR, SpO_2, DVAS, and HR was decided by change from baseline to last measurement on PEP-OT. The difference in baseline physiological parameters and at completion of PEP-OT trial (45 minutes) was compared using Wilcoxon signed-rank test. The trend of parameters from baseline to 45-minute value was estimated by generalized estimating equation analysis.

Results

Over the study period, 22 patients were screened. Seven patients were not included, 4 were excluded, and 3 denied consent. Fifteen patients were included in the study. The study flow is summarized in Flowchart 1.

Baseline Characteristics

Baseline characteristics of the patients are described in Table 1. COVID-19 pneumonia (86%) was the most common respiratory condition. Two-third of the patients were on nasal prongs support when started on PEP-OT trial.

Outcome of PEP-OT Trial

Twelve patients (80%) completed the 45-minute PEP-OT trial. Physiological effects of PEP-OT are described in Table 2. Most of the patients who completed the PEP-OT trial demonstrated decrease in RR, DVAS, HR, and increase in SpO_2. Individual patient trends of RR, SpO_2, DVAS, and HR values as percentage of baseline value over the period of PEP-OT trial are demonstrated in Figure 2. None of the patients developed adverse events of desaturations, shock, or air leak.

Table 3 describes the trend of RR, SpO_2, DVAS, and HR over the period of PEP-OT trial and 15 minutes after completion of the trial. The decrease in RR and HR from baseline to 45 minutes of PEP-OT trial (completion of PEP-OT) was statistically significant (p-value = 0.048 and 0.003, respectively).

The PEP-OT trial was discontinued in three patients based on request by the patients. One patient discontinued PEP-OT at 2 minutes, as she felt uneasy due to the NIV mask. Two patients discontinued PEP-OT at 15 minutes, both felt uneasiness in the chest. These two patients had underlying comorbidities (acute pancreatitis and metastatic renal carcinoma, respectively). None of these three patients developed any desaturation or adverse hemodynamic event.

Flowchart 1: CONSORT study flow diagram

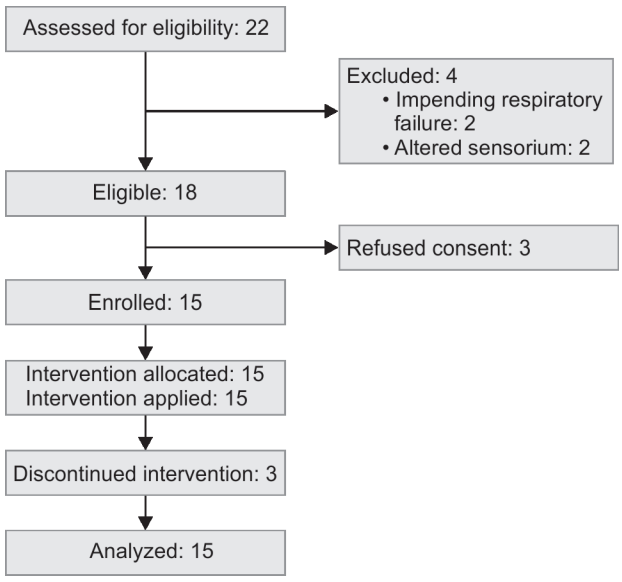


Table 1: Baseline characteristics

Characteristic	*N = 15*
Age, year, median (IQR)	42 (36, 48)
Male	6 (40)
Duration of admission, days, median (IQR)	4 (3, 18)
Diagnosis	
COVID-19 pneumonia	13 (86)
Pneumonia with effusion	1 (7)
Pulmonary edema	1 (7)
Comorbidities	10 (67)
Chest radiograph shadows	
Alveolar	10 (67)
Interstitial	5 (33)
Oxygen support	
Nasal cannula	10 (67)
Face mask	4 (26)
Partial rebreathing mask	1 (7)
Oxygen flow, L/min, median (IQR)	6 (4, 7)

Values described as number (%), unless specified; COVID-19, coronavirus disease 2019

