A multicomponent oxygen delivery strategy for COVID-19 patients in a step-down intensive care unit: A case series

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is the cause of the pandemic that has affected millions of people worldwide with pulmonary manifestations ranging from mild pneumonia to ARDS and characterized by hypoxia. This has led to questions regarding the most efficacious and least harmful oxygen delivery strategies that minimize exposure to health care workers. In this case series, we present the hospital course of 4 patients that were managed with a multi-component oxygen delivery method in a COVID-19 step down unit.

1. Introduction

In December 2019 a new strain of coronavirus, named severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2), emerged as the cause of Coronavirus Disease 2019 (COVID-19) and has since become a pandemic affecting 3,847,278 people worldwide as of early May 2020 [1].

The pulmonary manifestations of this disease range from mild pneumonia to severe acute respiratory distress syndrome (ARDS) complicated by shock or multiorgan failure [2]. As such this pandemic has presented several challenges in the optimal management of hypoxia, posing questions regarding the most efficacious and least harmful oxygen delivery strategies that minimize exposure to health care workers. The current COVID-19 management guidelines by Surviving Sepsis Campaign (SSC) suggest the use of supplemental oxygen if the saturation of peripheral oxygen (SpO2) is <92% and recommend its use once SpO2 is <90% [1].

If acute hypoxemic respiratory failure develops despite supplemental oxygen, guidelines suggest the use of high flow nasal cannula (HFNC) over non-invasive positive pressure ventilation (NIPPV) which includes continuous positive airway pressure (CPAP) ventilation and Bi-level positive airway pressure ventilation (bi-level or BiPAP) [1]. Studies have indicated a lower risk of intubation when HFNC is used compared with NIPPV, in patients with acute respiratory failure secondary to different etiologies [3]. Furthermore, NIV has been shown to be associated with an increased risk of respiratory disease transmission [4,5]. Guidelines also indicate that if HFNC is not available, a trial of NIV is suggested, however they recommend this be performed in a negative pressure room, since NIV is considered an aerosol generating procedure [1].

There are no clear guidelines on optimal timing of intubation for COVID-19 respiratory failure. The presence of increased work of breathing or signs of clinical fatigue in patients already on supplemental oxygen, HFNC, or NIPPV, may indicate the need for mechanical ventilation. For instance, the Chinese Society of Anesthesiology Task Force on Airway Management, recommend intubation for patients with persistent or worsening symptoms (tachypnea with respiratory rate >30/min, hypoxemia with PaO2/FiO2 (P/F) ratio <150 mmHg) despite the use of HFNC or NIV for 2 hours [6].

In this case series, we present a multi-component oxygen delivery method. We used a high flow cannula that can deliver up to 15 LPM and up to 75% FiO2 (Salter 1600HF-14) [7]. This cannula was connected to a high flow bubble humidifier, to prevent nasal irritation due to high flow oxygen delivery [8]. To our knowledge no study thus far has investigated the risks and benefits of using this type of high flow cannula in combination with a non-rebreather mask (NRBM) and awake prone positioning (PP). We present the hospital course of 4 patients that were managed with this oxygen delivery method in a COVID-19 step down unit.
2. Case presentations

2.1. Case 1

A 53-year-old man with a history of non-insulin dependent type-2 diabetes mellitus presented with a one-week history of gradually progressive fever, chills, dry cough, and shortness of breath. He had previously tested positive for COVID-19 by polymerase chain reaction (PCR) test, at an outside institution 3 days prior to this presentation. On admission, he was afibrile, blood pressure was 111/67 mmHg, heart rate 91 beats per minute (bpm), and oxygen saturation was 85% on room air. The hypoxia corrected to 98% with 15L on NRBM. Initial chest x-ray (CXR) showed moderate to severe bilateral perihilar infiltrates with bilateral ground glass opacities. An arterial blood gas (ABG) on 15L O2 via NRBM was 7.48/32/70 (pH/PaCO2/PaO2), with a P/F ratio of 77.76, meeting the classification of severe ARDS by Berlin criteria [9].

Over the first 12 hours of admission, his oxygen requirements to maintain goal saturation (SpO2) between 92 and 96% continued to increase without a concurrent worsening of respiratory rate or effort. Given his minimal work of breathing and comfortable appearance, the decision to intubate was deferred. He was started on 10L O2 via HFNC in combination with 15L O2 via NRBM and initiated on the awake proning protocol, which consisted of lying in prone position for at least 16 hours per day. Over the course of 8 days, his oxygen requirements gradually decreased. By day 7, he was able to lay supine and upright while maintaining an SpO2 of at least 92%. By day 8, he was weaned off the HFNC, requiring 8–10L O2 via NRBM. By day 9, he was able to ambulate in his hospital room without dyspnea/fatigue, while maintaining the goal oxygen saturation. During his hospital course, his renal function, liver function tests, and hematologic labs remained stable, with only mild abnormalities. He was concurrently treated with a 10-day course of hydroxychloroquine and 5 days of azithromycin. Serial ABGs and P/F ratios showed persistent improvement from severe to moderate ARDS, as shown in Table 1. CT chest (Fig. 1A) obtained on day 8 was negative for pulmonary embolism but demonstrated moderate to severe bilateral perihilar infiltrates with peribronchial thickening and ground glass opacities, minimally improved from the initial CXR. The patient was eventually discharged home without any oxygen requirements and to our knowledge has not required further admissions.

