Pre-Hospital Critical Care Management of Severe Hypoxemia in Victims of Covid-19: A Case Series

Jens Otto Mæhlen (jmaehlen@hotmail.com)
Akershus University Hospital: Akershus Universitetssykehus HF https://orcid.org/0000-0003-3917-8802

Jostein Hagemo
Oslo University Hospital, Air Ambulance Department

Marius Rehn
Oslo University Hospital, Air Ambulance Department

Hans Julius Heimdal
Oslo University Hospital, Air Ambulance Department

Roger Mikalsen
Vestre Viken HF, Air Ambulance Department

William Ottestad
Oslo University Hospital, Air Ambulance Department

Case report

Keywords: Prehospital management. Covid-19. Hypoxemia. Case series. Ventilation. Supplemental Oxygen.

Posted Date: October 21st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-92840/v1

Version of Record: A version of this preprint was published on January 12th, 2021. See the published version at https://doi.org/10.1186/s13049-021-00831-3.

Abstract

Objective: Despite critical hypoxemia, Covid-19 patients may present without proportional signs of respiratory distress. In this case series we describe the pre-hospital management of three patients with critical respiratory failure due to Covid-19. All presented with severe hypoxemia refractory to supplemental oxygen. The specific cause of hypoxemia in these patients is a matter of speculation, and several mechanisms have been suggested. We discuss possible strategies for ventilatory support in the emergency pre-hospital setting.

Methods: Three cases with similar clinical presentation were identified at two bases within the Norwegian national helicopter emergency medical service (HEMS) system. The HEMS units are manned by a consultant anesthesiologist, a HEMS crew member and a pilot.

Patients´ next of kin and the Regional committee for medical and health research ethics have approved the publication of this report.

Conclusion: Patients with Covid-19 and severe hypoxemia may pose a considerable challenge for the prehospital emergency services. Covid-19 patients with hypocapnic hypoxia and a high minute ventilation demand high oxygen flow rates in order to avoid dilution of oxygen with ambient air, which is difficult to achieve with non-rebreathers and disposable CPAP systems. Intubation may be associated with a high risk of complications in these patients and should be carried out with diligence when considered necessary.

Introduction

Covid-19 is characterized by an initial phase of unspecific symptoms such as fever and unproductive cough[1]. Due to risk of disease transmission, patients are advised to stay quarantined at home, unless medical care is needed. However, some patients develop severe respiratory failure and extreme hypoxemia, yet without proportional signs of respiratory distress or air hunger. Although anecdotal, a common clinical pattern has emerged; a remarkable discrepancy between relatively well-preserved lung compliance and severely compromised pulmonary gas exchange[2, 3]. A brisk ventilatory response with a rapid respiratory rate has been reported to lead to extreme hypocapnia in some of these patients, possibly contributing to lack of air hunger. Apart from a rapid respiratory rate, the clinical presentation in these patients may be misleading. Despite critical hypoxemia these patients tend to be awake, responsive, cooperative and hemodynamically stable. This particular clinical presentation has been coined “silent hypoxemia”[3]. In this pre-hospital case-series we report three Covid-19 patients with critical respiratory failure, and discuss possible strategies for ventilatory support.

Methods

The Norwegian national air ambulance system is governmentally funded and consist of 12 Helicopter Emergency Medical Services (HEMS) bases. These air ambulance units are all manned by a consultant anesthesiologist and a rescue man. Relevant cases were identified from clinical governance discussions and the attending consultant provided a focused narrative of the events. Publication of these case reports has been approved by the Regional committee for medical and health research ethics (Ref. ID: 142091) and written informed consent has been obtained from next of kin. The exact age of the patients remains undisclosed for privacy protection purposes.

