Supplemental oxygen therapy in COVID-19

F.E. Smit*, A.N. Oelofse*, A.L. Linegar*, H.A. Hanekom*, L. Botes# and E.W. Turton†

*The Robert W.M. Frater Cardiovascular Research Centre, Department of Cardiothoracic Surgery, University of the Free State, Bloemfontein, South Africa
#School of Health Technology, Central University of Technology, Bloemfontein, South Africa
†Department Anaesthesiology, University of the Free State, Bloemfontein, South Africa

Address for correspondence:
Dr F.E. Smit
The Robert W.M. Frater Cardiovascular Research Centre
Department of Cardiothoracic Surgery
University of the Free State
Bloemfontein
9300
South Africa

Email:
smitfe@ufs.ac.za

ABSTRACT

South Africa face a significant shortage of ventilator-supported intensive care (ICU) beds during the peak phase of the COVID-19 pandemic, further exacerbated by severe ICU-staff shortages. It is also recognised that the mortality rate for ventilated patients might be as high as 88%. In the absence of a vaccine and proven effective pharmacotherapy, it is important to understand the pathophysiological processes causing progression. Early type-L COVID-19, associated with pulmonary thrombo-embolism, may be amenable to treatment with careful anti-coagulation and supplementary oxygenation strategies. This could attenuate the severe hyperventilation phase causing patient self-inflicted lung injury (P-SILI) that contributes to the development of type-H COVID-19 pneumonia. Type-H is an ARDS variant requiring intubation and ventilation and is associated with a very high mortality rate. Stepwise non-invasive positive pressure ventilation strategies (NIPPV) providing supplementary oxygen have shown benefit and, in the South African context, may be the only realistic strategy to deal with high numbers of patients during the early type-L phase of the disease. To address this, a mobile wall unit has been created that allows for stepwise supplementary oxygen therapy according to protocol – including NIPPV as well as standard ventilation. The unit can support modified wards, field hospitals or high care areas in existing facilities. It allows for NIPPV support within a hood system linked to scavenger lines addressing aerolisation. Standard humidification, flow regulators, vacuum systems, HFNC and CPAP systems, as well as monitoring equipment that are readily available in South Africa, can be linked to the system addressing availability issues. SAHeart 2020;17:324-328

INTRODUCTION

Respiratory failure and respiratory support remain some of the most challenging aspects in the treatment of serious COVID-19. In low and middle income countries (LMIC) in general, and in South Africa specifically, this is further complicated by the inadequate number of ventilator-supported intensive care unit (ICU) beds.

In the *Business Day* of 11 April 2020, acting Director-General Anban Pillay is quoted as stating that 25 000 and 70 000 hospital beds as well as between 4 000 and 14 000 ICU beds would be required for COVID-19 patients when the pandemic reaches its peak. The Health Department's estimates reveal that South Africa (SA) currently has 3 216 ventilators, with 2 105 or roughly two-thirds being in the private sector. It puts the projected need at 7 000, based on modelling of the pandemic that puts the peak demand for hospital beds in June 2020.

This represents a serious challenge. It is unlikely that the SA public sector can expand its ICU beds, equipment and ventilators in the short to medium term to reach the number of beds required during this pandemic. More significantly, trained and qualified ICU staff are simply not available to man these additional beds. Merely training nursing personnel to care for a proned, sedated, paralysed, ventilated, ARDS patient with multi-organ failure requiring vasoactive drugs and maybe renal dialysis might just prove to be a bridge too far, even for all of those still in denial about the extent of this crisis. And nursing is only one component of critical care staffing. The mortality of ventilated patients remains very high (88% in a large New York patient cohort).[1]

Different respiratory strategies for different phenotypes of COVID-19 pneumonia have been proposed by Gattinoni, et al. (2020).[2] In the early phase of COVID-19 pneumonia, type-L, there is low elastance, a low ventilation to perfusion (VA/Q) ratio, low lung weight and low lung recruitability. The low VA/Q was explained as pulmonary vasoplegia by Gattinoni, et al. (2020).[2] However, this phenomenon might be better explained by extensive intra-pulmonary thrombo-embolism.[3]

