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Oxygen therapy and respiratory support in SARS COVID 19 infection in children

Abstract

Covid 19 pandemic has been a very dreadful experience and affected all of us badly. Although children are asymptomatic and less severely affected by covid illness as compared to adult population, however the patients presenting with severe symptoms require hospitalisation and need oxygen and respiratory support. Inappropriate, prolonged use and failure to monitor oxygen therapy can have serious consequences. Oxygen therapy in children requires the selection of proper oxygen delivery system that suits the patient's size, needs, and the therapeutic goals. Low flow and high flow oxygen devices are being used to deliver oxygen in children. High flow nasal cannula has been used proved to be wonderful modality for respiratory support in children. We need to follow all guidelines laid down by various agencies while delivering oxygen and respiratory support to sick children suffering from covid infection. All precautions should be taken to avoid aerosol generation. Close monitoring of oxygen therapy is a must. In this article we have tried to cover the indication and modes, it's relation with mucormycosis, monitoring and the precautions which we should take while giving oxygen therapy in covid era. Update of knowledge of indication of use and other modalities of treatment by treating doctors and patients are equally important so that we can fight a battle of third wave if it arrives.

Keywords: Covid 19, Oxygen therapy, delivery devices, monitoring

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Introduction

SARS 19 novel corona virus disease has affected large population throughout the world and has emerged as a global crisis and was declared a worldwide emergency by WHO on 11th March 2020. According to data's children has been found to be suffered less in number and severity as compared to adult population.[1] The rise of covid cases in second wave are definitely highest in india as compared to other countries. Maximum number of daily cases has been reported by India with high surge rate during second wave of covid in month of May 2021.[2] The clinical characteristics, disease progression and complications and overall case fatality rate in children and young patients are significantly milder as compared to adults.[3-5] Children of all ages are susceptible to COVID-19 with no sex predominance. Although clinical manifestations of children in COVID-19 are generally milder in pediatric population particularly but child below one year of age and patient who are in immunocompromised state are at higher risk of getting covid infection.[6] Severe symptoms has been found in patients who are premature, having any previous underlying chronic illnesses, cardio respiratory compromise and suffering from some immune related disorders.[7] The clinical presentation in children varies from mild cough, cold to severe respiratory involvement leading to acute respiratory distress syndrome like presentation.[8] Most of children remains asymptomatic may be because of less representation of ACE receptors over different epithelial cells and because of strong innate immunity. The GIT symptoms has now emerged as one of the main predominantly presenting clinical features in children.[9] Many of the children who had previous contact history of Covid in family or suffered from past covid infections are now a days landing up with a new hyper immune responsive clinical state, a new entity known as multisystem inflammatory syndrome of childhood associated with SARS covid virus.10The ARDS is found to be the most common presentation of SARS Covid infection with presentation of respiratory distress, increased work of breathing and hypoxemia.[11] Most of these patients require hospitalisation and need aggressive management with oxygen therapy and different modes of respiratory support.[11,12] Children with severe respiratory disease may land up into respiratory failure very early. So the early anticipation and timely intervention in form of respiratory support and oxygen therapy remains the primary modalities for treatment of COVID 19 presenting with ARDS like features.[13] The children with significant respiratory illness require ventilation and intubation on day one may deteriorate very quickly.[14] For children who require admission and are sick, the main line of treatment is supportive therapy, good nursing care, balanced diet and oxygen therapy.[15]

We had been passing through the phase of covid waves where it was said to be inevitable as announced and expected by many authorities. The availability of oxygen and the shortage of high flow nasal cannula, bipap and ventilators were seen during first and second wave of covid epidemic and our health system have drastically failed and crippled in managing patient during this epidemic. The reason was that everyone and even a layman was under the impression that oxygen and ventilators is the only treatment modality which can cure covid and needed in each and every patient. This rumour created an acute shortage of oxygen as people started purchasing and started stocking it even if it was not required and not advocated by doctors to everyone, so ultimately the patient who were in dire need of oxygen were devoid of it. People have falsely claimed that they have not received oxygen and ventilators during this phase.