Discussion

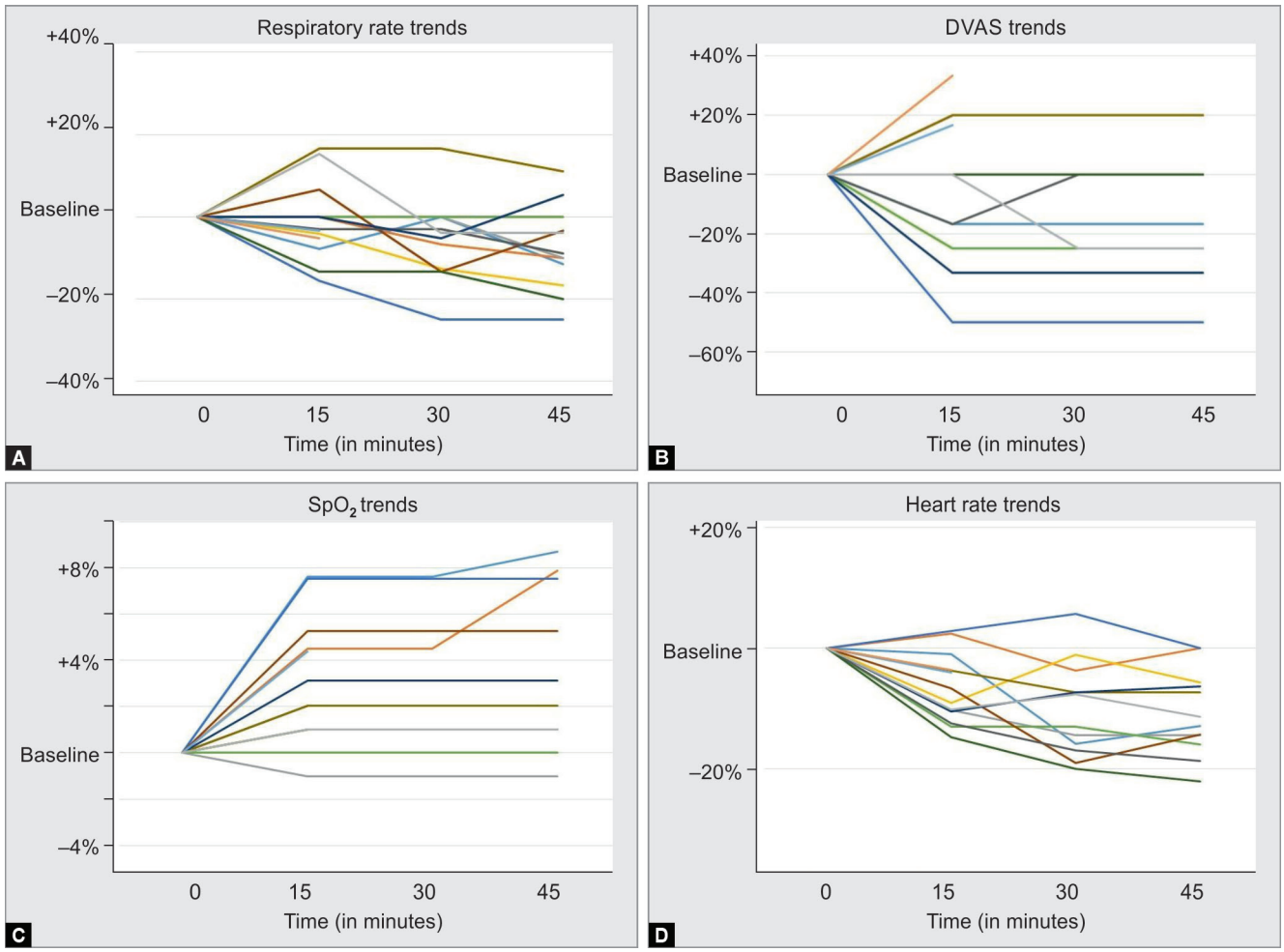
In this study, we demonstrated the feasibility of a novel oxygen therapy PEP-OT in acutely ill patients with respiratory distress. Positive expiratory pressure oxygen therapy showed physiological effects such as improvement in RR and HR. The therapy was safely delivered in all the patients.