2.2. Case 2

A 68-year-old man with a history of insulin-dependent type-2 diabetes mellitus and hypertension presented with dry cough, subjective fevers, and shortness of breath for one week. On admission, he was afibrile, blood pressure was 149/65, heart rate 95 bpm, and oxygen saturation was 80% on room air. Oxygen saturation improved to 98% on 10L O2 via NRBM. Initial CXR showed heterogeneous bibasilar airspace opacities. ABG on 15L NRBM was 7.44/34/64, with a P/F ratio of 71, meeting the definition of severe ARDS by Berlin criteria. Over the next 15 hours, while his work of breathing and comfort remained consistent, his oxygen requirement increased to 15L HFNC in addition to 15L NRBM to maintain a goal saturation of 92%. He was also initiated on the awake proning protocol. His CoVID-19 PCR test returned positive on day 2 of admission. Over the next week of hospitalization, his hypoxia improved while his oxygen requirements simultaneously decreased by 4–5L on the HFNC during and immediately after proning. However, these improvements were short-lived, and he required higher oxygen support while supine. By days 8, he became increasingly tachypneic and hypoxic even while prone, requiring 15L HFNC and 15L NRBM. CT chest (Fig. 1B) on day 8 showed bilateral ground-glass and interstitial infiltrates in all lung zones, left more than right, mostly peripheral in distribution, and was negative for pulmonary embolism. Viable lung tissue was noted only in the right upper and anterior lung zones. ABG showed a worsening PaO2 to 48 and he was therefore intubated on day 9. He was also treated with 10 days of hydroxychloroquine and 5 days of azithromycin. Serial ABGs for the days of hospitalization are as shown in Table 1. The patient remained intubated for a total of 15 days. During this period he developed oliguric acute kidney injury, and was transferred to another hospital to begin continuous veno-venous hemofiltration (CVVH). He was extubated on day 24 of hospitalization but had to be reintubated due to continued hypoxia. The patient failed subsequent spontaneous breathing trials (SBT) and on day 36 of hospitalization he underwent tracheostomy. During the submission of this manuscript, the patient’s disposition is to be transferred to a long-term acute care hospital (LTACH).

2.3. Case 3

A 62-year-old woman with no known past medical history presented with gradually worsening shortness of breath, cough, subjective fevers, chills, and a sore throat for 2 weeks. On presentation she was afibrile, blood pressure was 139/69 mmHg, heart rate 117 bpm, and oxygenation was 85% on room air, which improved to 100% on 15L NRBM. ABG on 15L NRBM was 7.42/36/111, with a P/F ratio of 123, meeting criteria for moderate ARDS per Berlin criteria. Admission CXR (Fig. 2A) showed moderate bilateral perihilar infiltrates with bilateral ground glass opacities. Her CoVID-19 PCR test returned positive on day 1 of admission. Over the first day of admission, her hypoxia worsened but her work of breathing and comfort remained stable, so decision to intubate was deferred and she was started on 10L of HFNC and 15 L of NRB in addition to the proning protocol. On day 2, the patient’s P/F ratio worsened to 77, thus the decision was made to pursue intubation. She was also treated with 5 days of hydroxychloroquine and 5 days of azithromycin. Her labs remained stable and within normal limits through her stay. Serial ABGs for the days of hospitalization are as shown in Table 1.

The patient remained intubated for 9 days, during this course she was transferred to another facility with more bed capacity and she was extubated on day 14 of hospitalization. The patient was finally discharged home without any oxygen requirements.

Table 1

|                    | CASE 1                  | CASE 2                  | CASE 3                  | CASE 4                  |
|--------------------|-------------------------|-------------------------|-------------------------|-------------------------|
|                    | Day 0 | Day 8 | Transfer | Day 0 | Day 9 | Intubation | Day 0 | Day 2 | Intubation | Day 0 | Day 7 | Transfer |
| PH                 | 7.48  | 7.4   |          | 7.44  | 7.53  |            | 7.42  | 7.45  |            | 7.47  | 7.47  |          |
| PACO2 (MMHG)       | 32    | 47    |          | 34    | 42    |            | 36    | 35    |            | 34    | 41    |          |
| PAO2 (MMHG)        | 70    | 80    | 64       | 56    | 111   | 70         | 62    | 78    |            |       |       |          |
| FIO2 (%)           | 90% via 15L NRBM | 50% via 10L NRBM | 90% via 15L NRBM | 100% via 15L HFNC and 15L NRBM | 90% via 15L (+) 10L NC | 123 | Moderate, transition to severe | 68.89 | 173.33 | Severe, transition to moderate |
| P/F RATIO ARDS SEVERITY | 77.78 |        |          | 71    | 46    |            |        |       |            |       |       |          |
discharged on day 23 to a nursing home for rehabilitation. It is unknown if she was discharged with supplemental oxygen.

