ORIGINAL ARTICLE

CTEX CPAP versus Conventional CPAP in Managing COVID-19 related Respiratory Failure: Experience from a Hospital

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ABSTRACT

Background: Continuous positive airway pressure (CPAP) is the preferred form of noninvasive ventilatory support in the management of type 1 respiratory failure in COVID-19 patients with a pure failure of oxygenation only. Limiting the inherent disadvantages, the improved and enhanced CTEX CPAP device may benefit the patients. ***Objective:*** To evaluate the clinical effectiveness of a new novel continuous positive airway pressure (CPAP) device CTEX in managing COVID-19-associated type 1 respiratory failure. ***Methods:*** This open-label, double cross-over, non-inferiority trial was conducted among COVID-19-positive patients with respiratory failure who required oxygen supplementation and were admitted to the intensive care unit (ICU), under Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh, between August 2020 and January 2021. A total of 39 patients with confirmed positive COVID-19 receiving standard CPAP (10-16cm of water) and entrained oxygen (2-15 L/minute) and having peripheral oxygen saturations ($SpO_{2)}$ <94% were included in this study. Patients were given standard CPAP for 1 hour followed by CTEX CPAP for 12 hours and then switched back to standard CPAP for 1 hour. The primary outcome measure was the evaluation of oxygen saturation ($SpO_{2)}$ over 12 hours, which was measured hourly across 11 hours starting at T0 for the initial value and ending at T11 for the final value. ***Results:*** The mean age of the patients was 60.25±11.70 years; male to female ratio was 3.3:1. Most of the patients 21(54%) had SpO_2 of 80-90% on admission. The average respiratory rate was 28.15±1.42 breaths per minute. SpO_2 before and after applying CTEX CPAP were observed 88% (ranged between 81% and 94%) and 95% (ranged between 91% and 100%) respectively. There was a significant improvement in SpO_2 and the value was increased over time and then plateaued. ***Conclusion:*** CTEX CPAP device was found to be significantly better at oxygenation for the treatment of COVID-19 patients with type 1 respiratory failure.

Keywords: COVID-19, continuous positive airway pressure, non-invasive ventilation, oxygen saturation, respiratory failure

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INTRODUCTION

Since the end of 2019, the whole world has been struggling with the epidemic of the new Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2), which was first detected in the Chinese province of Hubei[1]. Soon after its outbreak, the coronavirus disease (COVID-19) was declared a global pandemic by the World

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Health Organization (WHO) on March 11, 2020[1,2]. Since the disease was first identified, it has been accepted that a high number of patients with severe COVID-19 disease develop acute respiratory distress syndrome (ARDS)[3,4]. In COVID-19 patients, the lung pathology was heterogeneous, corresponding to the radiographic findings of patchy ground glass opacifications. The virus is believed to infect the epithelial lining cells of the respiratory tract using the ACE2 enzyme as a viral receptor leading to diffuse alveolar damage and edema[5]. In SARS-CoV-2 infection, the pulmonary parenchyma demonstrated a range of findings from patchy exudative hyaline membrane disease to extensive alveolar proteinaceous and serous exudation, hyaline membrane formation, and inflammatory infiltration with multinucleated syncytial cells[6].

A substantial number of patients with severe COVID-19 disease develop hypoxic respiratory failure requiring respiratory support[6,7]. During the initial outbreak, early reports from China suggested that early intubation and invasive ventilation were preferable to delaying care with the use of non-invasive ventilation (NIV)[7]. The mortality in COVID-19 patients requiring mechanical ventilation is very high; approximately 40% to 45% mortality has been observed internationally[8,9].

The improved understanding of severe COVID-19 disease has led to changes in the management of patients. Continuous positive airway pressure (CPAP), a form of NIV, appeared to have a more significant and positive role than initially thought[10]. The possibility of using CPAP, now already in very widespread use in homes to combat sleep apnoea, has been raised internationally as a device that may help during this upsurge of coronavirus cases. There is now growing evidence that CPAP avoids the need for invasive ventilation and may prevent deterioration. CPAP assists breathing by supplying a mixture of air and oxygen using positive pressure to help the patient take deeper breaths, thereby improving oxygenation without an airway adjunct[11,12].

Both non-invasive ventilation (NIV) and high flow nasal oxygen (HFNO) improve oxygenation in hypoxaemic COVID-19 patients but the evidence supporting the use of HFNO is still being debated and remains controversial in suspected and confirmed severe cases of COVID-19 disease[7,12]. Currently in the UK, the national guidance does not recommend HFNO in COVID-19 because of the lack of evidence of efficacy, the high oxygen usage, and the risk of infection spread[13-17]. The use of a negative pressure room is recommended when using HFNO for hypoxia associated with COVID-19 illness because the guidelines listed HFNO as an aerosol-generating procedure[18,19]. CPAP has other advantages which include: being simple and less expensive than hospital ventilators, allowing manufacturing capability can be increased far more quickly and at a much lower cost; increasing the amount of inspired oxygen; and normalizing the ventilation-perfusion inequality in the lung[8-10]. However, the CPAP device has several disadvantages that limit its clinical application including: viral aerosol generation with risk to staff and carers; high oxygen consumption, and cross infection[20].