We used the PEP-OT device primarily in parenchymal pathologies: pneumonia and pulmonary edema. The device was well-tolerated in these conditions. Among portable CPAP devices, Boussignac CPAP system is the most studied in clinical setting.

Table 2: Effect of PEP-OT on physiological parameters

Outcome	*N = 15 (Unless specified)*
Completion of PEP-OT trial	12 (80)
Change in respiratory rate (n = 14)	
No change	1 (7)
Decrease	11 (79)
Increase	2 (14)
Change in SpO_2 (n = 14)	
No change	2 (14)
Decrease	1 (7)
Increase	11 (79)
Change in DVAS (n = 14)	
No change	4 (29)
Decrease	6 (42)
Increase	4 (29)
Change in heart rate (n = 14)	
No change	2 (14)
Decrease	12 (86)

Values described as number (%). Change in physiological parameters was calculated for 14 patients, as one patient interrupted PEP-OT within 2 minutes. Change in values (no change, decrease, increase) is based on change from baseline to last measurement on PEP-OT; DVAS, dyspnea visual analog scale, PEP-OT, positive expiratory pressure oxygen therapy



Figs 2A to D: Individual patient trend over 45 minutes of use of PEP-OT in the RR, SpO_2, dyspnea visual analog scale, and HR represented as percentage change to the baseline value

Table 3: Trends in vital parameters

Parameter	*Baseline (n = 15)*	*15 min (n = 14)*	*30 min (n = 12)*	*45 min (n = 12)*	*60 min (n = 12)*	*p-value (value at 45 min vs baseline)*	*p-value for trend*
Respiratory rate, per min	30 (24, 32)	29 (23, 32)	25 (19, 29)	24 (20, 28)	29 (23, 31)	0.048	<**0.001**
SpO_2, %	98 (92, 99)	100 (99, 100)	100 (99, 100)	100 (99.5, 100)	96 (94.5, 98)	0.905	<**0.001**
DVAS	5 (4, 6)	4.5 (4, 6)	4 (3,6)	4 (3, 6)	4.5 (4, 5.5)	0.121	Estimate not obtained
Heart rate, per min	97 (82, 109)	86 (80, 100)	84 (75, 87.5)	83 (72, 89.5)	77.5 (89.5, 100.5)	0.003	<**0.001**

Values described as median (IQR); DVAS, dyspnea visual analog scale

It uses high-flow insufflation of oxygen to create turbulence and virtual pressure valve.[13] This device has also shown clinical feasibility in various scenarios, including pulmonary edema, acute hypoxemic failure, and prevention of postoperative atelectasis.[14,15] But pressure delivery in Boussignac CPAP system is dependent on patient efforts, and expiratory pressure can increase and inspiratory pressure can fall with increased respiratory efforts.[13] The PEEP valve used in PEP-OT is a physical valve with fixed resistance, and is unlikely to be affected by respiratory efforts. The expiratory pressure for PEEP valves has been demonstrated to be consistent when used in other scenarios like delivering CPAP in conjunction with CPAP machines or delivering PEEP with self-inflating bag.[16,17] Few other CPAP devices using PEEP valve utilize venturi effect for delivery of high flow, but the pressure delivered fluctuates in a scenario of raised inspiratory flow and effort.[8] Clinical studies of these devices are scarce.[9] Use of reservoir in PEP-OT for uninterrupted inspiratory flow prevents adverse effects of inadequate gas flow.

