CASE REPORT

The Use of High Flow Nasal Cannula and Awake Prone-positioning in COVID-19 Pneumonia in a Caribbean setting: A Case Series and Review of the Literature

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DOI: 10.48107/CMJ.2020.12.004

ABSTRACT

COVID-19 is associated with acute hypoxaemic respiratory failure and an ARDS like presentation. Traditional management generally involves the use of endotracheal intubation and mechanical ventilation. This approach can lead to significant resource consumption with the potential for patient morbidity. High Flow Nasal Cannula (HFNC) and prone ventilation can be used as alternative approaches. We present the successful use of this approach in three (3) COVID-19 cases. All patients had multiple co-morbidities and were older than 50 years. Two patients were classified as having severe ARDS. All patients had improved oxygenation after 4 hours of proning and throughout their course. All three cases were successfully discharged from the ICU. No complications were reported from proning. High Flow Nasal Cannula (HFNC) and awake pronation can be an effective modality in COVID-19 pneumonia.

INTRODUCTION

Trinidad and Tobago recorded its first case of COVID-19 on March 12th, 2020. To date, there are 4709 confirmed cases and 78 deaths recorded.[1] Complications of Coronavirus 2 (SARS-COV-2) infection include acute hypoxaemic respiratory failure and severe adult respiratory distress syndrome (ARDS). Generally, patients who require endotracheal intubation and mechanical ventilation for acute hypoxaemic respiratory failure have high mortality rates.[2] For COVID-19 ventilated patients, a case series reported mortality in the 18-65 and over 65-year age groups as 76.4% and 97.2% respectively.[3]

High Flow Nasal Cannula (HFNC) is a relatively new modality where a high concentration of humidified oxygen can be delivered safely and comfortably to patients. It also has the potential to prevent the need for intubation and mechanical ventilation. Initial international experience using this modality in COVID-19 has been promising so far.[4]

Additionally, prone ventilation, a known adjunct used to improve oxygenation in ARDS can also be combined with HFNC. Although research is underway on the combined use of these modalities, no large-scale trial data exists. We present three consecutive cases where prone ventilation was successfully combined with the use of HFNC. The current evidence on the role of HFNC and prone ventilation is also discussed.

CASE SERIES

This case series presents three consecutive patients with Polymerase Chain Reaction (PCR) confirmed COVID-19 and moderate to severe ARDS admitted to the Intensive Care Unit (ICU) in a parallel healthcare facility in Trinidad and Tobago. Cases 1, 2 and 3 are outlined below.

Case 1 was a 57-year-old obese female, bilateral amputee with pre-existing diabetes mellitus, hypertension, past-history of a pulmonary embolism and stroke with no residual deficits. She presented with a four day history of worsening dyspnoea, subjective fever and a non-productive cough together with generalized weakness.

Case 2 was a 66 year old obese male with a history of non-insulin dependent type 2 diabetes mellitus and hypertension with a four day history of dyspnoea, decreased appetite and generalized body pain. He was classified as having severe ARDS on presentation.

Case 3 was a 58 year old obese female with a history of non-insulin dependent type 2 diabetes mellitus with a nine day history of dyspnoea, worsening orthopnoea and a subjective fever associated with a productive cough. She was also classified as severe ARDS. She required an extended course in the ICU for a period of 11 days.

The relevant clinical features of all three patients are summarized in Table 1.

All three patients had pre-existing co-morbidities. Prior to being referred to the ICU, all patients received conventional low-flow oxygen therapy through face masks and nasal cannulae. All patients presented to the unit with mild to moderate dyspnoea and SpO_2 values ranging between 92-97%. The time between the onset of symptoms and admission to the ICU ranged between four to nine days.