Oxygen therapy and oxygenation parameters

Oxygen when administered correctly may be lifesaving. Hypoxia is a life threatening condition in which oxygen delivery to tissue is inadequate to meet the metabolic demands of body. Oxygen when given liberally and casually to patients may prove fatal. Giving oxygen to children requires the selection of proper oxygen delivery system that is suitable to patient's size, needs and the therapeutic goals

to maintain the desired saturation of body.[16] Oxygen delivery systems are categorized as either low-flow or high-flow systems. The Improper use and failure to monitor can have serious consequences, however O_2 should never be withheld from the severely hypoxic patients. The main goal of oxygen therapy should be to achieve adequate tissue oxygenation with the lowest fractional concentration of inspired oxygen possible with minimal complications.[17] To understand oxygen therapy, we must know the physiology of oxygenation first and oxygen indices should also be taken in to consideration.

1. Alveolar-arterial oxygen difference (A-aDo_2):

Atmospheric pressure at sea level is 760mmHg, Oxygen makes up 21% of inspired air.

Water vapor pressure due to oxygen which humidifies inspired air = 47mmHg.

PIO_2: (760 - 47) x 0.2094 = 149mmHg. (PIO_2: Partial pressure of inspired oxygen)

The alveolar partial pressure of oxygen (PAO2) can be calculated from the following equation: A-aDO_2 = PIO_2xFio_2 – ($PaCO_2$/R)-Pao_2. R (0.8) is the respiratory quotient.

The partial pressure of oxygen in arterial blood (PaO_2) is measured by blood gas monitor. In a healthy infant A-aDO_2 is 20 with FIO_2 of 20%. By this equation, we can determine whether hypoxia is because of ventilation perfusion mismatch or shunt.

2. Oxygenation index: In children use OI (Oxygenation Index) and OSI (Oxygenation Saturation Index) using SpO_2.

Oxygenation index is = MAPxFio_2x100/Pao_2.

Oxygen Saturation index = MAPxFio_2x100/SPO_2.

The advantage of OSI as opposite to SI is that this technique is non-invasive and allows continuous monitoring of oxygenation status. Practical relationship between two is OI =2XOSI.

3. The relationship between SPO_2 and Pao_2 can be understood by "S" shaped graph known as oxygen dissociation curve as shown in Figure 2.

4. Whole blood oxygen content:

The concentration of oxygen in arterial blood, often called the oxygen content is measured as: CaO_2 (ml O_2/ dl blood)= (1.34 x Hb x SaO_2) + (PaO_2 x 0.003).

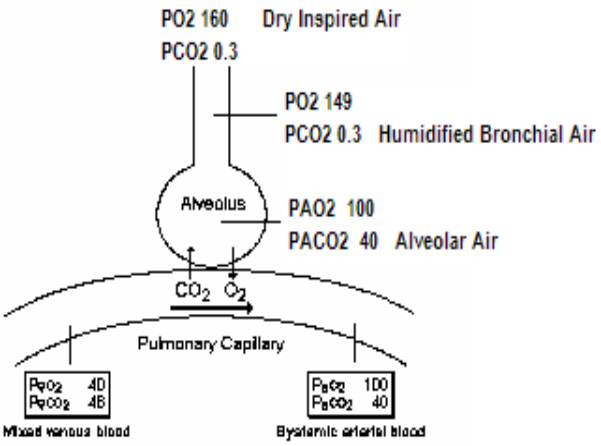

Figure 1 The oxygen cascade.