There is also a strong association between D-dimer levels, disease progression and features of chest computerised tomography (CT), suggesting venous thrombosis.[4] The treatment of thrombo-embolic complications as well as proposed anti-coagulation regimes are discussed in more detail in a report by the National Institute of Public Health of the Netherlands.[5]

The next phase is characterised by extreme hyperventilation with extreme swings in inspiratory pressure, resulting in patient self-inflicted lung injury (P-SILI). This, in combination with increased lung permeability due to inflammation then results in progressive lung oedema with increased lung weight and dependent atelectasis, concluding in COVID-19 pneumonia type-H. This is a very significant transitional stage in the development of the type-H, an ARDS-like condition.

The type-H pneumonia patient has high elastance, a high right to left shunt, high lung weight and high recruitability. Type-H pneumonia thus resembles acute respiratory distress syndrome (ARDS). Importantly, CT scans can clearly demonstrate the sub types and should be performed early on in the disease if possible, as demonstrated in Figure 1.

A rational treatment programme would thus include:

- Reversal of early hypoxemia.
- An early and aggressive anti-coagulation programme as dictated by D-dimers and other appropriate serology.
- If patients have dyspnea – non-invasive options, including high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP) and non-invasive positive pressure ventilation (NIPPV) should be considered. It should also include oesophageal pressure monitoring, if available. High positive end expiratory pressure (PEEP) might reduce pleural pressure swings, limiting patient self-inflicted lung injury (P-SILI). Gattinoni, et al. (2020) indicated that pressure swings of up to 5 - 10cmH20 are well tolerated.[2]
- Pleural pressure swings above 15cmH20 however require intubation and sedation to prevent serious and ongoing P-SILI using mechanical ventilation with low tidal volumes (6 - 7ml/kg) and moderate PEEP of 8 - 10cmH20.
- Type-H patients are treated as ARDS with higher PEEP, proning and extracorporeal membrane oxygenation (ECMO).

Thus, it is obvious that the availability of a stepwise supplementary oxygenation programme in conjunction with a well conducted anti-coagulation programme may be pivotal to the success of the treatment of early COVID-19 pneumonia. It may also reduce the onset or attenuate the severity of life-threatening type-H COVID-19 pneumonia, by limiting P-SILI. Once type-H COVID-19 pneumonia, associated with an inflammatory storm, ARDS and multi-organ failure is reached, outcomes are dismal – as mentioned above.[1]

The potential advantage of Helmet Non-invasive Ventilation compared to HFNC in acute hypoxemic respiratory failure is worth further consideration and study.[8]

In the absence of a vaccine and proven effective pharmacotherapy, the development of stepwise supplementary oxygenation programmes is essential to effectively treat early-onset COVID-19 pneumonia. A flow diagram of a prospective trial (UFS-HSD2020/0507) using a stepwise supplementary oxygen programme at the University of the Free State (UFS) is supplied in Figure 2. The possibility of conducting a multi-centre trial is being explored.

NEW DEVELOPMENTS

Supplementary oxygen delivery systems can be lifesaving in early COVID-19 pneumonia. It is therefore important that systems or alternatives be developed to provide this service as a multiplier in supplementary oxygen therapy availability. An example is a mobile wall unit concept that has been developed and tested at the Robert W.M. Frater Cardiovascular Research Centre at the UFS in conjunction with industry partners. This unit provides graded supplemental oxygen, a scavenger system, vacuum for suctioning and electrical connections for humidifiers, monitoring equipment and a nursing administration platform servicing 4 patients at the required 3 metre separation (Figure 3).

