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An alternative to ventilators to support critical COVID-19 patients

Gang Pan*[1, 2], Tao Lyu[1, 2, 3], John A. Hunt[4]

[1] *School of Animal, Rural, and Environmental Sciences, Nottingham Trent University, Brackenhurst Campus NG25 0QF, Southwell, UK*

[2] *Centre of Integrated Water-Energy-Food Studies, Nottingham Trent University, Brackenhurst Campus NG25 0QF, Southwell, UK*

[3] *Cranfield Water Science Institute, Cranfield University, College Road, Cranfield, Bedfordshire, MK43 0AL, United Kingdom*

[4] *Medical Technologies Innovation Facility, Nottingham Trent University, Nottingham NG11 8NS, UK*

* Correspondence: gang.pan@ntu.ac.uk (G.P)

The coronavirus disease 2019 (COVID-19) or the causative virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a potentially fatal infection which is now widespread throughout the world. The most seriously affected people have died due to a lack of oxygen from respiratory problems. Respiratory support by increasing the supply of oxygen using mechanical lung ventilation is one of the main methods to help critically ill patients through the acute phase of infection. A report from Imperial College London estimates that 30% of Covid-19 hospitalised patients are likely to require mechanical ventilation[1], which indicates that over 300,000 ventilators are needed for the current, just over 1 million confirmed cases. The overwhelming global demand for mechanical ventilators represents an urgent critical care challenge in the supply of medical equipment. More importantly, the efficacy of ventilation has been proven to be directly affected and restricted for COVID-19 patients who have impaired or complete loss of lung function due to the accumulation of large amounts of sticky sputum in the alveolus[2].

An alternative, method to improve the oxygenation of tissues, independent of alveolar gas exchange, involves the direct administration of dissolved oxygen into the cardiovascular system[3]. Currently, this IV therapy is hindered by the potential risk to human health resulting from intolerance to the large fluid loads required to deliver enough oxygen. The volume required being a function of oxygen solubility and the treatment being required to span days or weeks.

In recent years, nanobubble technology has broadly attracted studies from medicine[4], agriculture[5], and environment[6] specialists. Oxygen nanobubbles have been the subject of increasing attention due to the characteristics of high gas solubility and the long lifetime of retention of oxygen in liquid[7]. As opposed to microbubbles, the long-lived nano-scale bubbles can significantly increase oxygen concentration in water-based solutions without forming short-lived microbubbles[8], making it possible to oxygenate blood using a limited small volume of IV injection without gas bubble formation. Medical oxygen gas can be easily made into nanobubble water/saline solutions using physical means, such as ceramic nanofiltration membranes[9], temperature-swing[10] or microwaves[11], without the

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need to add any chemical or biological reagents. The oxygen concentration in a nanobubble solution can be 2 to 6 times higher than the normal solubility of oxygen in pure water, which makes it possible to deliver oxygen in a quantitative metrological way through the homogeneous oxygen nanobubble intravenous infusion for direct control of blood oxygen saturation pressure (SPO2) through the cardiovascular system rather than the lungs.

This blood oxygen infusion injection method is much simpler (no moving or powered parts) and cheaper than the manufacture and operation of the lung ventilator, making it easily available and applicable in many different healthcare environments around the world. The correct and optimised IV delivery rate could be determined from pulse oximeter readings for blood oxygen saturation. Thus, we propose an innovation utilising the intravenous injection route coupled with nanobubble technology, which could maintain blood oxygen pressure at normal levels safely and easily without the need for ventilators. Theoretical Data analysis indicated that intravenous delivery of 400 ml oxygen nanobubble physiological saline solution (ONPS) containing 40 mg O_2/L can improve low oxygen blood pressure (PaO_2) from 0.133 kPa (typical for critical patients) to a normal level of 13.3 kPa (normal people). Notably, the intravenous infusion contains only pure oxygen and physiological saline solution without adding any other chemical or biological reagents or drugs.

Increasing SPO2 by IV injection does not address the removal of carbon dioxide from patients, which is another essential function of the lungs. This may mean for some extremely severe cases, where patients have complete loss of lung function, the delivery of IV oxygen nanobubble treatment needs to be more carefully monitored as there may be an increased risk of hypercapnia. Clinically providing high SPO2 in a low volume of IV liquid may be crucial in the case of COVID-19 patients where the need maintain patients at the lower limits of hydration to reduce lung lavage is preferred. It could be applied in a controlled manner to augment lung function to get patients through the critical phase of the infection.

COVID-19 is causing significant impact to world economy. Manufacturing large numbers of ventilators in short period requires substantial investment by many countries whose economy and people's lives are already suffering under pressure. While saving critical COVID-19 patient's lives remains an exceptionally urgent task, we urge medical and clinical experts act quickly to conduct in vivo models and clinical trials to demonstrate this IV method of maintaining blood oxygen saturation pressure through intravenous injection during a limited dysfunctional period of lung capacity. Upon successful clinical trials, the method can be quickly and widely used in every country to save lives due to its easy implementation and exceptionally low costs using widely available intravenous protocols and equipment.

Conflicts of Interest: G.P. is the sole inventor and patent holder of a PCT application (Chinese patent application number 202010244781.4) related to the method described here. It is our intention to give favourable permissions or cooperation agreements to professional trials during this COVID-19 outbreak.

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