Is continuous positive airway pressure therapy in COVID-19 associated with an increased rate of pulmonary barotrauma?

Received: 27 Nov 2020
Accepted: 14 June 2021

To the Editor:

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has infected over 150 million people worldwide, with over 3 million deaths as of 6 May 2021 [1]. In the UK, approximately 15% of individuals affected by coronavirus disease 2019 (COVID-19) have required admission to hospital [2] and those with severe disease require advanced respiratory support including invasive mechanical ventilation (IMV) [3]. Due to the considerable scale of the pandemic, noninvasive continuous positive airway pressure (CPAP) has been utilised for COVID-19-related type I respiratory failure as a therapeutic strategy to improve patient outcomes [4, 5] and also to preserve IMV capacity during a challenging time for acute healthcare providers. However, its exact role is unclear and is the subject of a UK multicentre trial [6].

The UK, to date, has observed discrete surges of SARS-CoV-2 infection rates. We compared data from March to June 2020 (wave 1) with August to November 2020 (wave 2) [1]. For wave 1, there are limited reports of pneumothorax, pneumomediastinum and surgical emphysema (collectively referred to as pulmonary barotrauma) relating to positive pressure support in patients with COVID-19 [7, 8]. Martinelli *et al.* [7] conducted a retrospective multi-centre UK case series of patients admitted to hospital with COVID-19 in wave 1 and identified 77 patients with barotrauma (pneumothorax: n=60; co-developed pneumomediastinum: n=6; pneumomediastinum alone: n=11). Three of the patients were diagnosed on CPAP and 38 on IMV. Overall the authors estimated a pneumothorax incidence of 0.91% [7].

Our organisation, a large University hospital comprising two acute teaching hospitals in Liverpool, UK, delivered CPAP therapy both in established critical care areas and a dedicated COVID-19 Respiratory Support Unit managed by respiratory and infectious diseases teams. In wave 1, we retrospectively recorded one case of secondary pneumothorax from 112 (0.9%) patients in which the patient received CPAP, mirroring the incidence seen in the aforementioned case series. During wave 2, we observed a marked increase in pulmonary barotrauma cases with nine (6.6%) out of 136 patients developing this complication whilst on CPAP (table 1). Before commencing CPAP therapy, all nine patients had a high oxygen requirement, with a median p/f ratio of 72 mmHg (range 55–122 mmHg) and a median respiratory rate of 28 breaths per min. All patients had radiographic evidence of COVID-19 pneumonia and an absence of pneumothorax on initial chest imaging. All diagnoses were made with subsequent chest radiographs or computed tomography imaging. Pneumothoraces were seen in five out of nine patients (bilateral: n=4; unilateral: n=1) and three of these five patients required intercostal chest drain insertion. All nine patients had radiological evidence of pneumomediastinum. None of the patients were known to have significant underlying structural respiratory disease; additionally none were active smokers and only three had previously smoked. Development of barotrauma was a marker of poor outcomes with 100% mortality in all five patients who developed pneumothorax.

During pulmonary barotrauma, alveolar rupture leads to air leakage into the surrounding tissues and air spaces [9]. The mean duration from commencing CPAP to the diagnosis of barotrauma was 6.3 days (median (range) 6 (3–10) days), with affected patients receiving a median maximum CPAP pressure of 12.5 cmH_2O (range 10–15 cmH_2O, mean 12.1 cmH_2O). The pathophysiological explanation for the apparent increased rate of barotrauma in wave 2 is unclear; the combination of relatively high airway pressures and time on CPAP may be a precipitating factor. Additionally, withdrawal of CPAP therapy

Shareable abstract (@ERSpublications)
An increased incidence of pulmonary barotrauma in patients receiving CPAP for #COVID19 pneumonia was observed during the second peak of infections at this centre in the UK
https://bit.ly/3qeSTp9

Cite this article as: Jones L, Nightingale R, Burhan H, *et al*. Is continuous positive airway pressure therapy in COVID-19 associated with an increased rate of pulmonary barotrauma? *ERJ Open Res* 2021; 7: 00886-2020 [DOI: 10.1183/23120541.00886-2020].

TABLE 1 Characteristics of COVID-19 patients on continuous positive airway pressure (CPAP) with pulmonary barotrauma: wave 2

Summary	
Patients receiving CPAP, n	136
Barotrauma cases, n	9
Incidence, %	6.6
Demographics	
Age, years, median (range)	64 (27–82)
Male/female, n	6/3
BMI, $kg \cdot m^{-2}$, median (range)	28 (24–36)
Never-smoker/ex-smoker, n	6/3
Underlying respiratory diagnosis, n	
None	7
Asthma	1
Pleural plaques	1
Baseline characteristics before commencing CPAP	
Respiratory rate, $breaths \cdot min^{-1}$, median (mean; range)	28 (29.5; 20–40)[#]
P_{aO_2}/F_{IO_2} ratio, mmHg, median (mean; range)	72 (80.0; 55–122)
CPAP therapy	
Time from commencing CPAP to barotrauma diagnosis, days, median (range)	6 (3–10)
Maximum CPAP pressure received, cmH_2O, median (range)	12.5 (10–15)
Barotrauma cases	
Bilateral/unilateral pneumothorax, n	4/1
Requirement of intercostal chest drain insertion, n	3
Pneumomediastinum, n	9
Surgical emphysema (radiological diagnosis), n	8
Outcome, n	
Died	5
Inpatient	1
Discharged	3

COVID-19: coronavirus disease 2019; BMI: body mass index; P_{aO_2}: arterial oxygen tension; F_{IO_2}: inspiratory oxygen fraction. [#]: data available for eight out of nine patients.

for short breaks followed by re-application of pressure was an observed theme in wave 2 and may contribute to alveolar hyperinflation with increased alveolar pressures. In contrast to wave 1, all patients escalated to CPAP in wave 2, including the nine who developed pulmonary barotrauma, were also prescribed dexamethasone in keeping with the evidence base that emerged in wave 1 from the RECOVERY trial [10].