Pre-hospital Covid-19 Cases

Case 1

A man in his sixties presented to his general practitioner with tachypnea, high fever and a dry cough. The patient was admitted to hospital and ambulance transport was initiated. Despite receiving supplemental oxygen, the patient´s pulse oximetry readings decreased from 72% to 55% and the paramedics requested HEMS assistance. Upon HEMS arrival, the patient was awake and cooperative. The patient had been placed in an upright position. He was administered intravenous paracetamol due to a body temperature of 40°C. As the patient refused wearing a non-rebreather mask he received oxygen via a nasal cannula at a flow rate of 10 liters/minute. Physical examination revealed a respiratory rate of 20 – 25 breaths/minute, a peripheral oxygen saturation (SpO_2) of 55%, a heart rate of 80 beats/minute, a blood pressure of 120/60 mmHg, slightly cold peripheries and a body temperature of 38.9°C. Although tachypneic, he was able to speak in whole sentences. As the patient was alert and cooperative, no further treatment was initiated. His condition remained unchanged upon hospital arrival one hour later. He was admitted to the intensive care unit (ICU) where treatment with non-invasive ventilation (NIV) was initiated. After a few hours of NIV treatment the patient was intubated and mechanically ventilated due to exhaustion. He was later diagnosed with Covid-19 and died in the ICU approximately 3 weeks later.

Case 2

A woman in in her fifties with a previous history of hypertension, asthma and obesity presented with fever and a dry cough. One of her family members had tested positive for SARS-CoV-2. Her condition had deteriorated rapidly the last hour with worsening dyspnea. The paramedic crew arriving on scene requested HEMS assistance as the patient remained severely hypoxemic after receiving supplemental oxygen. Upon HEMS arrival, the patient presented with severe cyanosis and labored breathing. Despite this she was awake and cooperative. Physical examination revealed a respiratory rate of 50 breaths/minute, SpO_2 of 52% while breathing 12 liters/minute oxygen on a non-rebreather mask, heart rate of 142 beats/minute, blood pressure 200/110 mmHg, cold peripheries and a body temperature of 39°C. On route to hospital the non-rebreather mask was replaced and oxygen was administered with a bag valve mask (BVM) which was sealed tight around the patients mouth and nose. A positive end-expiratory pressure (PEEP) valve was connected to the BVM. The SpO_2 increased from 52 to 66% and the respiratory rate remained unchanged with an end-tidal CO_2 of 4,2 Kilopascal(kPa). As she became increasingly exhausted, she received assisted ventilation with the BVM. Shortly after arrival to the hospital she was intubated. The patient suffered temporary cardiac arrest during the intubation procedure. She was later diagnosed with Covid-19 and died in the ICU a few weeks later.

Case 3

A man in his fifties with a past history of hypertension, obesity and cerebrovascular disease was in home-quarantine due to symptoms of Covid-19. An ambulance was requested as his condition quickly deteriorated with increasing respiratory distress. Upon arrival the paramedics found the patient severely hypoxemic. They initiated treatment with a disposable CPAP system (pulmodyne O_2-Max®) before starting transport. Due to lack of effect, the CPAP was replaced by a non-rebreather mask and a HEMS unit was requested for assistance. The HEMS physician found the patient awake and cooperative, but with severe dyspnea. Physical examination revealed a respiratory rate of 50 breaths/minute, SpO_2 35% while breathing oxygen 10 liters/minute on a non-rebreather mask and a blood pressure of 120/80 mmHg. The patient was placed in a semi-upright position, the non-rebreather mask was removed and a BVM with PEEP of 10 cmH_2O and oxygen flow rate of 15 liters/minute was applied. SpO_2 increased from 35% to 50%. The decision to perform a prehospital intubation was made since the patient responded poorly to oxygen therapy and could no longer sustain adequate minute ventilation.
Prior to induction of anesthesia the patient became unresponsive, and assisted ventilations were given. Induction of anesthesia was performed with 250 micrograms fentanyl, 250 mg ketamine and 100mg rocuronium. The patient was ventilated in the apneic phase and intubated using direct laryngoscopy. First pass intubation was achieved quickly without further drop in SpO2. During loading into the ambulance, the patient became pulseless and CPR was commenced. A central pulse was identified after 20-30 seconds of CPR. A high minute ventilation with the BVM was maintained so that end-tidal CO_2 remained unchanged at 2.5 kPa. The oxygen saturation increased from 50 to 60%. Systolic blood pressure was 90 mmHg. The patient was positioned in a semi-upright position in the ambulance during transport. Shortly after hospital arrival the patient suffered circulatory arrest with a pulseless electrical activity as the initial rhythm. Despite 25 minutes of CPR a refractory asystole developed. The patient was diagnosed with Covid-19 post mortem.