The physiological effects of PEP-OT demonstrated a significant decrease in RR and HR and a trend toward improvement of DVAS and SpO_2. These effects are similar to cardiorespiratory effects of CPAP seen in other studies. Application of PEEP in spontaneously breathing ventilated patients has been shown to decrease RR by 0.4/minute for each 1 cm of water change in PEEP.[18] Continuous positive airway pressure applied to patients with acute hypoxemia has been shown to decrease RR, and the effect was more pronounced with longer CPAP of 60 minutes compared with 10 minutes.[16] The physiological basis for this effect includes improvement in FRC/lung compliance and gas exchange, Hering–Breuer inflation/deflation reflex, and stimulation of inspiratory muscle activity prolonging exhalation. Continuous positive airway pressure has been demonstrated to decrease HR in patients with heart failure.[19]

Our study suggests that PEP-OT is safe to use in patients with acute parenchymal diseases, but larger studies are needed to confirm these findings. In the three patients who interrupted PEP-OT, there were no adverse physiological changes. We used NIV mask with straps, and it is not uncommon to have intolerance to initial use of NIV mask.[20] Two patients had comorbidities that could contribute to discomfort in the chest and upper abdomen. Being a closed system, failure of oxygen delivery can lead to risk of suffocation. The device has to be used under direct observation, and in awake patients who should be instructed to remove the mask, if needed. Modification of device and use of open-end reservoir could solve this problem. We did not face any such episode during the study.

Lack of the need for special CPAP equipment and electricity are the major advantages of PEP-OT. Positive expiratory pressure oxygen therapy is also free of asynchrony commonly seen with NIV. The items used for assembly are readily available and low-cost. Reusable PEEP valves further decrease the cost in resource-poor settings.

The limitations of the study include use of 100% oxygen in the study, which could contribute to improved SpO_2 with PEP-OT. Use of blender or an open-end reservoir could help in delivery of lower oxygen concentration. We did not monitor the actual pressures delivered. We did not monitor changes in PCO_2 due to possible rebreathing.

Conclusion

The study suggests the feasibility of PEP-OT in acute hypoxia. Positive expiratory pressure oxygen therapy seems to be safe and has positive impact on respiratory mechanics in parenchymal respiratory pathology. Further studies of PEP-OT in specific clinical indications of CPAP, such as heart failure, are needed.

Supplementary Material

The Supplementary files are available online on the website of https://www.ijccm.org

Orcid

Nitin Dhochak https://orcid.org/0000-0002-3676-8930
Animesh Ray https://orcid.org/0000-0002-9434-5338
Manish Soneja https://orcid.org/0000-0002-8619-7929
Naveet Wig https://orcid.org/0000-0002-6603-601X
Sushil K Kabra https://orcid.org/0000-0002-8890-8261
Rakesh Lodha https://orcid.org/0000-0003-2608-1163

References

1. Grieco DL, Menga LS, Eleuteri D, Antonelli M. Patient self-inflicted lung injury: Implications for acute hypoxemic respiratory failure and ARDS patients on non-invasive support. Minerva Anestesiol 2019;85(9):1014–1023. DOI: 10.23736/S0375-9393.19.13418-9.
2. Yoshida T, Grieco DL, Brochard L, Fujino Y. Patient self-inflicted lung injury and positive end-expiratory pressure for safe spontaneous breathing. Curr Opin Crit Care2020;26(1):59–65. DOI: 10.1097/MCC.0000000000000691.
3. Ferreyro BL, Angriman F, Munshi L, Sorbo LD, Ferguson ND, Rochwerg B, et al. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: A systematic review and meta-analysis. JAMA 2020;324(1):57–67. DOI: 10.1001/jama.2020.9524.
4. Beitler JR, Mittel AM, Kallet R, Kacmarek R, Hess D, Branson R, et al. Ventilator Sharing during an acute shortage caused by the COVID-19