2.4. Case 4

A 58-year-old woman with history of pre-diabetes presented with URI symptoms, fever (100.5) and diarrhea for a week, with a reported positive sick contact. On admission, her blood pressure was 105/55 mmHg, pulse 78 bpm. She was tachypneic with a respiratory rate in the 30s and hypoxic to 84% on room air. The hypoxia corrected to >92% with 15L NRBM. ABG at admission was 7.47/34/62 (pH/PaCO2/PaO2) and calculated P/F ratio was 68.89, consistent with severe ARDS by Berlin criteria. The admission CXR (Fig. 2B) showed bilateral interstitial opacities suspicious for a viral/atypical pneumonia. On Day 2 of admission, she tested positive for CoVID-19 PCR test. By Day 2, her hypoxia worsened, requiring the addition of HFNC at 15L/min to 15L NRBM and awake proning. During the next week, she performed well with the protocol. Her ARDS improved to moderate (P/F ratio of 173.33). By the 2nd week of admission, her hypoxia gradually improved until she was able to maintain saturations >92% on room air to 1 L NC. She was treated with 5 days of azithromycin and 5 days of hydroxychloroquine. Her labs remained mostly within normal limits and stable throughout admission. ABGs on admission and on day of transfer out of the stepdown unit and to the floor are shown in Table 1.

The patient was eventually discharged home with 2L of supplemental oxygen.

3. Discussion

In this case series we describe the results of a multi-component respiratory management strategy for four COVID-19 patients with moderate to severe ARDS. The method consisted of a high flow nasal cannula, non-rebreather mask and prone positioning. The four patients presented with shortness of breath and were found to have bilateral pulmonary infiltrates on initial CXR. Three of the patients were classified as severe ARDS on admission, one as moderate. Two of the four patients transitioned from severe to moderate ARDS and did not require mechanical ventilation. Case 1 was discharged home without supplemental oxygen and case 4 was discharged with 2L of supplemental oxygen. Cases 2 and 3 required mechanical ventilation due to increased oxygen requirements despite being on high flow nasal cannula at 15 L, NRBM at 15L and PP.

The high flow nasal cannula system used in our patient population differs from the one most commonly described in COVID-19 pneumonia and ARDS literature [10,11]. Our system is the Salter 1600HF-14 cannula and provides up to 15 LPM and 75% FiO2 [7], which goes
improve ventilation to well perfused regions in the lung thereby improving the ventilation/perfusion mismatch [18]. For instance, we noticed that the patient in Case 2 had significant improvements in his SpO2 from 86% to 98% whenever he was on PP, which explains why he remained comfortable for a long period of time before finally intubating him on day 9 of hospitalization.

Our multi-component oxygen delivery strategy had various success rates (2 out of 4 required intubation). Prior literature has demonstrated the use of regular, non-humidified nasal cannula up to 15LPM in conjunction with NRBM at 15LPM as preoxygenation before intubation [14,19]. However, to our knowledge, this strategy has thus far not been studied for ARDS or COVID-19. The use of NRBM in conjunction with the nasal cannula was primarily to prevent aerosolization. Theoretically the combination of both nasal canula and NRBM could also provide higher flow rates and FiO2. We further maximized oxygen delivery via the prone position. With this multi-component oxygen delivery strategy, we may be able to achieve higher FiO2 than with any one strategy in isolation.

Our first case presented with features of severe ARDS, but this method improved his P/F ratio and consequently he was eventually weaned off oxygen. Our second case was also characterized as severe ARDS, but this patient was eventually intubated. Our third case was initially classified as moderate, but she transitioned to severe ARDS and required mechanical ventilation. Our last case was initially classified as severe but after the implementation of this method, her ARDS improved and she progressed to moderate ARDS and was finally discharged on 2L of supplemental oxygen. Interestingly, the four patients looked clinically comfortable on our method, so why did they have so different outcomes?