On admission to ICU, patients were immediately placed on HFNC with a starting flow rate of 60 L/min and the estimated fraction of the inspired oxygen concentration (FIO_2) ranging between 85-95%, and subsequently weaned to maintain a SpO_2 of 91-96%. Additionally, awake proning was commenced using the 'roast pig technique' as described by the Intensive Care Society.[5] Patients spent a period of four hours in the prone position, then alternated with the lateral position for two hours, followed by a period of 30 minutes to one hour in the supine position and the cycle was repeated. All patient-position changes were made during the day, while the patients remained either supine or lateral during night. All patients were able to position themselves without assistance and tolerated the positioning well. Cases 2 and 3 required intermittent morphine boluses (2.5-5 mg) while turning, due to musculoskeletal pain.

Improvement in PaO_2/FiO_2 gradient of oxygenation were noted in all patients, as depicted in Figures 1 and 2. Blood investigations revealed an elevated c-reactive protein in all three patients, with two patients displaying an elevated neutrophil to lymphocyte ratio. Dexamethasone 6 mg IV (once a day) was commenced on admission for a period of ten days. Antiviral therapy with Oseltamivir, together with antibiotic therapy utilizing a macrolide and cephalosporin was initiated in all patients. Additionally, prophylactic anticoagulation with Low Molecular Weight heparin, and supplements of Vitamin B-Complex and C were prescribed.

No patient required endotracheal intubation or mechanical ventilation. All patients were successfully discharged from the ICU, and at the time of writing all patients were still alive. No pressure sores or disconnections were reported during prone positioning.

DISCUSSION

The Surviving Sepsis guidelines Covid-19 update recommends the use of high flow nasal cannula (HFNC) in the treatment of acute hypoxaemic respiratory failure despite conventional oxygen therapy.[6] HFNC delivers warm, humidified oxygen at a peak flow rate of 60 L/min, achieving high fractions of inspired oxygen (FiO_2), low levels of positive pressure and a decrease in physiological dead space. Due to these benefits, patients experience relief from breathlessness, improved comfort and a reduced work of breathing.[4]

Evidence for HFNC in COVID-19 was initially derived indirectly from other acute hypoxaemic respiratory failure populations and its effect on intubation rates remain unclear. In the FLORALI trial, HFNC did not improve the rate of intubation but reduced all-cause mortality at 90

Table 1. The clinical features and hospital course of all three patients

	Patient 1	**Patient 2**	**Patient 3**
Age (y)	57	66	58
Comorbidities	Diabetes Mellitus, Hypertension, Past history of Pulmonary embolism (not currently on therapy) CVA (nil residual deficits) Bilateral BKA 2^0 peripheral arterial disease, Obesity	Diabetes Mellitus, Hypertension, Obesity	Diabetes Mellitus, Obesity
Onset of symptoms to admission (days)	4	4	9
Presenting symptoms	Dyspnoea Subjective fever Non- productive cough Generalized weakness	Dyspnoea Decreased appetite Generalized body pain	Dyspnoea Worsening orthopnoea Subjective fever Non-productive cough
CXR/CT Scan	CXR: Bilateral pulmonary infiltrates	CXR: Patchy opacifications bilaterally, present in the lower zones	CXR: Bilateral Interstitial markings
Previous O_2 therapy	NRFM	NRFM	NRFM
Lab investigations (On admission)	WBC: 10.1 x 10^3uL NLR: 1.7 CRP: 10mg/dl Cr: 1.1mg/dl	WBC: 9.6 x 10^3uL NLR:10.4 CRP:10.1mg/dl Cr:1.8	WBC: 19.7 x 10^3uL NLR: 6.3 CRP:25.1mg/dl Cr: 1.4mg/dl
Severity of SOB	Mild	Moderate	Moderate
SpO_2 on admission	97%	92%	97%
Medical treatment (×days)	Rocephin 1g IV od (×5) Azithromycin 500 mg PO od (×5) Tamiflu 75 mg PO bd (×5) Dexamethasone 6 mg IV od (×5) Clexane 80 mg SC od Aspirin 81 mg PO od Simvastatin 40 mg PO nocte Vitamin C 1g PO bd Vitamin B 2 mL IV od Nifedipine 20 mg PO od	Rocephin 1g IV od (×6) Azithromycin 500 mg PO od (×5) Tamiflu 75 mg PO bd (×5) Dexamethasone 6 mg IV od (× 6) Clexane 60 mg SC od Vitamin C 1 g PO bd Vitamin B 2 mL IV od	Rocephin 1g IV od (×7) Azithromycin 500 mg PO od (×5) Tamiflu 75 mg PO bd (×5) Dexamethasone 6 mg IV od (×10) Clexane 60 mg SC od Vitamin C 1 g PO bd Vitamin B complex 2 mL IV od
Days on HFNC	2	5	9
Days in ICU	5	5	11