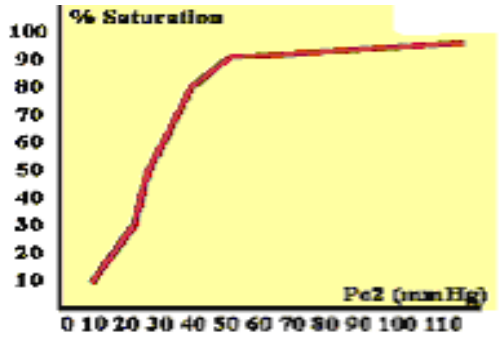

Figure 2 Oxygen dissociation curve.

Where Hb is in g/dl blood, SaO2 is expressed as fraction (i.e. 1.0 instead of 100%), PaO_2 is in mmHg, 1.34 is the O_2 carrying capacity of Hb in ml O_2/g, and 0.003 is the Bunsen solubility coefficients for O_2 in plasma at 37 C (16,17).

Indication of oxygen therapy[16]

The specific indication for oxygen therapy in acute care hospitals are as follows:

- Documented hypoxemia, in which arterial oxygen tension (PaO_2) of less than 60mmHg or oxygen saturation < 90% on room air or when PaO_2 & SaO_2 levels are below the ranges for specific clinical scenario.
- In neonates, PaO_2 levels of less than 50mmHg and/or SaO_2 levels of less than 88% or capillary oxygen tension (PCO_2) level of less than 40mmHg.

A. Indications for low flow oxygen delivery systems	B. Indications for high flow oxygen delivery systems
• FiO_2 requirement less than 0.45	• FiO_2 requirement more than 0.45
• Rate less than 25 breath/minute	• Respiratory rate more than 25 breath / minute
• Normal or near normal tidal volume	• High tidal volume
• Regular respiratory pattern	• Irregular respiratory pattern
	• Evidence of alveolar hypoventilation with CO_2 retention

Indications of hospitalisation of children in COVID 19:

All children who are sick looking and are not maintaining oxygen saturation should be admitted in PICU for monitoring. These patients should be started on oxygen therapy. Any of the following criteria should be considered for hospitalisation.[5,18,19]

1. Patient having significant respiratory distress
2. Oxygen saturation in room air <less than 92%
3. Presenting with sign of Shock
4. Poor feeding and dehydration child who are drowsy and poor responsive
5. Seizures/ encephalopathy/ severe illness.

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Critical disease: Child is considered very sick if he fulfils any of the below criteria.

ARDS, Sepsis, Septic shock, MODS, Acute thrombosis and MIS-C.

Sources of oxygen

The knowledge of various sources carries a lots of importance as acute shortage of oxygen was observed during second wave of covid epidemic in our country. If we know how it is being produced and what are the different sources hen we can surely increase production of oxygen at ground level and small health facilities in anticipation of third covid wave.

There are two typical sources of oxygen used therapeutically:

1) Oxygen cylinders 2) Oxygen concentrators.

Because of sudden surge in covid cases in second wave, there was a huge demand in oxygen concentrator at home due to insufficient supply of oxygen in hospitals and health care facilities.

Devices for oxygen delivery

Oxygen delivery systems are categorized as either low-flow (variable performance) or high-flow (fixed performance) systems.

A. low flow system

Low flow system, supply supplemental oxygen but at a flow rate below the patient's peak inspiratory flow demand, resulting in variable FIO2 and variable delivery of air to patient's airway. Low flow systems generally does not require humidification as compared to high flow devices. These includes nasal catheter, nasal prongs, nasopharyngeal catheter which are quite children friendly and well tolerated. Nasal prongs are the best oxygen delivering devices in developing countries.[20]