As represented by our cases, COVID-19 is a disease that has a wide spectrum of symptoms. A very interesting hypothesis postulated byGattinoni et al., [20] may help us understand why these patients had different outcomes despite applying the same measures of respiratory support. Although COVID-19 has been managed as ARDS, this condition has its own defining characteristics such as hypoxemia out of proportion to normal respiratory compliance, which is not observed in typical ARDS physiology [20]. It is hypothesized that COVID-19 can be characterized by 2 phenotypes: L and H. Type L is characterized by normal compliance, which may explain why patients can be hypoxic but not in severe respiratory distress. In these patients, supplemental oxygen is critical for correcting hypoxemia. For dyspneic patients, HFNC or NIPPV can be used. If these patients get intubated, high PEEP may be detrimental since they have near normal compliance. Once intubated, it is recommended to administer tidal volumes at >6 ml/kg and limit PEEP to 8–10 cmH2O, as alveolar recruitability in these patients is low. If these patients are intubated early, they may avoid transition from Type L to type H [20].

Type H is characterized by low compliance and high lung weight, resembling typical severe ARDS physiology. These patients should be managed as severe ARDS with high PEEP and prone position [20]. We may extrapolate this theory to our 4 patients as shown below in Table 2. We may assume that cases 2 and 3 progressed from L to H [20].

To our knowledge this is the first time that a study reports the combined use of nasal cannula, NRBM and PP. The use of HFNC remains controversial and is subject to ongoing debate. But studies have reported favorable outcomes with it, specifically when used in moderate ARDS [10,11].

Our case series suggests that considering the physiology of COVID-19 pneumonia is important in deciding on the best management strategy for our patients, as early detection of type L or H phenotype may prevent delays in intubation. More studies are needed to determine if the use of this method has a positive or negative impact on the outcomes of COVID-19 patients according to their physiologic phenotype on presentation.

Finally, we had our patients remain in PP for at least 16 hours per day. Mechanically ventilated patients with ARDS that were placed in PP, have been shown to have improved mortality [17]. Awake PP for COVID-19 patients is being increasingly reported in COVID-19 literature, demonstrating improvements in oxygenation when used with HFNC or NIPPV [10]. Physiologically, PP can decrease the formation ofatelectasis via the creation of more negative pleural pressure and the repositioning of the heart to rest in the sternal area. Also, PP can

connected to a bubble humidifier. The traditional HFNC systems reported in the literature can provide up to 60 LPM and up to 100% FiO2 [11]. The traditional Vapotherm [12] system was not utilized in this population due to supply shortages and also to minimize the risk of aerosolizing of COVID-19 particles. In our case series, this high flow cannula was set to deliver 15 LPM. In addition, we utilized a NRBM to provide flow rates of 15 L, with the capacity to deliver 60–90% FiO2 [13,14]. The NRBM was used to prevent aerosolization of particles that may have been generated by the high flow cannula. Studies suggest that NRBM has the least dispersed aerosols, with a maximum exhaled air distances of <0.1m at 10 LPM [15]. NRBM has also been suggested as a strategy to escalate oxygen therapy for COVID-19 patients [16].

Fig. 2. (A) Case 3. CXR on admission. Moderate bilateral perihilar infiltrates with bilateral ground glass opacities. (B) Case 4. CXR on admission. Bilateral interstitial opacities.

Table 2. We may assume that cases 2 and 3 progressed from L to H [20].
Table 2
Outcomes of the study patients with COVID-19.

| Case | Presumed type of pneumonia | Intubation | LOS | Transfer to another hospital | Disposition | Supplemental oxygen on discharge | Treatments (antibiotics, steroids) | 30-day Mortality (From admit date) |
|------|-----------------------------|------------|-----|------------------------------|-------------|----------------------------------|-----------------------------------|-----------------------------------|
| 1    | Type L                       | No         | 11 days | No                           | Discharged home | No                               | Ceftriaxone 5 days Azithromycin 5 days Hydroxychloroquine 10 days | Survived                          |
| 2    | Type L, transition to type H | Yes, on day 9 of hospitalization. Remained intubated for 15 days. Reintubated, failed SBT and now tracheostomy on day 36 of hospitalization | 37 days (still hospitalized) | Yes, due to oliguric AKI, for CVVH | Discharged to LTACH | Ventilator                       | Ceftriaxone 5 days Azithromycin 5 days Ceftepine 7 days Hydroxychloroquine 10 days | Survived                          |
| 3    | Type L, transition to type H | Yes, on day 5 of hospitalization. Remained intubated for 9 days. Extubated on day 14 | 23 days | Yes, due to bed shortages | Discharged to nursing home | Unknown | Ceftriaxone 5 days Azithromycin 5 days Hydroxychloroquine 5 days Ceftepine 7 days Hydroxychloroquine 5 days | Survived                          |
| 4    | Type L                       | No         | 16 days | No                           | Discharged home | 2L via nasal canula | Ceftriaxone 5 days Azithromycin 5 days Hydroxychloroquine 5 days | Survived                          |

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Author contributions

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Declaration of competing interest

No conflicts of interest exist for all authors. No source of funding present.

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