CVA: Cerebrovascular Accident
NRFM: Non-rebreathable Face Mask
SOB: Shortness of Breath
NLR:Neutrophil to lymphocyte ratio
CRP: C-Reactive Protein
BKA: Below Knee Amputation
CXR: Chest X Ray
HFNC: High Flow Nasal Cannula

days and increased ventilator-free days at day 28.[7] A systematic review and meta-analysis of nine randomized controlled trials (RCTs) involving 2093 patients in 2019 demonstrated lower rates of intubation compared with conventional oxygen (RR 0.85, 95% CI 0.74-0.99), but did not impact mortality rates or ICU length of stay (LOS).[8] Due to the large heterogeneity of critically ill patients, inadequate methodological quality and reporting, there are relatively few RCTs demonstrating a reduction in mortality in critical care and the validity of this endpoint remains uncertain.[9]

Despite showing no mortality benefit, the potential of avoiding invasive ventilation with an endotracheal tube in COVID-19 patients is an important finding in resource allocation, as it increases the availability ICU beds and ventilators as well as reduces the risk of infection in health care providers. It can also be hypothesized that HFNC will reduce nosocomial infections, complications

Figure 1: Table comparing PaO_2/FiO_2 ratio on admission and at 4 hours post awake-proning

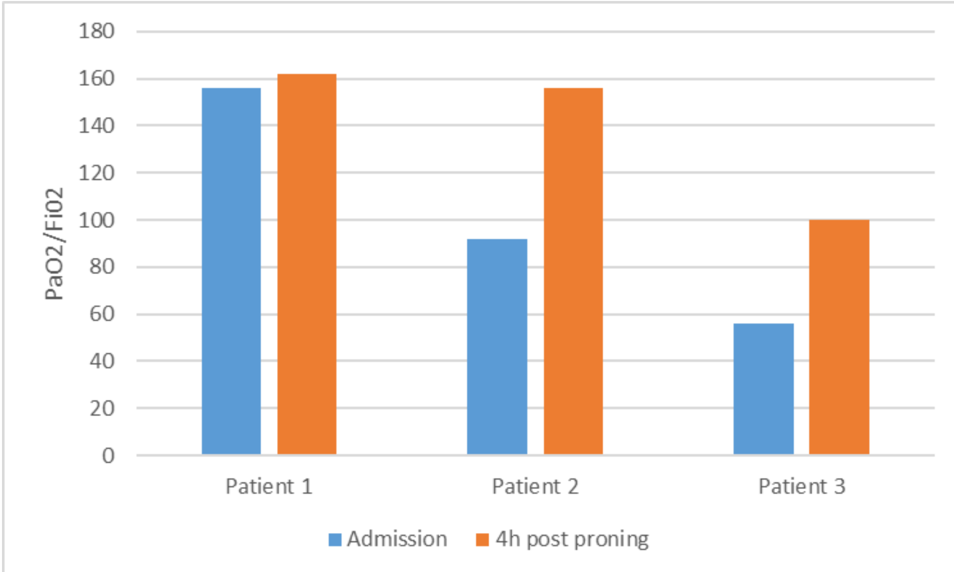
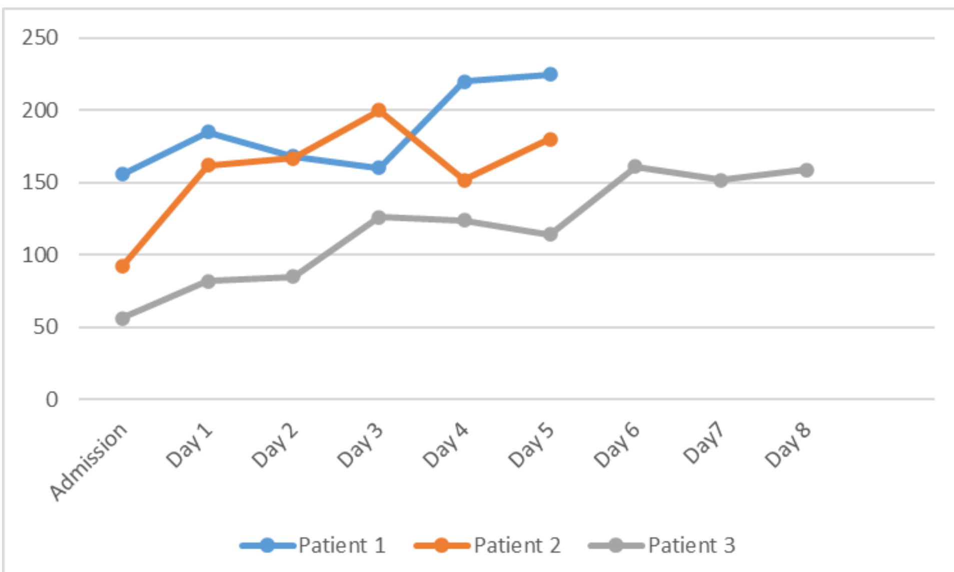