Discussion

We describe three Covid-19 cases presenting with critical respiratory failure managed in the pre-hospital setting. The cause of hypoxemia in these patients is a matter of speculation, and several mechanisms have been suggested. Two recent autopsy studies have reported interstitial thickening and congested capillaries, making both diffusion failure and a low V/Q ratio secondary to dead space ventilation plausible mechanisms[4, 5]. However, CT imaging studies also report consolidations in the majority of patients with Covid-19 pneumonia[6]. Consolidations may accordingly contribute to a substantial shunt fraction, which explains the failure of oxygen therapy in some of these patients. Prone positioning has been reported to improve oxygenation in COVID-19 patients[7], lending support to the notion that pulmonary shunting is a contributing factor to hypoxemia. Furthermore, Gatinoni et al. postulated dysregulation of pulmonary vascular tone with loss of hypoxic vasoconstriction and potentially increased pulmonary shunting[8]. Covid-19 patients are reported to have near normal lung compliance and consequently they can maintain large minute volumes for a prolonged period of time without succumbing to exhaustion.

Carbon dioxide (CO_2) diffuses through tissues about twenty times more rapidly compared to oxygen (O_2), and these properties likely underlie the disproportional pulmonary exchange of CO_2 and O_2 in these patients. The increased minute ventilation in these patients might be a sign of progressive respiratory failure with limited diffusion and increased dead space ventilation. Normal to increased end-tidal CO_2 in hypoxemic patients, might therefore be a sign of exhaustion or imminent respiratory collapse.

Despite being severely hypoxemic all three patients described in this case series were responsive and cooperative upon presentation. All cases presented with low pulse oximetry values in the 35% – 60% range. However, how well this reflects arterial oxygen saturation (SaO_2) is uncertain since pulse oximetry is not validated for SaO_2 values below 70% and tends to overestimate hypoxemia below this threshold[9].

Early intubation of Covid-19 patients have been recommended by some institutions, however this strategy has recently been challenged[10]. Anecdotal evidence suggest that favorable outcome can be achieved with NIV support even in patients with severe respiratory failure and persistent hypoxemia[11], and that NIV may reduce the need for intubation[12]. Several factors can contribute to a favorable outcome with NIV. First, as these patients seem to have near normal lung compliance, they do not necessarily have increased work of breathing implying that they can endure long periods with NIV support, without the need for heavy sedation. Second, prone positioning has been reported to be effective in Covid-19 and this can be easier to accomplish in awake patients on NIV compared to intubated patients which demands heavy sedation[7]. Further, profound hypoxemia, hypotension and even cardiac arrest have been reported in a significant number of Covid-19 patients during induction of anesthesia and tracheal intubation[13]. We argue that the decision to intubate Covid-19 patients in the pre-hospital setting should rely on a careful risk-benefit analysis, and one should consider NIV in patients with severe hypoxemia. We speculate that pre-hospital intubation should only be sought in hypoxemic Covid-19 patients with clear signs of decompensation, i.e. altered level of consciousness, increased work of breathing with apparent use of accessory respiratory muscles, or circulatory compromise.

