



Dr KK Aggarwal
5th September 1958 - 17th May 2021

Minutes of an International Weekly Meeting on COVID-19 in Association with Experts from CMAAO Nations

OXYGEN CRISIS AND PREPARATION FOR FUTURE

24th July, 2021 (Saturday, 9.30 am-10.30 am)

Key Points from the Discussion

A presentation on "Oxygen therapy – crisis and preparations for future" was made by **Dr Rahul Pandit**, Director-Intensive Care, Fortis Hospital, Mumbai; Member-National Task Force; Member-Maharashtra Task Force; Visiting Consultant-Wagga Base and Bathurst Base Hospital; NSW, Australia

- ⦿ In pediatric and neonatology, it's an established fact that too much of oxygen is bad. Oxygen is given only when it's necessary.
- ⦿ Research has looked at optimum level of oxygen to be delivered. There is a very thin line differentiating what will be useful and what will be probably harmful.
- ⦿ Oxygen saturation was the indicator relied upon to decide on oxygen therapy as arterial blood gas monitoring not available in many developing countries.
- ⦿ The oxygen cascade is the transfer of oxygen from atmospheric air to mitochondria. The oxygen partial pressure drops at each step of the cascade.
- ⦿ Hyperoxia is maintaining a partial pressure of oxygen (PaO₂) of more than 100 mmHg for a prolonged time; though the duration is unknown, it is probably in hours and not minutes.
- ⦿ Fraction of inspired oxygen (FiO₂) of 100%, there are good and bad effects. Good effects – vascular PO₂, pericapillary diffusion and oxygen delivery improve, inflammation starts to settle down. But vascular perfusion may also start decreasing, reactive oxygen species (ROS) increase leading to lipo-oxidative stress at the tissue level.
- ⦿ FiO₂ >60% causes lung atelectasis. There is Lorrain-Smith effect, where pulmonary oxygen toxicity may present as severe pulmonary inflammation, leading to pulmonary edema and is referred to formation of excess ROS and reactive nitrogen species (RNS).
- ⦿ Vascular effects include decrease in cardiac output, heart rate.
- ⦿ Paul-Bert effect can give rise to profound vasoconstriction and generalized tonic-clonic seizures. But these are very rare side effects.
- ⦿ Several trials have been published on the effect of hyperoxia in intensive care and emergency medicine in conditions like acute coronary syndrome (ACS), myocardial infarction (MI), stroke, cardiac arrest, including in the last 2 years of the pandemic.
- ⦿ A 50% increase in mortality has been observed in patients who spent 40% time in optimal oxygen

- saturation range versus patients who spent 80% time in optimal time.
- Trials in the past 24-36 months have also looked at restrictive oxygen strategy.
 - The American Heart Association (AHA) does not recommend oxygen therapy in patients of MI until the oxygen saturation is really low. Too much of oxygen may worsen the outcomes. Until recently, MI patients were routinely treated with oxygen. The rationale being that the increased oxygen delivery to the ischemic myocardium reduces infarct size and subsequent complication.
 - The Stroke oxygen trial showed no benefit of oxygen in stroke patients. No difference in mortality was observed.
 - For critically ill patients with an intensive care unit (ICU) length of stay of >72 hours, a conservative protocol for oxygen therapy compared with conventional oxygen therapy resulted in lower ICU mortality.
 - The reality however was the liberal oxygen strategy was followed. It was found that unnecessary oxygen to patients was not good and giving oxygen to patients to achieve oxygen saturation of 97-100% was not helping the patients.
 - The rapid increase in the numbers in the second wave did not help.
 - The oxygen requirement of the country increased by 9- or 10-folds as the pandemic worsened; hence, the failure to meet this high oxygen demand precipitating the oxygen crisis. But very soon, rational use of oxygen came in and allocation improved.
 - It is first important to calculate the oxygen demand. A survey of 30 hospitals has shown that for around 100 beds, 1.5 metric tonne of oxygen is needed per day during the pandemic.
 - The problem was a dynamic change in the need was not available. There was very little information about dynamic change in terms of oxygen requirement. This was dependent on the devices used ventilator, high-flow nasal oxygen (HFNO), noninvasive ventilation (NIV), etc.
 - Supply was limited to four ways: Liquid medical oxygen (LMO), oxygen cylinders, portable oxygen concentrators or PSA (pressure swing adsorption) plants. There were not many PSA plants in the country at that time.
 - The country had to turn to the industrial grade oxygen available. Lot of oxygen was sourced from steel plants. Industrial grade oxygen seemed to be as good as LMO, though the purity was around 92-93%. However, the problems were that these plants were in different parts of the country as well as the shifting pandemic, which moved from one part of the country to the other. The cryogenic tankers took longer to reach their destination (speed limit for safety) and so the crisis very quickly turned into an acute shortage.
 - There were limited refilling plants for oxygen cylinders; they are associated with ease of hoarding, questionable hygiene practices.
 - Oxygen concentrators helped but there is a problem of limitation of flow; many of them only give 5-10 L of oxygen. Hoarding is possible and also the oxygen purity declines after using it for sometime at the maximal capacity.
 - PSA plants are sustainable solutions, but the zeolite used has to be imported. They cannot be operationalized overnight. They are not the primary source of oxygen; they are best used as backup. The oxygen produced has 94-95% purity.
 - Solutions needed at that point of time were dynamic need calculation, allocation formula, distribution techniques, substores for ease of transport.
 - Every bed has to be mapped to calculate dynamic need. Real time data from hospitals was initially a problem, but it became available within 1-2 weeks.
 - The decentralization model for allocation worked best with an oversight from the center for equal allocation.
 - Empty tanks were airlifted via military aircrafts to filling stations and then put on RORO (roll-on, roll-off) express trains to their destinations. This helped ease the crisis quickly.
 - The Mumbai model of oxygen management has won much praise. It was a decentralized process. The city is divided into 24 wards. The real time data was available as every bed in the city was mapped. Six substores were created across the city. And smaller tankers, which could move easily in the city, were used to transport oxygen from hospital to hospital.
 - Oxygen stewardship program was introduced. One liter of oxygen saved is 1 liter produced. Keep oxygen restrictive strategy – keep oxygen saturation between 90 to 94% in patients who were monitored. Leaks, old pipes were repaired. Oxygen