Different types of masks like venturi mask, partial rebreathing mask, non-rebreathing masks are also used. Reservoir is generally added to increase oxygen concentration delivery to patient .These are mostly used in elder children where acceptance is good. The advantage of catheters is that no humidification is required. Partial rebreather devices achieve a maximum FiO_2 of 70 to 80%. Oxygen flow rate should be 6 L/minute. Non rebreathing masks are similar to partial-rebreathing masks but don't allow the mixing of exhaled gases with oxygen supply. The advantage being the good FIO_2 can be the one-way valve over the reservoir bag prevents entry of expired gas, and the one-way valve over one of the side ports limits entrainment of room air. It provides 95-100 % oxygen at flow rate of 6-15 L/minute. The provide different concentration at different flow rates as mentioned in Table 1 & Figure 3. Trans tracheal oxygen can be the better option for patient requiring oxygen for longer duration because of chronic illness. Mostly seen in patients in whom tracheostomy has been done. TRANS tracheal oxygen for long term was found to be better than prongs.[21]

B. High flow oxygen systems

High flow system, provide supplemental oxygen at a specified (fixed) FiO_2 and with sufficient flow to meet or exceed the patient's inspiratory flow rate. Here flow rate and velocity of oxygen is very high through a jet which generates high flow by using an air entrapment mask which tightly fits over patient's face. The cross-sectional area and the orifice decide and control the flow rate passing through the opening and an extra collar can be attached to provide humidification.

Table 1 Oxygen delivery device

Device	Flow rate (Lit/min.)	FiO_2
A. Low flow System		
• Nasal catheter	1-6	Max 0.45
• Nasal canula	1-6	Max.0.45
• Nasopharyngeal Catheter	0.25-1	0.24-0.35
• Simple Oxygen Mask	6-12	0.4-0.6
• Partial Rebreathing mask	6-15	0.4-0.8
• Non-rebreathing Mask	8-15	0.4-0.8
B. High Flow System		
• Air-entrainment mask	To supply fixed FiO2 level of 0.24,0.28,0.31,0.35,0.40, and 0.50	
C. Enclosure System		
• Oxygen Hood	>7	0.2-0.9
• Oxygen Ten	10-15	0.4-0.5

1. Oxygen hoods

It is the best method to deliver oxygen to infants. This is a transparent enclosure which surrounds the head of the baby or infant. Here continuous humidified oxygen is circulated through the port which create a higher oxygen concentration atmosphere inside the hood. Because of layering effect high concentration of oxygen is generated around the face of baby causing a risk of hypercapnia. The FiO2 achieved inside the hood varies from 22 to 90% and depends on the flow rate of O_2, air exit, size of side port openings and shape of hood. Ideally sensor should be placed and carbon dioxide concentration should be monitored to avoid its toxicity.

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2. Closed incubators:

This is a transparent enclosure mostly used in NICUs which create a warm, thermoneutral zone for baby. Humidification and oxygen can be added to this. This is an ideal equipment used for transportation of sick babies while referring the baby.

3. Oxygen tent

An Oxygen tent is similar a concept to a hood except that it's designed to encircle trunk and head of an older child. O2 concentration maintained within the tent depend on the rate of flow, the tent volume, the adequacy of the seal between the tent walls and bed, and the frequency with which this seal is broken to tend to the patients.

4. Heated humidified high flow nasal canula

This is the method which has been used in NICUs since long time but it became popular after covid pandemic. It has proved to be an wonderful modalities for respiratory support in children. Here heated, humidified oxygen is given under high flow via nasal canula to decrease work of breathing and airway resistance.

5. Ambu bag: It is a device which is generally used when patient is not breathing spontaneously. It always remains inflated unless squeezed fills spontaneously with air or gas when it is released. The main advantage is that it doesn't require any compression source of oxygen. The best thing is that it has got a puff off valves to avoid unnecessary high pressure which may damage lung and can lead to pneumothorax especially in neonates, mostly used at the time of resuscitation and transiently while suctioning when patient is on ventilator. It provides It provides 21% of oxygen without any reservoir or oxygen supply, 40% when oxygen source is attached but without reservoir and 100% when reservoir and sources of oxygen both are connected.

