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Continuous positive airway pressure in the treatment of COVID-19 patients with respiratory failure. A report of six cases with excellent outcome

Abstract

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently considered a significant threat to global health and global economy. This new rapidly spreading virus causes enormous stress to healthcare systems as large number of patients present with respiratory failure, needing intubation and mechanical ventilation. While the industry is racing to meet the rising demand for ventilators, all the alternative respiratory support modalities are employed to save lives in hospitals around the globe. We hereby report 6 patients who were diagnosed with SARS-CoV-2 and treated with continuous positive airway pressure in a negative pressure isolated room in a tertiary center in western Greece. The rapid progression of mild flu-like symptoms to respiratory failure in all patients was controlled with the use of continuous positive airway pressure making this strategy a reasonable alternative to respiratory failure due to SARS-CoV-2 as it may avert intubation and mechanical ventilation.

Key words: respiratory failure, coronavirus disease 19, continuous positive airway pressure

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Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently considered a significant threat to global health and global economy. This new rapidly spreading virus causes enormous stress to healthcare systems as large number of patients present with respiratory failure, needing intubation and mechanical ventilation. While the scientific community is concentrated on finding a specific treatment and/or a vaccine for the new virus, our only option is supportive therapy resulting in a high demand for intensive care unit (ICU) beds and ventilators. Attempting to mitigate this need, all the alternative respiratory support modalities are employed to save lives in hospitals around the globe. Continuous positive airway pressure (CPAP) devices are frequently used in patients with respiratory failure, and although conflicting data exist for their use in coronavirus infection, in a resource scarce environment, they could be a choice to avert intubation and save patients.

Case series

Six patients suffering from fever, cough, and mild respiratory distress, presented to the Emergency Department (ED) of a tertiary center in western Greece during March 2020. All patients were diagnosed positive for SARS-CoV-2, and on admission were alert, oriented, and hemodynamically stable. Their demographic data, past medical history, and clinical examination findings on admission are presented in Table 1. All patients were

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Table 1. Demographic data, past medical history, and major findings of clinical examination on admission

	Age/sex	BMI/tobacco use	Past medical history	Previous medication	Symptoms on admission
Patient 1	44 / M	29.3 / No	Hypertension	Olmesartan 20 mg od	Chest pain, temperature 38.3°C, dyspnea, mild productive cough. Chest auscultation: crackles on middle and lower lobes bilaterally
Patient 2	74 / M	23.4 / Yes (10 packs/year)	Benign prostate hypertrophy, hypertension	Tamsulosin 0.4 mg od, Amlodipine 10 mg od	Diarrhea, temperature 38.8°C , myalgias, non-productive cough. Chest auscultation: lower lung crepitations
Patient 3	74 / F	25.4 / No	Hypertension, hypothyroidism	Thyrohormone 0.1 mcg od, Amlodipine/valsartan 10/160	Fatique, non-productive cough, temperature 38.2°C. Chest auscultation: crackles on middle and lower lobes bilaterally
Patient 4	64 / M	23.8 / No	Coronary disease, hypertension, dyslipidemia	Carvedilol 12.5 mg bd, valsartan 160 mg od, simvastatin 20 mg od, ASA 100 mg od	Temperature 38.3°C , mild dyspnea, non-productive cough. Chest auscultation: crackles on left lower lobe
Patient 5	79 / M	26.9 / Former smoker	Hypertension, dyslipidemia, peripheral artery Disease	ASA 100 mg od, felodipine 5 mg od, rosuvastatin 5 mg od	Temperature 38°C, non-productive cough, fatigue, mild dyspnea. Chest auscultation: crackles on lower lobes bilaterally
Patient 6	50 / M	32 / No	Hypothyroidism	Thyrohormone 0.1 mcg od	Dyspnea, non-productive cough, temperature 38.3°C. Chest auscultation: some crackles on lower lobes bilaterally

ASA — acetylsalicylic acid; bd — twice a day; BMI — body mass index; od — once daily