stewards were appointed in each hospital. Each hospital had an oxygen committee.

- Mumbai had long-term sustainable solutions: increased capacity building and keep emergency oxygen stores for 2 weeks requirements.
- Many PSA plants have now been established by the government in rural and urban India.
- The country is now better prepared for the third wave in terms of oxygen requirement.
- Mucormycosis in India was found to be linked to poor glucose control, excessive use of steroids and use of immunosuppressive therapy (tocilizumab) and not oxygen supply in a series of 5,000 patients. Low immunity allowed the opportunistic fungus to grow. Now there are no mucormycosis cases in India.
- More than two-thirds of global cases of mucormycosis are in India. Reasons are not known.
- Mucor is found in soil.
- *Burkholderia pseudomallei*, which causes melioidosis, is found in soil in Singapore.
- High-flow nasal cannula is very recent in India and only few hospitals have this facility. Although they were not the cause of oxygen shortage, they could have contributed to it, so electively shifted to continuous positive airway pressure (CPAP) or bilevel ventilation with noninvasive ventilator use. HFNO has better patient compliance.
- Saving oxygen may be a strategy now.
- In a pandemic situation, in ICUs, oxygen saturation can be maintained at as low as 88% or up to 92% in a monitored environment and $\geq 93\%$ in an unmonitored environment. We should be targeting lesser oxygen saturation than what was being done before. As soon as the target is reached, oxygen can be reduced by a liter every time and see how the patient maintains at this level.
- Wastage needs to be taken care of hence oxygen stewardship programs are going to be necessary in the future.

Country updates

- **Bangladesh update:** The country is in a strict lockdown except for emergency services. The number of cases and deaths are increasing. Vaccines are now available. Vaccination of frontline workers has reduced deaths in this group.
- **India update:** India is still in the second wave and it is slowly plateauing. Situation, state-wise, is very different. Except for five states in the South and the North East part of India, the rest of India is mostly out of the second wave. Maharashtra and Kerala are two states, which show a different pattern. They are early starters. Floods have disrupted COVID care in Maharashtra. The Indian Council of Medical Research (ICMR) study has shown that antibody seropositivity is almost 67%, whereas seropositivity rate in southern states is 43%. The target is to vaccinate all those above 18 years by December end. If the vaccination is in order then it seems unlikely that the third wave will be explosive. It may be a mitigated third wave in unexposed geography, in unexposed people and is expected between September and January. Overall India is stable and cautiously optimistic. Lack of adherence to COVID-appropriate behavior is a major concern now.
- **Pakistan update:** Cases are rising; people are not adhering to standard operating procedures (SOPs). Serious restrictions will be implemented. Delta variant is present in the country. So far, only 5% of the population has been vaccinated.
- **Japan update:** There are around 5,000 daily positive cases and half of these are delta variant cases. Eighty-five percent of people aged ≥ 65 have been vaccinated at least once. One case of pediatric death has been reported.
- **South Africa update:** About 1.1 million have received the second dose and 4 million have received the first dose (Pfizer). About 1.1.6 people have taken the J&J vaccine. The country is slowly moving out of the third wave. ICU admissions are high. There have been massive superspreading events in Johannesburg and Durban areas and the effects will be seen in the coming week.
- **Hong Kong update:** Very few imported cases and almost no community cases. Two children from a consulate broke quarantine and travelled in a tourist bus tested positive. There were mandatory checks in many districts they had travelled to and so far, no community cases. Five million doses have been administered, more than half are Pfizer-BioNTech and the rest were Coronavac. More than 3 million (40%) have got the first dose and more than 2 million (30%) have got the second dose. The target is to achieve 70% vaccination with the first dose by September end. Teenagers (12-15 years) are also being vaccinated, though the response is not so good.