6. Bilevel positive airway pressure (BiPAP):

It is indicated for mild acute respiratory distress syndrome when patient is hemodynamically stable without having any multi-organ damage. It has been mostly used in adults and was used extensively in covid 19 era. Its use in children is limited because it is cumbersome but feasible only in an older, cooperative children who are tolerating oronasal mask well.

7. Contineous positive airway pressure (CPAP):

It is most commonly used non-invasive mode of respiratory support in neonates especially in respiratory distress syndrome. It provides distending pressure in both phase of respiration in spontaneous breathing distressed child. The PEEP and FIO_2 can be adjusted based upon the level of work of breathing and saturation.

8. Conventional and high flow oscillatory ventillators:

These are the next higher mode of respiratory support when NIV fails or patient is landing into severe respiratory failure. This is the invasive mode where patient need to be intubated. They can provide accurate Fio_2 as per the settings and requirement. These can be used with or without tracheostomy.

Criteria for selection of devices in paediatric patients in covid illness:[22,23]

Bilevel NIV or CPAP ≥5 cmH_2O via full face mask: PaO_2/FiO_2 ≤ 300 mmHg SpO_2/FiO_2 ≤264

Mild ARDS. 4 ≤ OI < 8 or 5 ≤ OSI < 7.5

Moderate ARDS. 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3

Severe ARDS =OI ≥ 16 or OSI ≥ 12.3

Principle of oxygen therapy and respiratory support in COVID-19 illness

The Principle of management of respiratory failure or Acute Respiratory Distress Syndrome in children in SARS COVID 19 are similar to that of ARDS due to any other underlying illness. All children should be hospitalised if they are looking sick or fall in any of the criteria as laid down in guidelines for management of covid illness. The criteria's and classification for identification of sick and critical patients have been well defined by WHO,MOHFW and Indian academy of paediatrics.[5,12,13,19,24]

Oxygen therapy should be started immediately to patients with acute respiratory distress, hypoxic patients or in shock. Our aim should be to maintain Spo_2 ≥94%.

Providing low flow oxygen modalities like nasal prongs should be the preferred method while starting oxygen in initial stage for respiratory support in small scale settings. In a study conducted in small hospital set up by Muhe L et al.[20] nasal prongs was found to be the initial choice of giving oxygen to patient in developing countries, with a target SpO_2 of ≥ 94%. At initial step the target for maintaining SPO_2 should be more than 94% in sick and critical children with emergency signs, otherwise it should be SpO_2 is ≥90%. Use all universal precautions while handling and delivering oxygen to patients with COVID19 (5,24).The methods and various oxygen delivery devices has already been discussed which provides different oxygen concentration at different flow rates. Conventional methods like nasal prongs/cannula, oxygen mask, hood should be the initial mode of starting oxygen at initial step. Non-rebreathing mask can provide up to 95% FiO_2 at oxygen flow rate of 10 -15 L/ min and can be used for short periods initially. High flow nasal canula for giving oxygen is the choice of therapy when child is not improving with low oxygen flow.[25,26]

Non-invasive Ventilation are methods of providing oxygen and respiratory support to the patients where intubation is not required. This is less invasive and the advantages being are good compliance, easy to remove, easy to implement, patient friendly and generally well tolerated by the patient. These are well accepted method of oxygen delivery and support in older and cooperative children.[5,19,22,25,26] Heated high flow nasal cannula which is a commonly used modality of respiratory support in bronchiolitis and pneumonia.[25] In HFNC flow of oxygen is 1–2 L/min in infants, 2–4 L/min in young children and 4–6 L/min in older children which cam maintain the desired SPO_2 level. Because of risk of spread of infection and contamination by aerosol generation, they are not advisable in covid era. Every effort should made to reduce the spread of aerosol generation from the oxygen delivering methods.[19]

In a comparative study conducted by Luo J et al.[26] on children less than 5 years of age with respiratory distress presenting with mild

hypoxemia to determine the efficacy of different mode of giving oxygen therapy. In this study HFNC was found to be better than simple oxygen therapy in reducing the risk of treatment failure, however risk of treatment failure was seen less with nasal CPAP as compared to HFNC in patients of age group 1-6 months who are having moderate-to-severe respiratory distress. There were no differences in mortality or increase chances of intubation in all 3 groups.