However, despite prior experience in treating patients with COPD exacerbations on oral steroids with noninvasive ventilation at high pressures, we have not seen barotrauma to the extent that we have seen in COVID-19 patients and therefore postulate that treatment with dexamethasone combined with the acute inflammatory insult of COVID-19 pneumonitis may contribute to increased lung tissue friability.

Overall, CPAP appears to have been a beneficial intervention in the outcome of patients with COVID-19 seen at our centre during both wave 1 [5] and 2. However, given our observations, caution and vigilance regarding the risk of pulmonary barotrauma should be undertaken. A low threshold for a chest radiograph after starting CPAP and routine examination for surgical emphysema may aid early recognition of barotrauma. Daily review of progress, including time on CPAP, delivered pressure, and response to therapy is mandatory. In particular, we would suggest that increased work of breathing should prompt review of therapy and discussion about the transition to IMV; barotrauma may be seen as a type of patient self-induced lung injury and IMV with sedation and paralysis may allow driving pressures to be reduced and lung injury to be limited.

Observing data from patients at our centre has enabled a descriptive analysis of a possible increased risk of pulmonary barotrauma associated with CPAP in patients with COVID-19 pneumonitis. Our small sample size precludes meaningful statistical analysis and we recognise that this is an important limitation of this study. Outcome data of the RECOVERY-RS trial [6], comparing CPAP, high-flow nasal oxygen and standard care may support our observations. The possible association of a higher rate of barotrauma with the widespread use of dexamethasone may also require further exploration. CPAP therapy is an

important intervention for patients with COVID-19 pneumonitis within healthcare settings; therefore awareness of potential development of pulmonary barotrauma is key for acute clinicians managing this patient cohort.

Lewis Jones[1], Rebecca Nightingale[1,2], Hassan Burhan[1,2], Gareth Jones[1], Kimberley Barber[1], Helena Bond[1], Robert Parker[1], Nick Duffy[1], Peter Hampshire[1] and Manish Gautam[1]

[1]Liverpool University Hospital NHS Foundation Trust, Liverpool, UK. [2]Liverpool School of Tropical Medicine, Liverpool, UK.

Corresponding author: Manish Gautam (manish.gautam@liverpoolft.nhs.uk)

Provenance: Submitted article, peer reviewed.

Conflict of interest: L. Jones has nothing to disclose. R. Nightingale reports grants from the Medical Research Council outside the submitted work. H. Burhan reports a grant from AstraZeneca (Respiratory High Risk Asthma Clinic Proposal – 2019-055), personal fees from Novartis (advisory board attendance fee), AstraZeneca, Chiesi and GSK (speaking fees), and travel, accommodation and attendance fees for European Respiratory Society Meeting, Paris, 2018, from the Health Foundation Innovating for Improvement (Round 6 grant: Improving Heroin Smokers' Access to COPD Community Services), outside the submitted work. G. Jones, outside of this work, has previously received honoraria from GSK, AstraZeneca, Chiesi and Pfizer, and nonfinancial support from Napp. K. Barber has nothing to disclose. H. Bond has nothing to disclose. R. Parker has nothing to disclose. N. Duffy has nothing to disclose. P. Hampshire has nothing to disclose. M. Gautam has nothing to disclose.

References

1 Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* 2020; 20: 533–534.
2 Gov.UK. Coronavirus (COVID-19) in the UK. Deaths in United Kingdom. https://coronavirus.data.gov.uk/details/deaths. Date last accessed: 10 November 2020.
3 World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance. *Pediatria i Medycyna Rodzinna* 2020; 16: 9–26.
4 Burns GP, Lane ND, Tedd HM, *et al.* Improved survival following ward-based non-invasive pressure support for severe hypoxia in a cohort of frail patients with COVID-19: retrospective analysis from a UK teaching hospital. *BMJ Open Respir Res* 2020; 7: e000621.
5 Nightingale R, Nwosu N, Kutubudin F, *et al.* Is continuous positive airway pressure (CPAP) a new standard of care for type 1 respiratory failure in COVID-19 patients? A retrospective observational study of a dedicated COVID-19 CPAP service. *BMJ Open Respir Res* 2020; 7: e000639.
6 Perkins, GD, Couper, K, Connolly B, *et al.* RECOVERY – respiratory support: respiratory strategies for patients with suspected or proven COVID-19 respiratory failure; continuous positive airway pressure, high-flow nasal oxygen, and standard care: a structured summary of a study protocol for a randomised controlled trial. *Trials* 2020; 1: 687.
7 Martinelli AW, Ingle T, Newman J, *et al.* COVID-19 and pneumothorax: a multicentre retrospective case series. *Eur Respir J* 2020; 56: 2002697.
8 Udi, J, Lang, CN, Zotzmann V, *et al.* Incidence of barotrauma in patients with COVID-19 pneumonia during prolonged invasive mechanical ventilation – a case-control study. *J Intensive Care Med* 2021: 36: 477–483.
9 Ioannidis G, Lazaridis G, Baka S, *et al.* Barotrauma and pneumothorax. *J Thorac Dis* 2015; 7: Suppl. 1, S38–S43.
10 Horby P, Lim WS, Emberson JR, *et al.* Dexamethasone in hospitalized patients with Covid-19 – preliminary report. *N Engl J Med* 2020; 58: 133.