The unit connects to standard hospital air and electricity facilities. This unit can support low flow oxygen, HFNC and CPAP systems. Although aimed at supplementary oxygen supply, it can obviously also support standard ventilators. This system uses standard equipment freely available in most hospitals or in the market to provide an option, which can rapidly expand supplementary oxygen delivery programmes. This may include new high-care areas, modification of existing wards, newly designated areas within hospitals or in field hospital situations to provide a stepwise supplementary oxygen platform. CPAP can be provided up to 14cmH20, which is

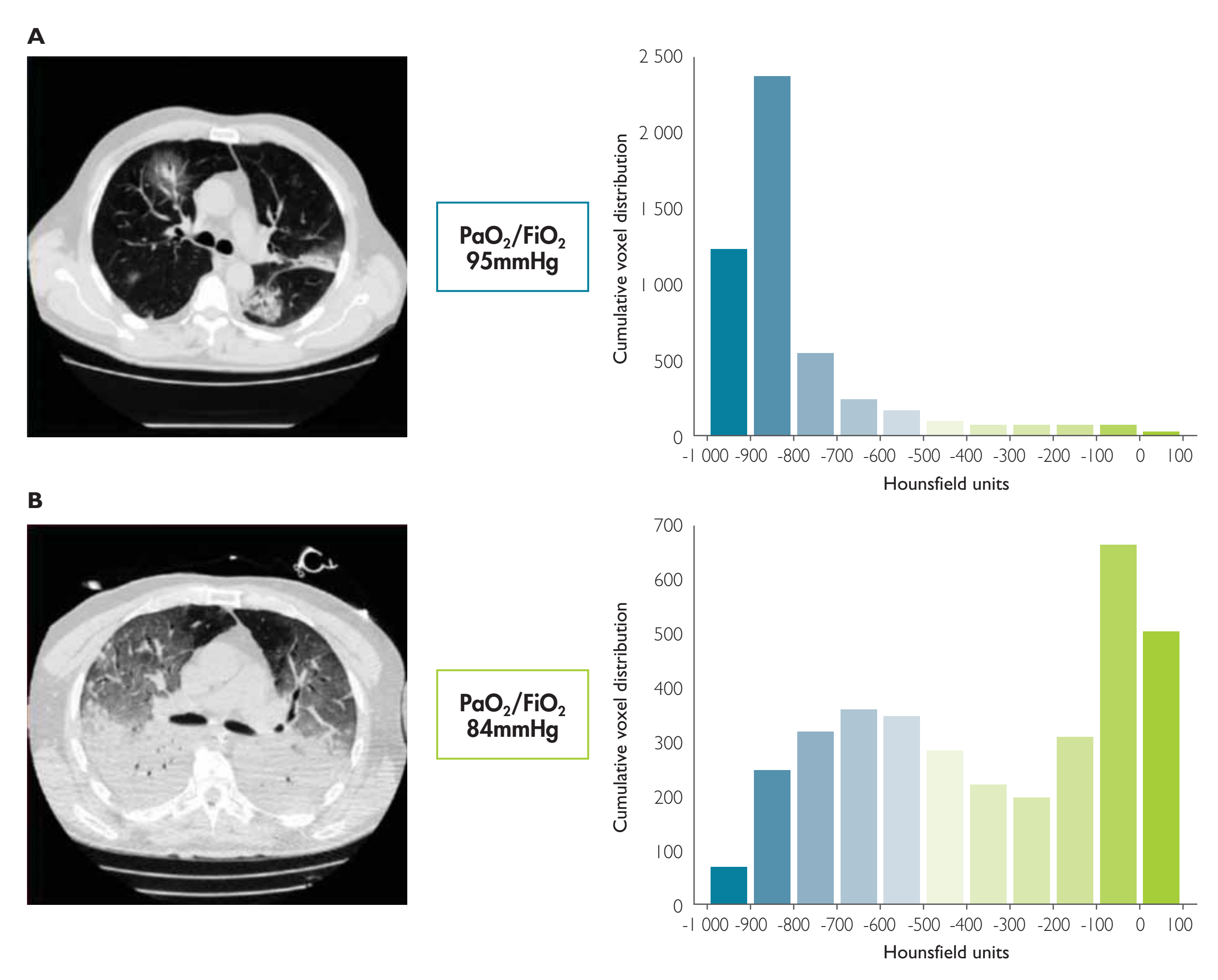

FIGURE 1: A CT scan acquired during spontaneous breathing.
A: The cumulative distribution of the CT number is shifted to the left (well-aerated compartments), being the 0 - 100HU compartment, the non-aerated tissue virtually 0. Indeed, the total lung tissue weight was 1108g, 7.8% of which was not aerated and the gas volume was 4 228ml. Patients receiving oxygen with venturi mask inspired oxygen fraction of 0.8.
B: CT acquired during mechanical ventilation at end-expiratory pressure at 5cmH_2O of PEEP. The cumulative distribution of the CT scan is shifted to the right (non-aerated compartments), while the left compartments are greatly reduced. Indeed, the total lung tissue weight was 2 744g, 54% of which was not aerated and the gas volume was 1 360ml. The patient was ventilated in volume controlled mode, 7.8ml/kg of tidal volume, respiratory rate of 20 breaths per minute, inspired oxygen fraction of 0.7 (reproduced from Gattinoni, et al., 2020).

perceived to be the upper limit tolerated during spontaneous ventilation. The intra-pleural pressure swing can be attenuated theoretically by increasing the mixed air flow to 60l/min and above.

Staff requirements for semi ambulatory patients can be calculated at 1:4, with a qualified or experienced nurse supervising 8 - 12 patients (three mobile wall units).

Dealing with aerolisation remains a concern. It is therefore suggested that the systems be used in conjunction with a containment device connected to the scavenger system ("12" in Figure 3). Alternatively, patients can be admitted to a COVID-19 designated area with full aerolisation personal protective equipment (PPE), ideally combined with negative pressure or extractor fans with HEPA filters.

CALCULATING THE NEED FOR SUPPLEMENTARY AND ADVANCED OXYGEN DELIVERY

The epidemiological modelling worldwide is an evolving science as data are required and models updated. It is accepted that the distribution of hot spots might be highly variable, may occur either at the same time period or may be highly chaotic. However, it remains useful to use general data available to attempt a needs calculation.