Though low flow nasal prongs and nasal cannula is the preferred mode of therapy in children with mild respiratory symptoms in initial phase for respiratory support however if it fails the BiPAP or invasive ventilation should be started without wating much of the precious time. Use of nasal prongs or nasal cannula is preferred in young children, as they may be better tolerated but risk of aerosol generation will always be there with high flow nasal cannula[28] but the evidences are not so strong.[19] With strict routine universal precautions for aerosol generation and spread of infection, this method is found to be most useful and most accepted method of oxygen delivery in covid patient requiring oxygen support.[29]

In Mild respiratory distress high Flow Nasal Oxygenation, Non-invasive ventilation may be given but in severe respiratory distress or respiratory failure, mechanical ventilation may be given with low tidal volume less than 6 mL/kg and high PEEP. If the child does not improve clinically even with mechanical ventilation, then we should consider High Frequency Oscillatory Ventilation. If child still doesn't improve and hypoxic, then extracorporeal membrane oxygenation should be started as it can be a lifesaving modality at the worsening stage.[27,29] All health care centres where patient infected with covid 19 patients are kept should be well equipped with pulse oximeters, functioning oxygen cylinders, high flow oxygen supply and even oxygen plants (recommended for bigger hospital set ups) and disposable and various oxygen-delivering systems. All universal precautions should be followed while handling the contaminated equipment and interfaces.[30]

Precautions to be taken during intubation and mechanical ventilation

The following precautions should be followed:

Special precautions are needed to take while intubating the child. Our concern should be to intubate as quickly as possible and to minimise aerosol generation and limit spread of infection to other patients. It is recommended that we should pre-oxygenate the child with 100% FiO_2 for 5 minutes before intubation. Filters are now recommended to avoid generation of aerosol. If non-invasive ventilation fails then patient should be intubated promptly. We should use cuffed endotracheal tubes, head box and filters in older children while intubating.[5,29,30] Avoid bag and mask ventilation if possible, to limit aerosolization but if unavoidable then low tidal volumes should be used. Intubation should be done by experienced and trained person to decrease contact time and to limit spread of infection with minimum attempt. Rapid sequential intubation along with analgesia and muscle relaxant should be done to ease the process of intubation. If affordable then video laryngoscope should be available at health facility which can maintain a safe patient doctor distance.[31]

Now seeing the surge and continuous waves of covid infection, doctors should focus on universal use of head box, plastic sheets, viral filters, disposable ventilator circuits, close suctioning and negative pressure rooms with adequate air circulation in all ICUs taking care of covid patients.[32] In adults nasal mask, oronasal mask, full face mask and helmets have been tried to limit spread of droplet infection. In adults patient initial flow rate should be 5 litre per minutes to maintain SPO_2 target of >93%.In stable adult patients, target should be >90 % and 92–95% in pregnant ladies.[32,33]

Prone position

Oxygen therapy is the best treatment of choice patient having hypoxemia. Gentle ventilation should be done to avoid volutrauma and barotrauma. If there is no improvement with ventilation, then prone positioning and ECHMO should be tried.[34] Awake prone position may be considered in older persistent hypoxemic children if they are able to tolerate.[35] Patient who are on HHHFNC or ventilators for long time and saturation is not improving significantly, then prone position can be the other option to increase oxygen saturation and to overcome hypoxemia. Various studies has shown prone position a good intervention for improving lung oxygenation.[19,36]

Precautions to be taken by health care workers to avoid risk of aerosol generation

All health care workers should wear personal protective equipment (PPE) to limit aerosol transmission. There should be a separate negative pressure isolation room where sick infective children are kept. A medical mask should be put on face of the child receiving who are receiving oxygen therapy with nasal prong or HFNC, the condition being child is comfortable and tolerating it well.[4,21]

One attendant per person should be allowed in intensive care units. The ICU should be well ventilated and should follow all guidelines while oxygenating the patient. All precautions should be taken to avoid spread of infections from nasal prongs while receiving oxygen therapy. In infants, it is recommended that an oxygen hood should be placed over the head along with nasal prongs to decrease spread of aerosols and it can be secure by tight mask to avoid unnecessary spread of infection due to leaks around the cannula.

