

Oxygen Therapy in COVID-19

Netra Mankar, Guddi Laishram*

Department of Community Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha, Maharashtra, India

ABSTRACT

One of the main causes of death in COVID-19 is hypoxia which occurs due to damage to the lungs. For this damage we need to give a patient oxygen therapy which is essential for saving the life. In the following article we have given information about different oxygen therapy and combinations which shows improvement in patient's status. Prone ventilation has also shown beneficial effect in homogeneous ventilation and can be performed at home based management. With the help of dual therapy and nocturnal therapy we have focused on benefits which have been noticed while using this therapy. By comparing risk benefit ratio high flow nasal cannula and non-invasive ventilation has gotten more attention as these proven to be machine of need. As numbers of cases rises suddenly intubation is not possible due to increased risk of transmission of infection so in early phase of disease high flow nasal cannula and non-invasive ventilation have been tried so that patient's status can improve and severity of disease will decrease. In article we have tried to explain importance of early intervention with high flow nasal cannula and non-invasive ventilation before intubation. With the help of these methods along with combination and prone position maximum benefit and improvement have been achieved and all these methods and techniques are inter dependent for achieving highest possible response in patient's condition. Oxygen therapy is the preferred treatment in moderate to severe cases as main sign of infection is hypoxia which is the main culprit in this scenario.

Key words: Hypoxia, Oxygen therapy, COVID-19

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Corresponding author: Dr. Guddi Laishram

E-mail: drguddi2015@gmail.com

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LITERATURE REVIEW

Epidemiology

Outbreak of COVID-19 had been occurred in Wuhan province of China which ultimately spread to all over world leading to the dreaded pandemic. Initially this pandemic had affected mainly people of age more than 65 but it further progressed in all age groups. It has been noticed initially that men were affecting in more number. But after increase in number of cases no gender bias has been observed. After China many countries were affected like USA, Italy, Germany and France. Italy was badly suffered from this pandemic with case fatality rate of 7.2 [2].

Pathogenesis

When SARS-CoV-2 enters in nasal cavity it starts replicating by attaching to epithelium. Receptor which helps virus to bind is ACE-2. This is the initial stage of infection. As infection proceed by entering into conducting airway which further triggers innate immunity. CXCL 10 is a type of cytokine which maybe use as predictive for clinical course of infection. It helps in monitoring innate immunity response against virus. Some patients may escalate to stage three of infection. In this stage virus reaches to gas exchange unit and affect type II

INTRODUCTION

On 31st of December 2019 cluster of cases of pneumonia of unknown origin were noticed in Wuhan, China. It was declared as pandemic on 11th of March 2020 after global spread. Till now it has speeded very rapidly and occurred in two waves. Among this wave last one was so devastating and dangerous. So many people lost their life in second wave due to hypoxia. In COVID-19 main mechanism is damage to the lungs which ultimately leads to hypoxia. It has been observed that 86 percent mortality in patients who are on ventilator and 61 percent mortality in critically ill patients [1]. COVID-19 causes atypical ARDS. For these reason different types of oxygen therapy has been tried in the patients for maximization of benefits.

pneumocystis which will form pulmonary infiltrate. Viral particles are released in large number along with toxin. Fibrosis along with diffuse alveolar damage is main pathology seen in lungs [3].

Oxygen nasal cannula

It is used in mild hypoxia as initial step. Main advantage of using this is decreases aerosol production which further spread of the virus. It provides FiO_2 40 percent and 6 litre per min oxygen which is not that efficient if patient gets critical [1].

Face mask

Compare to oxygen nasal cannula it can provide high FiO_2 to the patient but not that efficient because it can't increase oropharyngeal pressure [1].

High flow nasal cannula

It has mainly used before giving patient invasive ventilation [1]. It has capacity of giving FiO_2 up to 1.0 and flow rate up to 70 litres per min. A study has shown that 85 percent survivors and 50 percent non survivors received HFNO [9]. It is more effective than conventional oxygen therapy. It has been seen that risk of treatment failure and 30 day mortality are almost same for HFNO and Non Invasive Ventilation (NIV). Best thing about HFNO is it decreases chances of invasive ventilation. One randomised control study has been done on patients having non hypercapnia acute hypoxemic respiratory failure which showed HFNO is more effective in reducing 90 day mortality rate than NIV. Pneumothorax cases have been increased in COVID-19 so HFNO is more helpful than NIV [4].

It can provide heated and humidified air which the best for respiratory mucosal function. Because of this mucociliary clearance and integrity of epithelium in non-compliant lung can be maintained. It has been seen that due to tracheal gas insufflation dead space decreases which further increases effective minute ventilation. As it provides high flow rate of oxygen which ultimately meet the need of pathological lung. This maybe the main reason for reduction in incidence of intubation [5].

In mild to moderate type of respiratory failure high flow nasal cannula gives positive end expiratory pressure. It can reduce metabolic work by warming and humidifying the gas. It can be used in isolation ward without any fear of Claustrophobia which is seen mainly in non-invasive ventilation. In elderly patients it has been seen that man to machine co-operation is poor which is pre-requisite of non-invasive ventilation. High flow nasal cannula is good option to tackle increasing vases in short period.