isolated in the COVID-19 ward of our hospital, and during their stay they developed respiratory failure. Their PO_2/FiO_2 ratio varied between 130 to 160, they were tachypneic with bilateral infiltrations on chest X-rays. Based on the clinical status and single organ involvement, a decision was made to support them with CPAP oxygen therapy via face mask. StarMed's Ventumask 30 CPAP mask with a Venturi flow driver and adjustable PEEP valve was used in all patients, and to minimize the risk of virus dispersion, all subjects were treated in a negative pressure room (Figure 1). Upon admission all patients were on hydroxychloroquine, lopinavir/ritonavir, azithromycin and ceftaroline or ceftriaxone. Oxygen saturation, blood pressure, heart rate and urine output were continuously monitored. Additionally, the respiratory rate and patient's compliance with CPAP therapy was recorded by the staff nurse. CPAP therapy was well tolerated by all patients and no signs of superinfection of any etiology were noticed based on daily clinical examination and laboratory tests. Blood gas analysis was performed twice daily and in case of any clinically significant event. The attending physicians adjusted the fraction of inspired oxygen and the level of CPAP in accordance to patient's respiratory improvement. All persons were monitored with chest X-rays. Patient number 6 was the only one that received a chest CT scan during his hospitalization (Figures 2–4). Their stay in the negative pressure room and CPAP treatment ranged from 3 to 10 days and 3 to 9 days, respectively (Table 2). All 6 patients, representing 10.3% of the total COVID-19 admissions of that period, were discharged from the negative pressure room with nasal cannula or Venturi face mask, clinically improved. Finally, after a short stay (up to ten days) in COVID-19 ward, all patients were discharged from our hospital.

Discussion

The clinical spectrum of COVID-19 is broad, ranging from asymptomatic to severe disease with high mortality. In severely ill patients exhibiting signs of cytokine storm, respiratory function can deteriorate rapidly, and the current evidence proposes that dyspneic patients over 60 years old with comorbidities have to be monitored closely, especially during the first weeks after symptoms onset [1, 2]. Respiratory viruses can cause acute respiratory distress syndrome (ARDS), and in the last decade, zoonotic coronaviruses were

A

Requirement		Setting	Flow delivered
O_2% approx	PEEP cmH_2O	Flow O_2 L/min A + B	Flow approx L/min
40%	5	11 + 8	78
	7.5	11 + 8	72
	10	12 + 6	70
	12.5	12 + 4	65
	15	12 + 4	60
	20	13 + 2	60
50%	5	10 + 18	80
	7.5	10 + 18	77
	10	10 + 16	72
	12.5	10 + 14	65
	15	10 + 12	60
	20	12 + 10	60
60%	5	9 + 26	80
	7.5	9 + 26	74
	10	10 + 24	75
	12.5	10 + 22	72
	15	10 + 22	70
	20	10 + 18	60
100%	Feed with a minimum O_2 flow of 40 L/min		

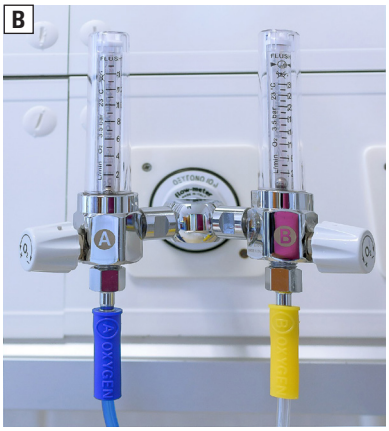

Figure 1. StarMed's Ventumask 30 CPAP mask with Venturi flow driver (black arrow) and adjustable PEEP valve (white arrow). The device is connected to a dual oxygen flow meter (**B**) and using the settings table (**A**), flows can reach up to 80 L/min and FiO_2 can be adjusted from 30% to 100%. The positive end-expiratory pressure can be set up to 20 cmH_2O and is monitored with the pressure gauge (*)

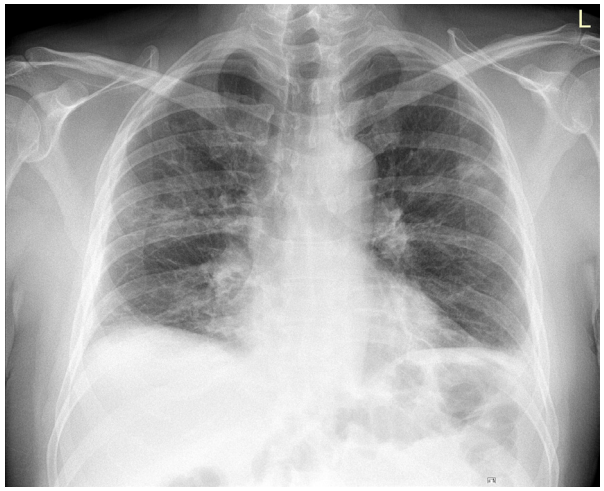

Figure 2. Chest X-ray on hospital admission (day 0)

able to cross the species barrier causing severe acute respiratory Syndrome (SARS), Middle East respiratory syndrome (MERS) and recently the pandemic COVID-19. In the event of respiratory failure, prior to intubation and mechanical ventilation in carefully selected patients, a non-invasive ventilation (NIV) or a CPAP trial could be attempted. CPAP and NIV therapy are well documented in patients with respiratory failure, in immuno-compromised patients, in weaning patients from mechanical ventilation, and in critically ill patients with mild ARDS [3, 4].

