"Happy hypoxia" of COVID-19: Are we Happy with our Oxygen Reserves?

Oxygen can be termed one of the most basic requirements in a hospital facility. It is also the most important need of any organism. A review of the oxygen cascade reminds us that all there needs to be is about 2–3 mm Hg of oxygen in our mitochondria. This is termed the Pasteur point below which anaerobic metabolism begins. To get to this Pasteur point, we usually begin with an alveolar oxygen partial pressure of about 100 mm Hg and an arterial oxygen partial pressure of 90–100 mm Hg when the lungs are normal.

The situation changes with the development of ventilation-perfusion mismatch. In general, an increase in shunt fraction is related to the development of an increased alveolar to arterial oxygen tension gradient. The novel corona virus disease 2019 (COVID-19) disease primarily causes an increase in dead space rather than a shunt. Currently, the mechanism is thought to be due to formation of microemboli, resembling pulmonary embolism. This would cause an increase in alveolar dead space and thus alveolar hypoventilation, if the minute volume remains unchanged. Impaired alveolar diffusion of oxygen will lead to 'silent hypoxia' and a consistent drop in oxygen saturation. Unlike other diseases, the body tries to compensate by increasing tidal volume and to a lesser extent, the respiratory rate in COVID-19 disease. The increase in tidal volume is achieved by increasing the inspiratory flow and consequently the work of breathing. The patient may be completely unaware of the increased respiratory load and this is a state called "happy hypoxia." This can be easily diagnosed with a pulse oximeter. However, a cautious interpretation of pulse oximetry values is required, as the COVID-19 patients often have "hypocapnic hypoxia." Even with an oxygen saturation of around 93%, they may be at the brink of respiratory failure, and a low end-tidal carbon dioxide should alert the clinician.

The dual need of increasing inspired oxygen concentration as well as higher inspiratory flows often makes the high-flow nasal oxygen a lifesaving equipment. The initial fears of spread of the corona virus using high-flow nasal cannula (HFNC) have been dispelled. The risk of bioaerosol spread during the use of HFNC even with oxygen flow rate of 60 L/min is not greater than that of oxygen masks with oxygen at 15 L/min.[1] The aerosol dispersion distance with an HFNC is in fact much lesser than that of a nonrebreathing mask or a venturi mask.[1] The realization that mechanical ventilation is largely detrimental to the progress of the disease has made high-flow nasal oxygen much more acceptable in the management of patients in respiratory failure due to COVID-19.

This issue of IJRC has two articles relevant to this situation. "High Flow Nasal Cannula – COVID 19 and beyond" by Dr. Rali *et al*. is an interesting article.[2] They mentioned that HFNC is a safe treatment modality with low risk of exposure to aerosolized viral particles for health-care workers, if used appropriately. HFNC must be used preferably in negative pressure room with the patient wearing a surgical mask. If a negative pressure room is not available, the patient should be in a single room with high-efficiency filtration system with a surgical mask over the nasal cannula with droplet/contact isolation and health-care workers must be wearing proper personal protective equipment (PPE). A high limit of 30–40 L/min is often used to reduce the risk of droplet travel distance at rest which increases with cough, but if the health-care workers have adequate PPE protection, and the patient is in the negative pressure room, higher flows may be considered.

The other article in this issue that is relevant to this discussion is "Hospital oxygen supply-A survey of disaster preparedness of Indian hospitals" by Dr. Paul *et al*.[3] Oxygen is a reasonably cheap but lifesaving commodity. The hospital supply could be in the form of bulk cylinder manifold, oxygen concentrators, or liquid oxygen. Their calculation for oxygen requirement at a hospital is as follows: at any point of time, approximately 25% of patients admitted to a hospital may require about 6 L of oxygen per minute. Thus, even if areas of high oxygen requirements such as operation theaters, intensive care units, and emergency medicine areas are excluded, the oxygen requirement of a 100-bedded hospital is about 150 L/min or 2.16 lakh L/day. However, the areas that have high oxygen requirements cannot be excluded and therefore the amount of oxygen required is much more. The requirement is also not static and will have to be monitored very closely, especially when the demand is high on ventilators.