As the covid 19 disease is mainly an air borne. So we should be very cautious while delivering oxygen and drug therapy through nebulisers. All aerosolized generating procedures should be avoided. Use of nebulisers should be discouraged but if required then metered dose inhalers (MDI) should be prescribed and they should be promoted for patient who are on inhalational therapy.[37,38] All guidelines as laid down by WHO, MOHFW, ICMR, IAP and other institute to prevent spread of infection and to reduce aerosol generation during intubation, nebulisation, suctioning and resuscitation procedures should be followed however it's very difficult to find the appropriate sizes masks, nasal cannulas, suctioning catheters that fit well to each and every child. The next problem is maintaining adequate seal without sedation is also quite difficult task in children.

Use of aerosol box should be promoted which is having a transparent plastic hood enclosure which helps us to visualise the procedures clearly. Closed suction catheters are preferred. All health care workers should wear head cap, face mask, goggles, gloves, full body gown, shoe cover and helmets in aerosol generating areas and PICUs. Risk assessment and of close contacts for healthcare workers should be assessed once exposure has occurs.[30] All treating paediatrician should follow all practical advisory and recommendation of safety measures issued by IAP while practicing safely during covid era in their clinics and PICUs to cut down the risk of infections. Key recommendations has been recently issued by Indian Academy Of Paediatrics and printed in journal INDIAN PEDIATRICS.[30]

Oxygen toxicity

Oxygen toxicity probably result from increased production of hydrogen peroxide and reactive agent such as superoxide anion, single

oxygen and hydroxyl radicals that attack and damage lipids, proteins, and other macromolecules, especially those in biological membranes.

a. Oxygen induced hypoventilation:

When a normal patient breathes 100% O_2 the peripheral chemoreceptors remain essentially inactive. Because blood O_2 levels are high and less reduced hemoglobin is available to carry CO_2, a slight rise in $PaCO_2$ increase the minute ventilation by 5-20%. This worsening of hypoventilation has been attributed to suppression of hypoxia peripheral chemoreceptor reflex.

b. Atelectasis:

When 100% O_2 is used within minutes "nitrogen wash out" occurs from the lungs. Patients with any degree of airway obstruction as may result from secretions, may experience diffusion of oxygen from alveoli to pulmonary circulation at a rate greater than that which can be replaced by circulation. This promotes a loss of alveoli volumes and atelectasis.

c. Retinopathy of prematurity:

Oxygen free radicals attack the incompletely developed retinal tissue and result in vasoconstriction which can progress to complete obliteration of retinal detachment. It is primarily a condition of prematurity and low birth weight babies.

d. Pulmonary oxygen toxicity:

Pulmonary O_2 toxicity, seen after inhalation of high concentration of O_2 for prolonged period, is due to cellular injury of lung parenchyma and airway epithelium.

e. Central Nervous System: central nervous toxicity of oxygen is rarely seen in adult patients. Some patients may have hypercarbia because of CO2 retention either due to hypoventilation or due to inadequate V/Q mismatch leading to CO2 retention that may lead to raised intracranial tension. In neonates oxygen toxicity may lead to intraventricular haemorrhage.