The Covid-19 patients reported in this paper responded poorly to oxygen therapy and due to their high minute ventilation high oxygen flow rates were required. With the delivery systems applied in the pre-hospital context, oxygen flow rates are often limited to 15 liters/minute. Non-rebreather masks and CPAP systems will dilute oxygen with a highly variable volume of ambient air, depending on the patient´s minute ventilation, oxygen flow rate and degree of mask seal. In a study in healthy volunteers the FiO_2 obtained with a non-rebreather mask with oxygen flow of 15 liters/minute was approximately 0.6 and fell rapidly with increasing respiratory rate and tidal volume[14]. The FiO_2 delivered via a BVM is variable depending on the manufacturer. One study reported a FiO_2 in the range of 0.43–0.54 at flow rates of 10 and 15 liters/minute, but at higher O_2 flow rates an FiO_2 above 0.9 was achieved[15]. We would like to highlight two factors which must be taken into consideration in order to deliver a high FiO_2 with the BMV. First, a tight seal between the patients face and the mask is necessary in order to avoid ambient air being drawn in during inspiration. Second, the oxygen flow rate must exceed the patient´s minute ventilation. If not, the reservoir bag collapses, and ambient air will be pulled into the bag diluting the oxygen and reducing the FiO_2. This is an important point in the context of COVID-19 patients as they often have a high minute ventilation and thus require a high oxygen flow rate to achieve a high FiO_2. A PEEP valve may be connected to the BVM, however we would like to stress that a BVM with a PEEP-valve is not able to generate a continuous positive airway pressure. The PEEP-valve only applies positive airway pressure during expiration and not continuously throughout the respiratory cycle. Lastly, attaching a viral filter to the BVM will cause increased airway resistance during inspiration compared to spontaneous breathing with a non-rebreather. This increased airway resistance will increase the work of breathing and may cause atelectasis. Assisting the patient's breathing by pressing the bag during inspiration may compensate for this and may even facilitate lung recruitment. However, doing this synchronously with the patient's spontaneous effort requires practice and focus and is especially challenging in patients with a high respiratory rate.

Hypoxemic patients may fail to respond adequately to supplemental oxygen despite a high $FiO_{2,}$ reflecting a considerable shunt fraction or compromised diffusion. Reducing the shunt fraction can be achieved by recruiting non-ventilated lung volume or by facilitating redistribution of perfusion to areas of the lung with better ventilation. Several non-invasive interventions can be applied in the pre-hospital context in order to reduce shunt fraction.

In an in-hospital setting CPAP has shown to be effective in improving hypoxemia in Covid-19 patients[11], however the time required from onset of CPAP-treatment to an increase in oxygen saturation has not been specifically studied in these patients. Unfortunately, disposable CPAP systems generally fail to deliver a high $FiO_{2,}$ and we speculate that this contributes to the ineffective use of CPAP in one of our patients. Adding extra oxygen via a nasal cannula underneath the CPAP may improve the $FiO_{2,}$ however this set up requires two oxygen sources. A transport ventilator in CPAP mode could permit a FiO_2 close to 1.0 as these ventilators draw oxygen to match the patients inspiratory flow rate without the need for ambient air. Additionally, a mechanical ventilator may sustain a more stable positive airway pressure. This could also be used as a bridge to intubation in patients with critical hypoxemia requiring optimal preoxygenation.

Prone position has been reported to improve outcome in intubated patients with acute respiratory distress syndrome (ARDS)[16]. In awake patients the evidence is scarce, possibly reflecting the less severe nature of ARDS in non-intubated patients. Prone position can theoretically improve oxygenation via several mechanisms. Perhaps the most immediate effect is due to redistribution of blood from atelectatic dorsal areas of the lungs to less atelectatic ventral lung tissue. Proning may also help in recruitment of dorsal atelectasis and help in mobilization of secretions and thereby preventing further atelectasis. Several studies have reported that Covid-19 patients have dorsal consolidations whereas the ventral parts of the lungs are less affected[6, 17]. This may explain why many Covid-19 patients respond favourably to prone positioning. Caputo et al reported the effects of awake prone position in 50 patients with confirmed Covid-19 presenting to the emergency department[7]. A majority showed improvement in oxygenation within 5 minutes. Awake prone positioning appears to be a safe and effective intervention in cooperative hypoxemic Covid-19 patients when done in an in-hospital setting[11]. It requires little or no specialized equipment and little extra resources. Awake prone positioning for hypoxemic Covid-19 patients has already been implemented in some EMS protocols in the United States[18].