pandemic. Am J Respir Crit Care Med 2020;202(4):600–604. DOI: 10.1164/rccm.202005-1586LE.
5. Fagevik Olsén M, Lannefors L, Westerdahl E. Positive expiratory pressure – common clinical applications and physiological effects. Respir Med 2015;109(3):297–307. DOI: 10.1016/j.rmed.2014.11.003.
6. Brilhante SA, Florêncio RB, Gualdi LP, Resqueti VR, Aliverti A, Andrade A de FD, et al. Comparison of different levels of positive expiratory pressure on chest wall volumes in healthy children and patients with fibrosis. Fisioter Pesqui 2017;24(3):311–320. DOI: 10.1590/1809-2950/17015824032017.
7. Tracy M, Shah D, Priyadarshi A, Hinder M. The effectiveness of Ambu neonatal self-inflating bag to provide consistent positive end-expiratory pressure. Arch Dis Child Fetal Neonatal Ed 2016;101(5):F439–F443. DOI: 10.1136/archdischild-2015-308649.
8. Vargas M, Marra A, Vivona L, Ball L, Marinò V, Pelosi P, et al. Performances of CPAP devices with an oronasal mask. Respir Care 2018;63(8):1033. DOI: 10.4187/respcare.05930.
9. Uz İ, Kiyan GS, ÖzÇete E, YalÇinli S, Korgan MB, Altunci YA, et al. Is the flow-safe disposable continuous positive airway pressure (CPAP) system as effective as non-invasive mechanical ventilation (NIMV) in the treatment of acute cardiogenic pulmonary Oedema? Am J Emerg Med 2021;39:109–113. DOI: 10.1016/j.ajem.2020.01.034.
10. Dhochak N, Lodha R, Kabra SK. Positive expiratory pressure oxygen therapy (PEP-OT): Innovation in acute respiratory support. OSF Preprints; 2020 [cited February 13, 2022]. Available from: https://osf.io/65jr7/.
11. Ambrosino N, Scano G. Dyspnoea and its measurement. Breathe 2004;1(2):100–107. DOI: 10.1183/18106838.0102.100.
12. Hartung JC, Wilitzki S, Thio-Lluch M, te Pas AB, Schmalisch G, Roehr CC. Reliability of single-use PEEP-valves attached to self-inflating bags during manual ventilation of neonates: An in vitro study. PLoS One 2016;11(2):e0150224. DOI: 10.1371/journal.pone.0150224.
13. Sehlin M, Törnell SS, Öhberg F, Johansson G, Winsö O. Pneumatic performance of the Boussignac CPAP system in healthy humans. Respir Care 2011;56(6):818–826. DOI: 10.4187/respcare.01015.
14. Dieperink W, Jaarsma T, van der Horst ICC, Nieuwland W, Vermeulen KM, Rosman H, et al. Boussignac continuous positive airway pressure for the management of acute cardiogenic pulmonary edema: Prospective study with a retrospective control group. BMC Cardiovasc Disord 2007;7:40. DOI: 10.1186/1471-2261-7-40.
15. Puente-Maestú L, López E, Sayas J, Alday E, Planas A, Parise DJ, et al. The effect of immediate postoperative Boussignac CPAP on adverse pulmonary events after thoracic surgery: A multicentre, randomised controlled trial. Eur J Anaesthesiol 2021;38(2):164–170. DOI: 10.1097/EJA.0000000000001369.
16. Wagstaff A, Glover C, Soni N. Continuous positive airway pressure in acute respiratory failure: The importance of the valve. J Intensive Care Soc 2012;13(1):17–24. DOI: 10.1177/175114371201300107.
17. Gomo ØH, Eilevstjønn J, Holte K, Yeconia A, Kidanto H, Ersdal HL. Delivery of positive end-expiratory pressure using self-inflating bags during newborn resuscitation is possible despite mask leak. Neonatology 2020;117(3):341–348. DOI: 10.1159/000507829.
18. Haberthür C, Guttmann J. Short-term effects of positive end-expiratory pressure on breathing pattern: An interventional study in adult intensive care patients. Crit Care 2005;9(4):R407–R415. DOI: 10.1186/cc3735.
19. Sin DD, Logan AG, Fitzgerald FS, Liu PP, Bradley TD. Effects of continuous positive airway pressure on cardiovascular outcomes in heart failure patients with and without Cheyne-Stokes respiration. Circulation 2000;102(1):61–66. DOI: 10.1161/01.cir.102.1.61.
20. Girault C, Briel A, Benichou J, Hellot MF, Dachraoui F, Tamion F, et al. Interface strategy during noninvasive positive pressure ventilation for hypercapnic acute respiratory failure. Crit Care Med 2009;37(1):124–131. DOI: 10.1097/CCM.0b013e3181928706.