Figure 2: Line graph showing the trend of PaO_2/FiO_2 ratio during ICU course



with sedation, delirium and venous thromboembolism.

As the current COVID-19 pandemic continues, more evidence is emerging for the role of HFNC in the management of acute hypoxaemic respiratory failure. In an observational study of 28 COVID-19 patients conducted in Italy, the outcome and safety of HFNC was assessed in hypoxemic patients unresponsive to conventional oxygen therapy.1[0] Nineteen patients (67.8%) were successfully treated and discharged, nine (32.2%) failed HFNC and progressed to NIV of which five required intubation. Three of the intubated patients subsequently died. A $PaO_2/FiO_2 < 100$ mmHg was found to be associated with an increased risk of HFNC failure.

In a multicentre, retrospective cohort study in China which followed 43 COVID-19 patients, 20 patients (46.5%) had failure with HFNC of which 13 required endotracheal intubation. Successful HFNC patients had higher median oxygen saturations (96% vs 93%;

p=0.001) at admission (similar to our patients) compared to those with HFNC failure.[4] Expert evidence also supports the use of HFNC in COVID-19 with multiple professional societies advocating their use.[11]

Another major benefit with the use of HFNC is the ease in performing awake proning in the treatment of refractory hypoxemia. Awake proning avoids many of the logistic challenges and difficulties that exists in proning a sedated and mechanically ventilated patient, which can be technically challenging, as the patient co-ordinates and performs the position change themselves. Prone positioning improves ventilation/perfusion mismatch, reduces shunting and improves hypoxaemia in ARDS patients. Its use is generally regarded as part of the standard of care for hypoxaemic ARDS patients.[12]

Recent evidence suggests that early awake proning with HFNC may avoid intubation in patients with moderate to severe ARDS.[13] Preliminary data in COVID-19 patients also suggest that awake proning and HFNC improves oxygenation and reduces need for intubation and mortality rates. In a small, single-centre cohort study it was found that prone positioning with HFNC improved oxygenation in COVID-19 severe hypoxemic respiratory failure. This study also found that patients with a SpO_2 of 95% or greater after one hour of proning was associated with a lower incidence of intubation.[14] With evidence being limited to case series and small observational studies, questions still need to be answered surrounding the efficacy of awake proning in both ARDS and COVID-19 hypoxaemic respiratory failure.