A pilot study from 2004 reported that inhaled nitric oxide had an immediate effect on oxygenation in spontaneously breathing SARS patients with hypoxemic respiratory failure[19]. A randomized controlled trial investigating the effects of inhaled nitric oxide in mechanically ventilated patients with Covid-19 is underway[20]. Administering pulmonary vasodilators like inhaled nitric oxide drugs is logistically challenging in a pre-hospital setting. In situations with critical hypoxemia were the appropriate equipment is readily available this could be an option.

The risks of a pre-hospital intubation may outweigh the benefits in cooperative and alert patients despite severe hypoxemia. Although early intubation was initially recommended in Covid-19 patients that were hypoxemic despite supplemental oxygen, WHO guidelines now suggest a trial of NIV before proceeding to invasive mechanical ventilation in selected patients[21]. There are many possible explanations why intubating these patients is considered high risk. Initially, several guidelines advised against mask ventilating these patients through the apnoeic period prior to laryngoscopy due to the risk of aerosolization. This may however lead to an unnecessary long apnea time potentially causing a critical drop in oxygen saturation. In line with this, some international guidelines now recommend mask ventilation through the apneic period[22]. Another possible mechanism by which apnea leads to a rapid deterioration in oxygen saturation is the effect of increased $PaCO_2$ on haemoglobin oxygen affinity. In Covid-19 patients with a high minute ventilation, hypocapnic hypoxia causes a left shift in the oxygen dissociation curve implying that at a given PaO_2 the hypocapnic patient has a higher oxygen saturation than the normocapnic patient. If the $PaCO_2$ suddenly rises due to apnea this may cause a reduction in haemoglobin oxygen affinity at the level of the lung thereby leading to a sudden drop in SaO_2[23]. A sudden drop in SaO_2 to a critically low level accompanied by a simultaneous drop in coronary perfusion pressure secondary to the vasodilatory and cardiodepressive effects of the anesthetic drugs, may contribute to hemodynamic collapse.

Conclusion

Patients with Covid-19 and severe hypoxemia may pose a considerable challenge for the prehospital emergency services. We have reported three Covid-19 patients with severe hypoxemia that proved refractory to oxygen therapy and NIV. Covid-19 patients with hypocapnic hypoxia and a high minute ventilation demand high oxygen flow rates in order to avoid dilution of oxygen with ambient air, which is difficult to achieve with non-rebreathers and disposable CPAP systems. Intubation may be associated with a high risk of complications in these patients and should be carried out with diligence when considered necessary. Further, the decision to intubate these patients may dictate a long ICU course with substantial mortality risk, and NIV has been reported as a safe alternative in selected patients.

Declarations

Ethics approval and consent to participate

Publication of these case reports has been approved by the Regional committee for medical and health research ethics (Ref. ID: 142091).

Consent for publication

Written informed consent have been obtained from next of kin. The exact age of the patients remains undisclosed for privacy protection purposes.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

None of the authors received any funding for writing this manuscript.

Authors' contributions

All authors have contributed in the writing of the manuscript. RM, HJH and MR contributed with cases and retrieval of consent. MR contributed with comments to structure and language. JSH contributed with retrieval of consent, approval by the Regional committee for medical and health research ethics and to the submission process. JOM and WO contributed with the writing of the text as a whole and to the submission process. All the authors have seen and approved the submitted manuscript.

Acknowledgements

Not applicable.

References

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet.* 2020.
2. Wilkerson RG, Adler JD, Shah NG, Brown R. Silent hypoxia: A harbinger of clinical deterioration in patients with COVID-19. *The American Journal of Emergency Medicine.* 2020.