Mucormycosis, oxygen and COVID 19:

After SARS covid infection the opportunistic infection both bacterial and fungal infections are on rise in India. Both candida and aspergillosis has been emerged a new challenge as a co infection.[39] There is also sudden surge in mucormycosis cases in India after the second covid wave and India has reported maximum number of mucormycosis cases worldwide which has contributed 71% of total cases of muccormycosis.[40] Though the reasons are multifactorial but main causes are mutated covid infection, diabetes mallitus,excessive use of steroids, hypoxia and immunocompromised state.[41-43]

Other associated factors may be attributed like contaminated industrial oxygen supply, shortage of oxygen leading to hypoxic tissue state where fungal infections are more prone to grow in tissues in human body. Contaminated Oxygen in pipe lines and infrequent change of water in bottle and humidifiers may be the possible reason given by some experts for sudden increase in black fungus in India. To find the exact causes and corelation of rising of mucormycosis case with covid infections, further studies and research are still going on. The covid infection is definitely the cause of invasive fungal infection.

Fungal infections are more common in tissues having localised hypoxemia which create a microenvironment of hypoxia leading to growth of hyphae. There will be an adaptation of fungus to this hypoxic micro environment .When oxygen is given there will be switch over to alternative pathway which can decrease the invasiveness of fungus. So by avoiding hypoxia at tissue level, invasive mucormycosis can be prevented.[44] Although hyperbaric oxygen had been explorated for the treatment of rhino cerebral mucormycosis in era of 90s, it can prevent growth of mucor as it reduces tissue hypoxia and acidosis. It was found to be beneficial in prevention of growth of mucor because of different mechanism of action.[45]

When to stop oxygen therapy?

Oxygen therapy should be discontinued once patient is able to breath comfortably at room air and arterial oxygenation is maintained.

Patients who doesn't have hypoxia in blood but at risk of tissue hypoxia, oxygen should be stopped when blood gas is normal.

Oxygen therapy at home can be given to some chronic patient s in whom there is further requirement of oxygen. Oxygen therapy at home can be dangerous strategy as its very poorly monitored at home. There are no definite evidence for regarding initiating, monitoring and continuation of oxygen therapy at home.[46]

Monitoring of oxygen therapy

Parameters which should be monitored are:[47,48]

- Clinical state and level of consciousness of the patient.
- Continuous Spo_2 monitoring.
- Arterial blood gas analysis.It should be performed before oxygen therapy if possible.
- Fio_2 level should be adjusted as per the SPO_2 level.
- ETCO 2 monitoring.
- Chest X-ray and blood gas should be done one hour after extubating.
- Blood gas monitoring, oxygen saturation, Fio_2 and capnography remains the main parameter of importance in monitoring in respiratory failure.[48]

To meet the demand of oxygen scarcity and ventilators in a fight with covid epidemic in a developing countries like us, all practitioners and patients must know that oxygen and ventilators are not required for each and every patient. The approach should be target based oxygen delivery should and it should be titrated with oxygen saturation, flow and FIO_2. The high flow nasal oxygen can be a good mode of respiratory support in Covid patients which can spare some of the ventilators which can be offered to those patients who are really needing them. So this article basically helps in updating the knowledge of treating doctors regarding proper and judicial use of oxygen, high flow nasal oxygen, Bipap and ventilators, as the indications of each are different and well defined. So update of knowledge of treating doctors and patients are equally important so that we can fight a battle of third wave if it arrives.

Conclusion

Oxygen is a lifesaving drug in patient of respiratory pathology and should be used judiciously and monitored. Nasal prongs followed by high flow nasal canulla are the best initial method of choices of giving oxygen. If non-invasive ventilation fails, then invasive ventilation should be considered in patients with respiratory failure. All treating paediatrician should follow all practical advisory and recommendation of safety measures issued by various agencies. Saturation targeted oxygen therapy will eventually cut down oxygen consumption and by selecting the proper treatment modalities we will be able to save so

many people in a limiting sources in a developing countries like us. It will also help agencies to plan oxygen production strategies and to procure good equipment which are really needed to fight a war with covid if third wave arises.

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Conflicts of interest

None.

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