If the 100-bedded hospital is using bulk cylinder manifold with J type cylinders with a capacity of approximately 7000 L of oxygen/cylinder, we would need 300 such cylinders per day. The recommendation is to keep at least four days' supply available which inflates the numbers by another four times (1200 cylinders). The practical solution to such requirements would be liquid oxygen.

A typical sized vacuum insulated evaporator (VIE) contains 5000–10000 L of liquid oxygen. A full 10000 L tank of liquid oxygen could be approximately equal to 1200 "J" type cylinders of 7000 L, amounting to 8,400,000 L. Thus, in the example given above, one would need one VIE flask with 10000 L capacity every 40 days. One would obviously have to have a few bulk cylinders also available to last a few hours at least if there is any delay in refilling the tank.

Many patients on home oxygen use oxygen concentrators, but they are of limited capacity and are meant for individual use. A hospital oxygen concentrator is much bigger and delivers 95% oxygen USP. Its disadvantage is that the maximum flow output may be less than the oxygen requirements during peak hours of its use in the hospital. The heat generated and the requirement of water to cool it is also a problem. Liquid oxygen has largely replaced oxygen concentrators in the big hospitals. Being self-sufficient in oxygen production with only electricity required for working is the biggest advantage of oxygen concentrators.

As the authors in that article have stated, in case of any disaster situation, an urgent meeting of the gas supply committee should be convened to assess the available oxygen supply.[3] Elective procedures requiring oxygen should be suspended until adequate external supply reaches. Assessment to determine the remaining time to end of supply should be done. The use of telemetry can be useful for both the hospitals and the vendors to monitor and initiate supply. They have also a table in the article that helps to estimate the number of days of oxygen stock needed depending on the distance from the liquid oxygen plant and availability of telemetry.

The Corona Virus Disease 2019 Infection And Oxygen Preparedness

The COVID-19 infection is a novel infection with no known definitive treatment. The disease process is such that oxygen is the only therapy that works currently and is essential for the patient to survive. Appropriate oxygen therapy at the appropriate time may avert mechanical ventilation. The weekly magazine Outlook had published in April 2020 that such an eventuality could happen.[4] The article warned that there are only weeks for vulnerable nations in Africa and South Asia to prepare for this pandemic, not necessarily with ventilators but oxygen itself. The initial focus on acquiring ventilators by many governments would not be useful unless oxygen issues are tackled. The article goes on to mention that nearly 20% of patients with COVID-19 require oxygen. While 14% were managed with just oxygen therapy, 5% needed mechanical ventilation.

The COVID-19 infection around the globe has put a strain on oxygen requirements in many countries. It is important for each individual hospital to check its requirement, anticipate, and prepare for increased needs and plan in advance for such contingencies. COVID-19 has been around for 3 months at least now and many countries have passed their peak of the infection. The USA, in particular, New York, Italy, Spain, UK, have all had their woes.

An informal inquiry with the respiratory therapists and intensivists in these countries was conducted. They were asked whether any of them had any issues at their hospital with oxygen supplies. None of the respondents saw any situation due to lack of oxygen in the hospitals where they worked, except for one situation in a hospital in New York, where they did run out of oxygen and had to shift all their patients to another hospital for that reason.

To the question of whether they planned ahead of time, all answered affirmatively. For example, the actions taken at one of the hospitals in the Middle East were as follows:

- All oxygen storages were rechecked and filled to the maximum capacity, including the liquid and alternate system (cylinder)
- All cylinders used in various departments (small size), ambulances, and other transport units were rechecked and filled appropriately to the fullest capacity and stored
- The respiratory therapy (RT) supervisors were instructed to refill immediately without any delay in process to restore, and the gas supply units were given authority to proceed with the filling in coordination with the supply agencies
- Emergency funds were also allocated for the same to avoid any delay
- Additional cylinders were purchased and stored; equipment capacity was increased in the emergency units and ambulance units
- Regulators, wall outlets, zone valves, flow meters, and all the other delivery devices were checked for accuracy and leakage. All damaged devices were replaced or repaired
- Oxygen calibration sensors of the ventilators were checked and certified by the manufacturers' service units, and also the wall connections and threaded joints were checked
- Respiratory therapists (RTs) were instructed to turn off the ventilators and keep standby once the calibrations are done, since many ventilators consume oxygen when kept on standby
- Consumption statistics reports were circulated weekly and analyzed
- Available numbers of oxygen concentrators were gathered and prepared for use in the wards and general care areas
- Training to the health-care practitioners were provided for oxygen therapy
- The RTs and nurses were instructed to use only nebulizer machines only for aerosol therapy, not by using oxygen source
- All elective surgeries were discontinued to conserve oxygen.

While the developed countries seem to have planned reasonably well and overcame these difficulties, some others have not been so fortunate. A newspaper dated June 7, 2020, published an article about how Peru is running out of oxygen for its COVID-19 patients.[5] The article mentions that even if they turn oxygen meant for industrial use to medical oxygen, Peru will still fall short of what it needs.

The Indian Scenario

The Ministry of Home Affairs and Family Welfare and the Drug Controller General of India have taken several measures to ensure medical oxygen would be readily available during the COVID-19 pandemic, if required. The Union Health Ministry has issued guidelines to the states on

the methods of supplying oxygen to the medical facilities handling COVID-19 patients.[6] A list of 17 medical oxygen gas manufacturers/suppliers, 7 cylinder manufacturers for medical oxygen, and 4 manufacturers of liquid oxygen under the umbrella of the All India Industrial Gases Manufacturers' Association (the national representative body of industrial gas manufacturers and allied industries in India) has also been given to the states.

The guidelines from the Ministry of Family Health and Welfare include advice regarding the volume of oxygen generated/ required depending on their oxygen source. For a 200 bedded hospital, output from the liquid oxygen tank (Vacuum insulated evaporator) should be 20,400 cubic meters of oxygen per month. If using a pressure swing absorption generator (which uses a power load of 40 KW and a space of 4m x 5m), 475 L/min of oxygen must be generated. If the hospital is relying on oxygen cylinders alone , it will need 90 jumbo cylinders, each with a capacity of 7.25 cubic meters. In addition another 90 cylinders with a similar capacity is required as a backup, irrespective of the primary source of oxygen.[5] Other measures include allowing industrial manufacturers to manufacture oxygen for medical use without compromising on permissible impurities.[6]

Many hospitals and district administrations are also procuring oxygen concentrators for use if all else fails. For example, the Delhi government has ordered for 2000 oxygen concentrators. These could be more useful for use in makeshift hospitals that may be constructed if the existing hospital facilities are overwhelmed.[7]

An interesting innovation of the naval dockyard in Visakhapatnam is the 'Portable Multi-feed Oxygen Manifold (MOM)'. It has a six-way radial header that can be fitted to a single oxygen cylinder enabling delivery of oxygen to six patients simultaneously from that single oxygen cylinder.[8] However, considering the large amount of oxygen required in the Covid setting, it is better to have cylinders dedicated to single patients rather than multiple patients.

An article published by News 18 on 7th of June 2020 was very reassuring.[9] The article goes on to say that India has enough supply of oxygen in stock. Since elective surgeries have been curtailed, oxygen that would have been used by these patients is also available. Apparently, India has currently 80,000 tons of oxygen in stock, about 100 times the usual consumption.

The air that we breathe is free and taken for granted. The thought of this commodity becoming rationed or unavailable itself is alarming. While oxygen may be available in the operation theaters and intensive care units, the wards may not have it. Similarly, pulse oximeters, which are vital in diagnosing hypoxia, also may not be freely available, enhancing the danger. In spite of all advances in medicine, health-care personnel can feel completely helpless in treating patients when they are unable to administer the most basic, yet most essential medicine of all, oxygen. It is very reassuring to know that the Indian government and the industry have been planning for contingencies. One can only remain hopeful that the corona virus is soon stopped in its tracks in this nation of a billion people.

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