3. Ottestad W, Seim M, Mæhlen JO. COVID-19 with silent hypoxemia. *Tidsskrift for Den norske legeforening.* 2020.
4. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *New England Journal of Medicine.* 2020.
5. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao S-Y. Pulmonary pathology of early phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. *Journal of Thoracic Oncology.* 2020.
6. Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, Ling Y, Jiang Y, Shi Y. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology.* 2020;295(1):210-217.
7. Caputo ND, Strayer RJ, Levitan R. Early Self-Proning in Awake, Non-intubated Patients in the Emergency Department: A Single ED's Experience During the COVID-19 Pandemic. *Academic Emergency Medicine.* 2020;27(5):375-378.
8. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, Camporota L. COVID-19 pneumonia: different respiratory treatments for different phenotypes?: Springer; 2020.
9. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. *Respiratory medicine.* 2013;107(6):789-799.
10. Tobin MJ, Laghi F, Jubran A. Caution about early intubation and mechanical ventilation in COVID-19. *Annals of Intensive Care.* 2020;10(1):1-3.
11. Sun Q, Qiu H, Huang M, Yang Y. Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province. *Annals of intensive care.* 2020;10(1):1-4.
12. Oranger M, Gonzalez-Bermejo J, Dacosta-Noble P, Llontop C, Guerder A, Trosini-Desert V, Faure M, Raux M, Decavele M, Demoule A. Continuous positive airway pressure to avoid intubation in SARS-CoV-2 pneumonia: a two-period retrospective case-control study. *European Respiratory Journal.* 2020.
13. Yao W, Wang T, Jiang B, Gao F, Wang L, Zheng H, Xiao W, Xu L, Yao S, Mei W. Emergency tracheal intubation in 202 patients with COVID-19 in Wuhan, China: lessons learnt and international expert recommendations. *British Journal of Anaesthesia.* 2020.
14. Farias E, Rudski L, Zidulka A. Delivery of high inspired oxygen by face mask. *Journal of critical care.* 1991;6(3):119-124.
15. Zamora I, Newhart J. The Influence of Variable Flows on FIO2 Delivery via Self-Inflating Resuscitation Bags: Respiratory Care; 2018.
16. Guérin C, Reignier J, Richard J-C, Beuret P, Gacouin A, Boulain T, Mercier E, Badet M, Mercat A, Baudin O. Prone positioning in severe acute respiratory distress syndrome. *New England Journal of Medicine.* 2013;368(23):2159-2168.
17. Wu J, Wu X, Zeng W, Guo D, Fang Z, Chen L, Huang H, Li C. Chest CT findings in patients with coronavirus disease 2019 and its relationship with clinical features. *Investigative radiology.* 2020;55(5):257.

18. Heightman AJ. (https://www.jems.com/2020/05/08/the-ems-today-show-prone-positioning-of-patients-found-to-be-beneficial-to-covid-19-patient-care/).
19. Chen L, Liu P, Gao H, Sun B, Chao D, Wang F, Zhu Y, Hedenstierna G, Wang CG. Inhalation of nitric oxide in the treatment of severe acute respiratory syndrome: a rescue trial in Beijing. *Clinical infectious diseases.* 2004;39(10):1531-1535.
20. Lei C, Su B, Dong H, Bellavia A, Di Fenza R, Fakhr BS, Gianni S, Grassi LG, Kacmarek R, Morais CCA. Protocol of a randomized controlled trial testing inhaled Nitric Oxide in mechanically ventilated patients with severe acute respiratory syndrome in COVID-19 (SARS-CoV-2). *medRxiv.* 2020.
21. Organization WH. *Clinical management of COVID-19: interim guidance, 27 May 2020*: World Health Organization; 2020.
22. Cook T, El-Boghdadly K, McGuire B, McNarry A, Patel A, Higgs A. Consensus guidelines for managing the airway in patients with COVID-19: Guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists. *Anaesthesia.* 2020;75(6):785-799.
23. Ottestad W, Søvik S. COVID-19 patients with respiratory failure: what can we learn from aviation medicine? *British Journal of Anaesthesia.* 2020.