Further research with high quality RCTs is warranted to assess the benefits and risks, as well as the patient population which benefits the most.[15] There is also limited data regarding the optimal awake proning and HFNC regime in COVID-19 patients. The COVAYDE trial is currently underway to provide more information on the benefit of awake proning and HFNC in severe COVID-19 infections.[16]

Negative aspects of HFNC in the treatment of COVID-19 hypoxemic respiratory failure include failure and need for intubation with a severely decompensated patient and the potential risk of infection with aerosolization.

A challenge exists in identifying patient characteristics that will predict HFNC failure and ensure intubation is not delayed. Vianello et al. found that a $PaO_2/FiO_2 < 100$ was associated with an increased risk of HFNC failure.[10] The recently described ROX index is defined as the ratio of SpO_2 /FiO_2 to respiratory rate and is a useful bedside tool to predict HFNC failure and need for intubation. Generally, all patients with a ROX>4.88 were less likely to be intubated.[4] A retrospective study involving 129 COVID-19 patients investigating the use of ROX index, confirmed the validity of this simple tool to predict need for intubation.[17] Patients 1, 2 and 3 in our case series had a ROX index of 8.27, 5.28 and 4.95 respectively at 12 hours, which is in keeping with predicting the success of HFNC in our patients.

The Chinese Society of Anesthesiology Task Force on Airway Management recommends intubation for COVID-19 patients with persistent or worsening symptoms (tachypnoea with respiratory rate >30/min, hypoxemia with PaO_2/FiO_2 (P/F) ratio <150 mmHg) despite the use of HFNC or NIV for two hours.[18] However, adopting this strategy can lead to unnecessary intubations. Paying close attention to individual patient physiology and work of breathing may lead to more accurate assessments of the need for intubation.[19]

Patients number 2 and 3 in our case series had admitting P/F ratios of less than 100 when started on HFNC, with patient 3 having values in the 50's indicating very severe hypoxaemia. If classical criteria were applied, both patients would have been urgently intubated, paralyzed and proned. However, their lack of severe dyspnoea and increased work of breathing allowed for the trial of HFNC. After four hours of prone ventilation, cases two and three had an almost doubling of their P/F ratio – a significant improvement. Additionally, all three cases were obese with multiple co-morbidities, making a course of mechanical ventilation and subsequent weaning potentially challenging.

Another major controversy with the use of HFNC in COVID-19 patients is the potential for transmission of infection, as HFNC may be regarded as an aerosol-generating procedure (AGP). Jie Li et al. reviewed the literature regarding HFNC as an AGP.[20] It was concluded that HFNC did not pose any additional infection risk when compared to conventional oxygen therapy. There is to date, no published evidence that HFNC leads to an increase in transmission of nosocomial respiratory infections.[6,20] At our institution, HFNC is currently used as first line in the management of acute hypoxaemic respiratory failure. To date, 21 doctors, 26 nurses and other axillary staff have been involved in the management of COVID-19 patients with HFNC and we report no infections to the staff involved.

Limitations of our case series include the small number of patients in the population and the retrospective nature of the study that may result in significant bias. Indeed, our experience in this modality is limited. Further high quality RCTs are warranted to evaluate the use of HFNC and awake proning in COVID-19 patients.

CONCLUSION

We report the successful use of HFNC and prone-positioning to avoid endotracheal intubation in all 3 patients in our case series. HFNC together with proning was well tolerated and safe to staff and patients. HFNC combined with awake self-proning has the potential to be a cost-effective and efficacious treatment option that should be investigated further in larger trials.

Ethical Approval statement: Obtained or not applicable
Conflict of interest statement: None declared
Informed Consent statement: informed Consent was obtained from all patients/relatives
Funding statement: none
Authors Contribution: KS conceptualized the topic, RC, KS and SB wrote the manuscript

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