With improved and enhanced CPAP equipment, early intervention with this technique may be of benefit to the patients by reducing the risk of mortality. This study aims to evaluate the clinical effectiveness of a new novel continuous positive airway pressure (CPAP) device CTEX in the management of type 1 respiratory failure associated with COVID-19.

METHODS

This study was conducted in the intensive care unit (ICU) under Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh, between August 2020 and January 2021. Positive COVID-19 patients with Type 1 Respiratory failure receiving standard CPAP (10-16cm of water) and entrained oxygen (2-15 L/minute) with peripheral oxygen saturations of less than 94% were included in this study. The chosen standard machine to compare against was the Yamind DM28 CPAP device. This was a new device on the market with advanced features and had gained CE and FDA authorization for its use in the treatment of COVID-19 patients. Baseline data including age, sex, duration of symptoms, on-admission pulse, blood pressure, respiratory rate, and oxygen saturation (SpO_2) were recorded. At first, patients were given Yamind DM28 CPAP for 1 hour and then crossed over to CTEX for 12 hours. After switching to CTEX, hourly heart rate, blood pressure, respiratory rate, oxygen

saturation, oxygen flow, CPAP pressure, and adverse incidents were documented. Thereafter, the patient again crossed over to DM28 CPAP for 1 hour. Evaluation of oxygen saturation over a 12-hour period was the primary outcome.

Values were expressed as mean±SD (standard deviation) or as percentages. The results were presented using tables and/or figures. All analysis was conducted in R v3.6.1 using the following packages: ggplot2, car, Rmisc, tolerance, lme4, performance, AICcmodavg, PairedData, FSA, and reshape2. As multiple measurements were taken from the same subject, a repeated measures model was fitted to determine whether the SpO_2 changed over time. About 74.3% of the random variation (random effects variation accounts for the variation that's "leftover" after the variance explained by the fixed effects in the model) was explained by subjects, 0.7% by time, and 25.0% by unknown variables. The variation (in standard deviations) in the model due to subject was 2.240, due to time was 0.220, and that of unknown variables was 1.298. The goodness of fit using Nakagawa's R2 for mixed models was 84%. Comparisons between models were also conducted using the Akaike Information Criterion (AIC) and the restricted log-likelihood. The next step of the analysis was to only look at the start and end values, therefore investigating the relative change in SpO_2, which also accounts for multiple subjects. A paired Student's t-test was run to determine the differences in means whether it was greater than 0 or lesser than or equal to 0 (confidence intervals: 95%).

RESULTS

A total of thirty-nine patients were included in this study. Patient demographics and clinical information are summarized in Table 1. The mean age of patients was 60.25±11.70 years, median age was 63 years (range 43-80 years) and male to female ratio was 3.3:1. The average body weight was 68.82±9.21 Kg.

Patients had suffered from COVID-19 infection for several days and the average duration of symptoms was 8.6±3.63 days. About 27(69%) patients had one co-morbidity, 9(23%) had two or more co-morbidities and 3(8%) had no other diseases. Sixty-nine percent of patients had hypertension, 61% had diabetes mellitus, 15% had ischemic heart disease, 10% had a history of bronchial asthma and chronic obstructive pulmonary disease, and 8% had kidney disease. On admission, 21(54%) patients had SpO2 of 80%-90%, 16(41%) had SpO2 of less than 80%, and only 2(5%) patients had SpO2 of more than 90%. The mean systolic and diastolic blood pressures were 129.41±16.65 and 81.33±9.58 mmHg, respectively. The average pulse rate and respiratory rate were 79.70±11.56 beats per minute and 28.15±1.42 breaths per minute, respectively. Figure 1 shows the average SpO2 for each time point along with a general trend line, confidence intervals (in black), and tolerance intervals (in red). Confidence intervals describe the uncertainty around the population mean value. Tolerance intervals describe the uncertainty around a set proportion of the population data (in this case 90%), which means there is 95% confidence that 90% of the population data would fall within the limits. The average initial SpO2 was 88% (range 81%-94%) and the final SpO2 was 95% (range 91%-100%).

Table 1: Patient demographics and clinical characteristics (n=39)

Characteristics	Values
Age (in years)	60.25±11.70
Gender Male Female	 30 (77%) 9 (23%)
Body weight (in kg)	68.82±9.21
Duration of symptoms (in days)	8.6±3.63
Comorbidities[a] None One Two or more	 3 (8%) 27 (69%) 9 (23%)
Blood pressure (in mm of Hg) Systolic Diastolic	 129.41±16.65 81.33 9.58
Pulse rate	79.70±11.56
Respiratory rate	28.15±1.42
Admission SpO_2 >90% 90-80% <80%	 2 (5%) 21 (54%) 16 (41%)

Values were expressed as mean±SD or proportions. [a]Comorbidities included: hypertension, diabetes mellitus, ischemic heart disease, congestive heart failure, chronic obstructive pulmonary disease, asthma, end-stage renal disease, smoking, hypothyroidism, and coagulopathy.