- **Australia update:** One hundred sixty-three cases in NSW; the state of Victoria has 12 cases. Half of the country's population is in lockdown. There are cases of Delta variant in the country, especially in NSW, which has only partial lockdown. Pfizer vaccine is in short supply, but there is excess of AstraZeneca.
- **Singapore update:** Seventy-five percent vaccinated with one dose, 51% vaccinated with two doses; 70,000 vaccinations per day; 130 cases in a day, lot of Delta cases are coming from Indonesia. Those who had received both doses, 0% needed oxygen; single dose 3.4% needed oxygen, and the vaccinated 5.4% needed oxygen. Delta virus seems to be coming down in terms of severity.

Participants - Member NMAs: Dr Yeh Woei Chong, Singapore, Chair-CMAAO; Dr Ravi Naidu, Malaysia,

Immediate Past President-CMAAO; Prof Ashraf Nizami, Pakistan, First Vice President-CMAAO; Dr Alvin Yee-Shing Chan, Hong Kong Medical Association, Treasurer-CMAAO; Dr Marthanda Pillai, India Member-World Medical Council; Dr Angelique Coetzee, South Africa; Dr Akhtar Hussain, South Africa; Dr Qaiser Sajjad, Pakistan; Dr Marie Uzawa Urabe, Japan; Dr Salma Kundi, Pakistan; Dr Md Jamaluddin Chowdhury, Bangladesh

Invitees: Dr Russell D'Souza, Australia UNESCO Chair in Bioethics; Dr Shashank Joshi, Mumbai, India; Dr Rahul Pandit; Dr Monica Vasudev, USA; Dr Mulazim Hussain Bukhari, Pakistan; Dr Li Ling Lim; Dr Yau Onn Voo; Dr Vanessa Phua; Dr Benny Tan; Dr Catherine Ng; Dr Cheng Jew Ping; Dr S Sharma, Editor-IJCP Group

Moderator: Mr Saurabh Aggarwal



J&J COVID-19 Vaccine Recipients may Need a Booster

Individuals who have been administered the single-dose Johnson & Johnson (J&J) COVID-19 vaccine may require a booster jab to tackle some of the concerning coronavirus variants, suggests a new study.

A significant proportion of blood samples taken from people who had received the J&J vaccine showed low neutralizing antibody levels against the Delta, Delta Plus, Beta and Lambda variants, noted the study posted on the medical website bioRxiv which is yet to be peer-reviewed. Neutralizing antibody levels were found to be so low that the vaccine may not provide even 50% protection against infection with these variants, stated investigators from the New York University Grossman School of Medicine.

A 50% efficacy is the least to get an emergency-use approval from the US FDA, which the J&J vaccine has received. On the basis of studies conducted with other vaccines, investigators speculate that neutralizing antibody levels in J&J vaccine recipients could be improved either with a second dose of the same vaccine or a dose of the Pfizer/BioNTech or Moderna mRNA vaccine... (Reuters)

COVID-19 Vaccine Booster Shots may be Needed for Emerging Variants, Says AIIMS Chief

Chief of AIIMS, Dr Randeep Guleria, has said that amid different mutations of the coronavirus emerging in the near future, the country might need to embrace a booster shot of second-generation vaccines against COVID-19. He said that the immunity is waning and we may need to have a booster dose that will tackle the emerging variants. He added that the booster dose will be a second-generation vaccine, which would be better with respect to the immunity it provides, cover the new emerging variants and have a better efficacy overall. Dr Guleria said that trials of booster vaccine shots are underway and people will possibly require a booster dose by the end of this year. However, that will happen only once the population is vaccinated. The next step then will be the administration of a booster shot... (NDTV - ANI)

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