A CPAP machine maintains a positive pressure in the airway, which can be adjusted while the fraction of inspired oxygen can be raised up to 100%. A tube carries the oxygen-air mixture

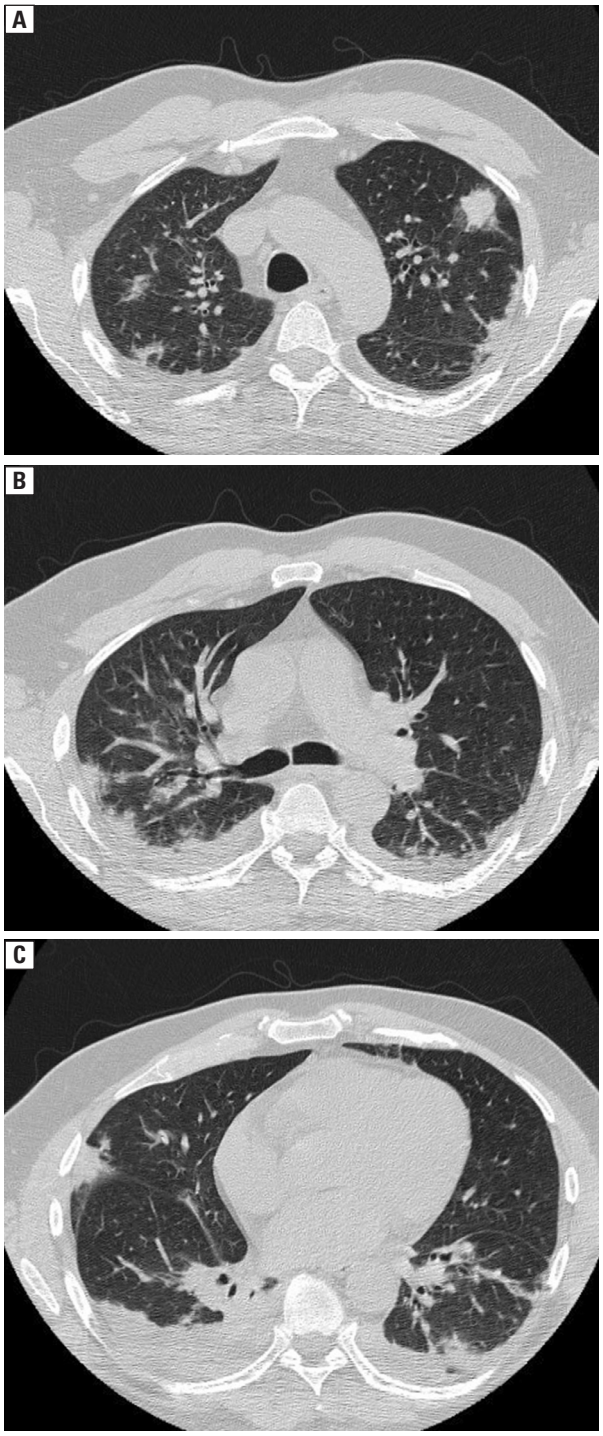

Figure 3. Chest computed tomography scan before his admission to the negative pressure room (day 4)

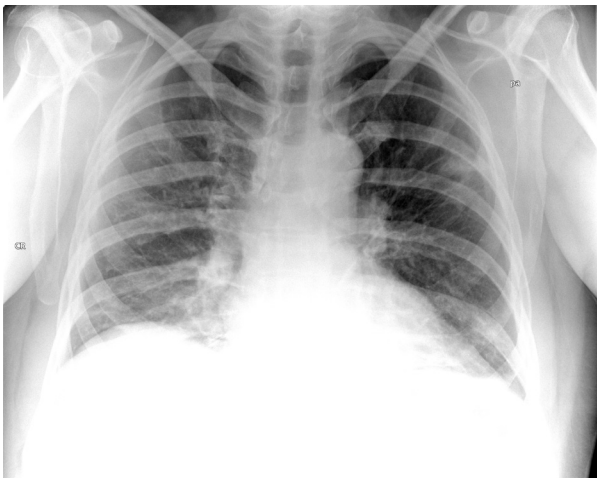

Figure 4. Chest X-ray upon discharge from the negative pressure room (day 8)