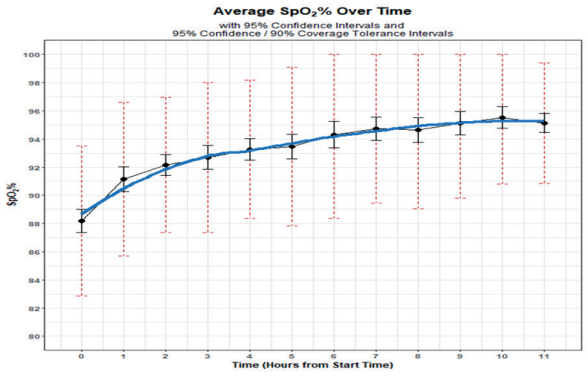

Figure 1: Average SpO_2 changes over time after starting CTEX CPAP.

DISCUSSION

COVID–19 pandemic was associated with high morbidity and mortality since its first outbreak in China in December 2019[21]. The severity of the pandemic has been extensively affected by age, sex, and concomitant diseases echoing the views of Wu et al. and Guan et al[22,23]. In Southeast Asia, including Bangladesh where it was first identified on March 8, 2020; the figures had been worsening as evidenced by securing the 17th position in the WORLDOMETER list[21]. While the majority of COVID-19 patients had a self-limited type of disease, 1 in 5 COVID-19 patients especially the older group required hospital care. The requirement of intensive care among COVID-19 hospitalized patients varies between countries from 5% to 32%[24]. In Bangladesh, the intensive care unit (ICU) utilization rate was 23.8% and patients were significantly older compared to non-ICU patients[25].

The present study demonstrated that most of the patients were older and male (77%). Several studies done in the Indian subcontinent and Europe have found similar age and gender predominance[21,25-27]. We have found that 69% of the enrolled patients had one or more comorbidities, similar to findings reported from studies in Italy and China[28,29]. The most common comorbidities were hypertension (69%) and diabetes mellitus (61%). In previous studies in Bangladesh and other countries, these two diseases were the most prevalent comorbidities[21,25].

All the enrolled patients were supported by non–invasive ventilation. Because high mortality rates and prolonged ventilator days associated with invasive mechanical ventilation were reported in COVID-19 patients[30]. At the start of this pandemic, CPAP was considered inferior to early intubation and ventilation. But later it was found that CPAP was associated with significant improvement in oxygenation and reduction of respiratory distress[31]. Ing et al. also suggested that CPAP might be a safe, effective strategy in the management of hypoxemic respiratory failure associated with COVID-19[32]. However, CPAP is considered an aerosol-generating procedure (AGP) and increases the risk of viral transmission[20]. This risk is lower in CTEX CPAP as a viral filter is incorporated into the heart of the device developing a sealed patient consumable circuit and using the virucidal capabilities of copper.

This trial shows that introducing COVID-19 patients to CTEX CPAP provides an improvement in oxygen saturation and brings the majority of patients back to near-normal oxygen values within 12 hours. We have found that after using standard CPAP for 1 hour, the average SpO2 increased up to 88%. After applying CTEX CPAP, SpO_2 increased up to 91% at the end of 1 hour, and after 12 hours the final SpO2 was 95% (ranged between 91% and 100%). It may be because the flow of the device was tuned to deliver the highest possible inspired Oxygen >0.7 while only consuming 15L per minute of oxygen at the source.

Virtual Ward Technologies Ltd. has come up with a new first principles design on the old CPAP technology, which would capture all the benefits while limiting the disadvantages. The improvements in design brought about by CTEX, make the uptake of CPAP far more attractive to clinicians and carers worldwide in the management of severe COVID-19. CPAP still has its limitations, if the patient presents too late and is exhausted and in Type 2 respiratory failure, then we still do not have any alternative than to commence invasive ventilation.

However, CPAP not only reduces the need for tracheal intubation and invasive mechanical ventilation but also reduces the pressure on intensive care unit beds[6,9,10,30-32]. Bangladesh is one of the most densely populated countries, consisting of 4.7% of the total population aged 65 years or more[21]. With limited resources, the number of ICU beds is insufficient to treat such a large population. In view of the projected shortage of ventilators and medical oxygen supplies due to the upsurge in coronavirus cases, CTEX CPAP may play a significant role in managing COVID-19 patients. However, this study was conducted in a single

center over a small group of patients so that the result might not reflect the entire population.

CONCLUSION

CTEX CPAP demonstrated clinical effectiveness for COVID-19-related type 1 respiratory failure. In comparison to the conventional Yamind DM28 CPAP device, this novel device showed significantly better oxygenation.

Competing interests: There were no potential conflicts of interest relevant to this study.

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Ethical clearance: The study was approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Author's contribution: Concept of the study: AKMA, SMM; Study design: AKMA, DKB, MSI; Data gathering: AKMA, MMK, DKB, MSI, SMM; Writing, editing and finalizing the manuscript: AKMA, MMK, DKB, MSI, SMM.

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