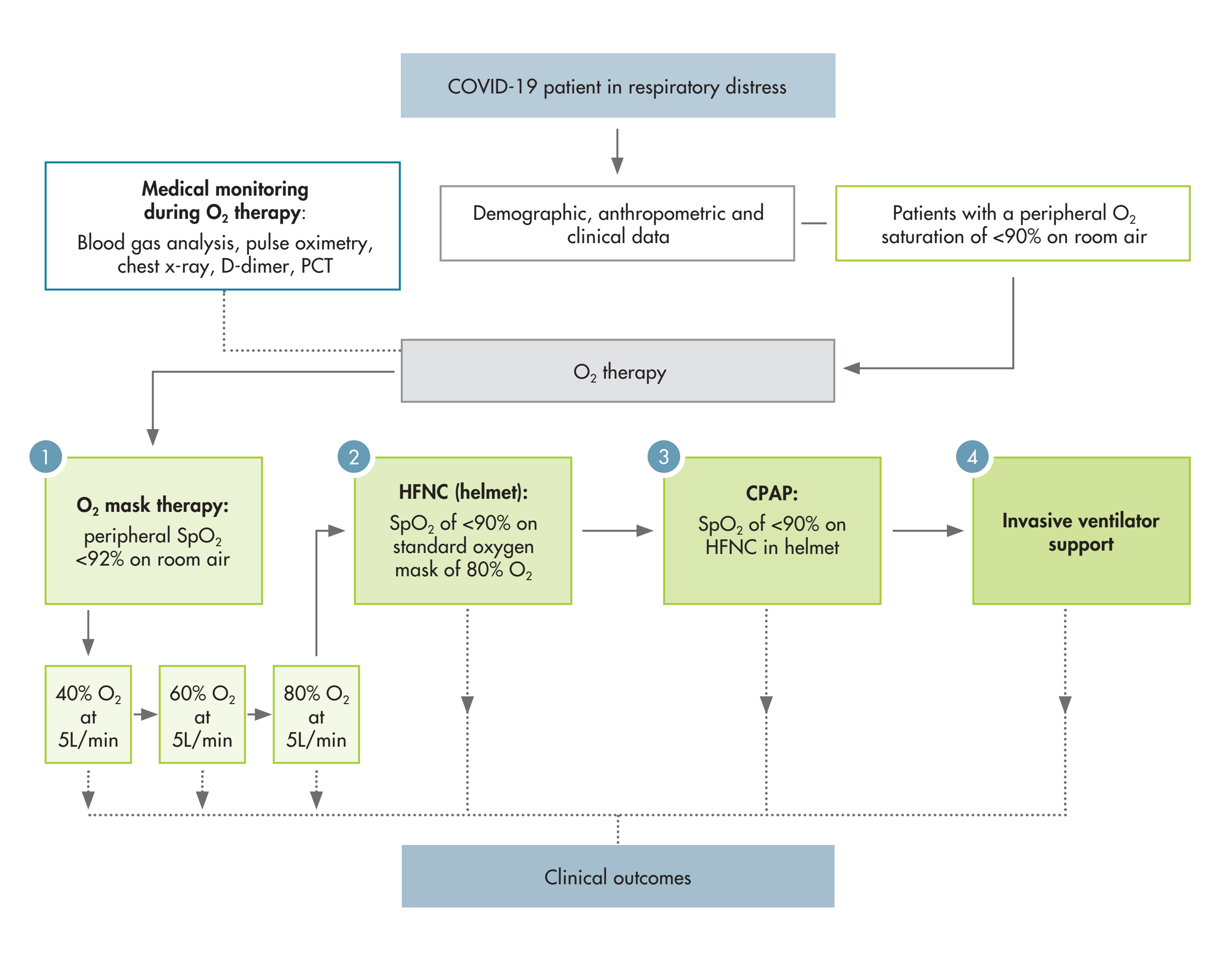

FIGURE 2: Flow diagram of a prospective trial using a stepwise supplementary oxygen programme at the UFS.

There is general consensus that the expected mortality rate over the entire pandemic in SA, would reach approximately 45 000 to 80 000 people at the current mortality rate of 1.97%.[6] Reported data show that 15% of infections are serious and 5% of patients require critical care support.[7]

This implies that 112 500 - 200 000 patients will require supplementary oxygen as part of their treatment. Assuming a national 90-day peak period and assuming that each patient requires five days of oxygen therapy, this translates to a requirement of 562 500 - 1 000 000 oxygen day beds over 90 days. This means that one could realise a demand for 6 250 - 11 000 oxygen-supplied beds per day during the nationwide peak lasting 90 days. These figures fall within the National Department of Health projections above.

However, a simultaneous national peak across all metropoles seems to be unlikely and it is thus important to consider supplemental oxygen delivery systems as described above, which can be moved to the areas of need as required.

CONCLUSION

In the absence of vaccines and proven pharmacotherapy, well-coordinated stepwise supplementary oxygen programmes and judicious anti-coagulation programmes at all levels of care might be lifesaving in cases presenting with early type-L COVID-19 pneumonia. This may provide a system that can attenuate P-SILI contributing to the development of type-H COVID-19 pneumonia, an ARDS type of disease requiring sophisticated ventilation equipment and techniques. Apart from the fact that the SA public sector is under-resourced in terms of ICU beds and ventilators, advanced type-H COVID-19 pneumonia, associated with an inflammatory storm, ARDS and multi-organ failure, has a prohibitive mortality rate – even in the best of hands.