to an oronasal mask usually that must create a good seal with the patient's face. Beside oronasal masks, other frequently used interfaces include helmets, nasal masks, and full-face masks. CPAP decreases the work of breathing and improves oxygenation by ameliorating lung compliance, allows alveolar recruitment, counteracts the intrinsic positive end expiratory pressure (PEEP) and decreases preload and afterload in cases of congestive heart failure [4]. In patients presenting to the emergency department (ED) with acute respiratory failure and without signs of neurologic and/or hemodynamic compromise, a trial of CPAP should be attempted before intubation and mechanical ventilation [5]. Continuous positive airway pressure (CPAP) should be preferably used in a negative pressure isolated hospital room when treating cases of SARS-COV-2 infection due to the high dispersion of the virus when using high flow devices. Alternatively, CPAP therapy could be applied with the use of a helmet combined with a filter on the exhalation port [6].

There are limited and conflicting data regarding the use of NIV or CPAP in respiratory viral infections (RVI). In the study by Kumar *et al.*, the use of NIV in patients with severe influenza A (H1N1) showed NIV failure in up to 85% [7]. In a multicenter observational study of critically ill patients due to influenza infection hypoxemic respiratory failure, 806 of 1898 patients underwent initial NIV, and 56.8% of them required finally intubation and invasive ventilation. The more severe cases (SOFA ≥ 5) had a higher risk of NIV failure. Also NIV failure was associated with increased ICU mortality compared to invasive mechanical ventilation [8]. NIV has been shown to have positive results in the management of some patients with SARS, while in a study based on a multicenter cohort of 302 MERS critically ill patients, NIV was used initially in 35% of subjects, but the vast majority of them (92.4%) required invasive mechanical ventilation [9, 10].

In a recent retrospective observational study that included 24 patients with respiratory fail-

Table 2. Patients' data during stay in negative pressure room

	PO_2/FiO_2 on admission	Days in negative pressure room	Days on CPAP	CPAP cm H_2O	Hours per day on CPAP	Side effects	Antibiotic treatment	Anti-viral agent	Hydroxy chloroquine	PO_2/FiO_2 on discharge from negative pressure room
Patient 1	145	10	9	5–7.5	24	Nasal bridge pressure ulcer	Ceftaroline, azithromycin	Lopinavir/ ritonavir	Yes	200
Patient 2	160	6	5	5	24	None	Ceftarolin, azithromycin	Lopinavir/ ritonavir	Yes	320
Patient 3	140	7	7	7.5–10	24	Nasal bridge pressure ulcer	Ceftriaxone, azithromycin	Lopinavir/ ritonavir	Yes	250
Patient 4	150	5	5	7.5–10	24	None	Ceftarolin, azithromycine	Lopinavir/ ritonavir	Yes	180
Patient 5	160	3	3	7.5	24	None	Ceftriaxone, azithromycin	Lopinavir/ ritonavir	Yes	205
Patient 6	120	4	4	7.5	24	None	Ceftarolin, azithromycine	Lopinavir/ ritonavir	Yes	170

CPAP — continuous positive airway pressure

ure type 1 due to SARS-CoV-2, CPAP treatment successfully averted intubation in over half of the patients. All the patients were treated in a negative pressure room at the Royal Liverpool Hospital. 14 patients were weaned off CPAP and discharged. Their median time on CPAP and bed stay were 4.5 and 10.5 days, respectively [11]. Furthermore, a small two period retrospective case control study that included 52 patients (14 controls and 38 cases) showed that CPAP is feasible in deteriorating COVID-19 patients and can avoid intubation at 7 days and at 14 days. More patents in the control group were intubated or died in comparison to the experimental group (57% *vs* 23%, p = 0.043). Median use of CPAP was 5 (2–7.5) days and for 8 (4–11) hours daily [12].

Finally, new data for COVID-19 are becoming available, raising concerns regarding the lack of ICU beds worldwide, and the high mortality rates observed after intubation and mechanical ventilation [13, 14]. The current available evidence indicates that a CPAP therapy can be used in COVID-19 respiratory failure, and this strategy may avert intubation.

Conclusions

In anticipation of new studies that will shed more light on a definitive COVID-19 treatment, management principles for this new clinical entity in case of ARDS are mainly supportive and should be similar to the management of ARDS from other causes. Until a specific antiviral treatment is available, the use of invasive and non-invasive ventilation should be tailored according to patient's needs and clinical status. There is a true need for efficient trial designs to test the role of continuous positive airway pressure support in patients with respiratory failure due to SARS-CoV-2, alone or in combination with other treatment options.

Conflict of interest

None declared.

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