It is therefore imperative that every effort should be directed at early detection and treatment of Type-L COVID-19 pneumonia. The proposed system provides a flexible, mobile and transportable alternative to provide stepwise supplementary

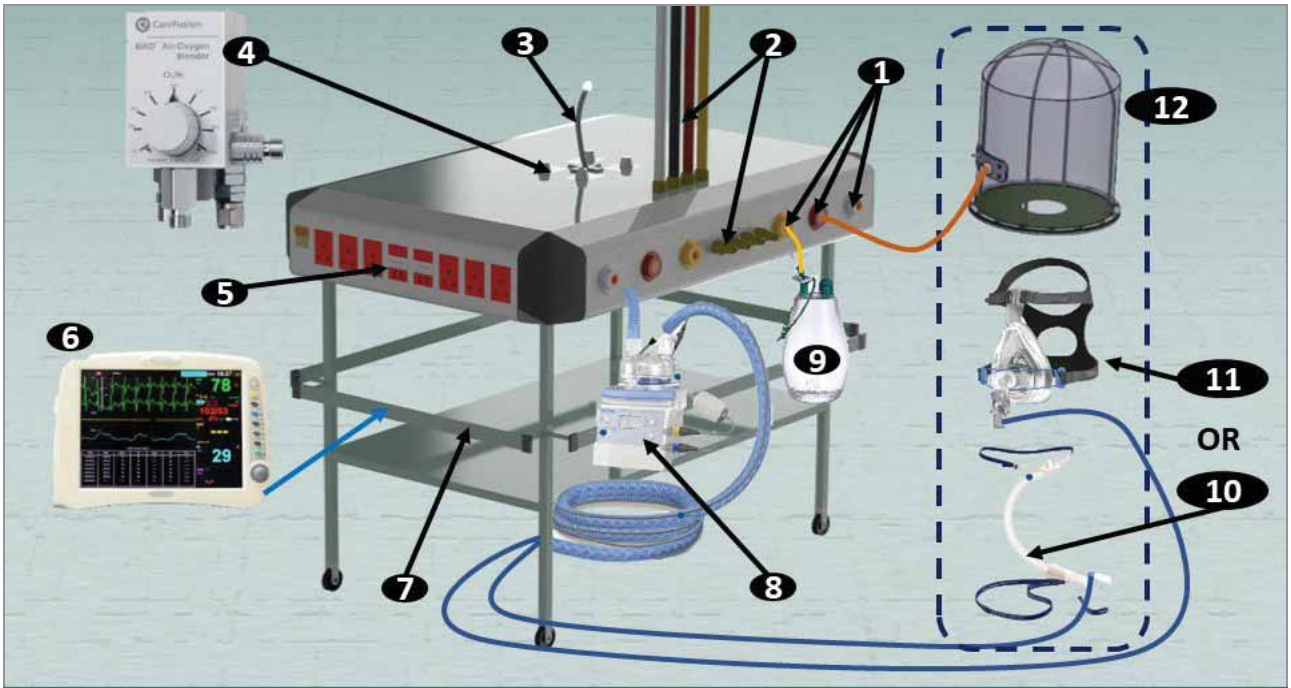

FIGURE 3: Mobile wall unit concept developed and tested at the Robert W.M. Frater Cardiovascular Research Centre at the UFS in conjunction with industry partners.
1 = Standard connecting ports for blended air and oxygen, scavenger and vacuum; 2 = Inlet of medical air and oxygen from the main supply, scavenger line and a vacuum line; the inlets can be connected from the top or the side; 3 = Flexible night light for nursing staff; 4 = Air/oxygen blender allowing a variable blend of 21% - 100% oxygen; 5 = Electrical sockets for devices such as monitors and humidifiers, as well as USB sockets for mobile device charging; 6 = Monitor; 7 = Mounting rails for monitors, humidifiers; 8 = Active humidifier with temperature control attached to supplementary oxygen point with regulator providing up to 120l/min flow; 9 = Vacuum drainage bottle; 10 = HFNC or 11 = CPAP mask connected to the humidifier; 12 = Containment hood connected to the scavenger line.

oxygen in areas of need, using standard equipment readily available in SA. Nursing and staffing requirements as well as expectations will also be more realistic. Aerolisation challenges can be addressed by using a hood and scavenger system.

A multi-centre trial is suggested to verify the efficacy of this system. It may also be the only system available to the rural population.

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