Aerosol production is the main concern for transmission of virus. Study shows that virus can be vial and highly infectious in aerosol. Nasal cannula has higher chances of aerosolization. This same concern is seen for HFNO but randomised controlled crossover trial proved that HFNO is not associated with air or contact contamination. In patients with cardiogenic pulmonary oedema or

hypercapnia treatment failure is seen in HFNO as compared to NIV. If patient is not showing any signs of improvement then mechanical ventilation or ET intubation should be done [1].

Non invasion ventilation

Early invasive ventilation was said to be preferable choice but due to limited machine, resources and weaning off challenges non-invasive ventilation came into light. It helps to prevent deterioration if applied in early cases [6].

It comprises of Continuous Positive Airway Pressure (CPAP) or Bi-Level Positive Airway Pressure (BIPAP) ventilation [1]. 70 percent patients have given the trial of NIV before invasive mechanical ventilation [2,3]. HFNO is recommended over NIV as NIV benefit to risk ratio is lower [6].

Continuous positive airway pressure

This machine provides oxygen at constant flow both during inspiration and expiration. Normally positive end expiratory pressure is 2.5-3 centimetre of water. In the patient who requires continuous positive airway pressure 5 centimetres of water of positive end expiratory pressure is set. The main mechanism is to prevent collapse of alveoli and helps in distension of lungs. Pre requisite for continuous positive airway pressure is that it requires sealed system which can be achieved through tight fitting mask or hood. But this can lead to complications like damage of nasal bridge due to prolonged use. Oxygen leak can lead to reduction in inflation of lung and dryness of conjunctiva and cornea and oedema of same is also seen. Other method is continuous positive airway pressure hood. Straps are used for supporting the hood which is tied under the armpits. Advantages of hood are reduction in incidence of facial sores but this can create the feeling of claustrophobia in the patients. Because of complications frequent protective dressing is needed. Risk of aspiration is seen in these patients as air cause gastric distension. Barotrauma can also be noticed due to poor compliant lung [6].

Bi-level positive airway pressure

It is mostly used in chronic obstructive pulmonary disease patients and it is seen that patients who have comorbidities it gives satisfactory results. It can improve work of breathing. Barotrauma can be due to inappropriate use which causes increase intake of tidal volume. Exclude pneumothorax before use of bi-level positive airway pressure because it will lead to increase transmission of infection. For sufficient tidal volume inspiratory positive airway pressure should be in range of 12 to 35 centimetres of water. Expiratory positive airway pressure has same setting as of continuous positive airway pressure. 8 centimetres of water difference should be present between inspiratory positive airway pressure and expiratory positive airway

pressure. If bi-level positive airway pressure fails then intubation should be done [6].

Helmet ventilation

Other mode for NIV with helmet. It has proven to be advantageous over face mask in COVID-19 patients:

- Decreases air leak
- Reduces aerosol production
- Tolerance rate is more.

Limitations

- High consumption of CO₂ supply
- Rebreathing of CO₂ [1].

Conventional mechanical ventilation

High mortality rate after tracheal intubation is reported then also 10-17 percent patients lastly require it. Risk factor

- Multiple organ injuries and late intubation
- **Complications:** pneumothorax etc. [1].

High frequency jet ventilation

Open system, high frequency, small tidal volume and low airway pressure makes it more reliable for airway surgery. It is used in atrial fibrillation ablation, ARDS treatment and assessment of CVS function. Limitations: difficult to monitor FiO₂, airway pressure, Pet CO₂. For these all reason it is not much in use [1].

High Frequency Two-Way Jet Ventilation (HFTJV)

It has two phase active inspiratory and expiratory. It is seen that during inspiratory phase a jet pulse is injected into lung while jet pulse is injected out during expiratory phase. It helps in elimination of SARS-CoV-2 virus out of lungs by Venturi effect [1].

Supra Glottis Jet Oxygenation and Ventilation (SJOV)

HFTJV is infraglottic jet ventilation which requires tracheal intubation. But SJOV with jet pulses originated above vocal cord and has same result. It is demonstrated in patient with respiratory suppression, GI endoscopy under propofol and emergent difficult airway management especially in OSA. It provides similar results of oxygenation in apnea patients and also maintenance of blood carbon dioxide level as compared to HFNO.

Advantages

- Easy to use
- Requires less sedation.

It can also produce aerosol so PPE kit use is must [1].

Dual oxygen therapy in SARS CoV

It has been seen that five to six percentages of COVID 19 patients shown sever hypoxemia. To tackle this problem use of non invasive ventiu is must. But it has been noticed

that some patients having sever COVID-19 infection are failing to maintain oxygen level even if patients are on 100 percent FiO₂. One study shows that main reason behind this is hypercapnia which increases alveolar dead space. To overcome this problem Kumar et al suggested dual oxygen therapy. In this therapy mechanism on which high flow nasal cannula and non-invasive ventilation works are combined. As COVID causes disseminated intravascular coagulation like clinical features. So initial treatment consist of administration of oxygen through oxygen nasal tube or high flow nasal cannula. If the patient deteriorates then oxygen demand increases and then continuous positive airway pressure or ventilation has to use. As increase in dead space in non-invasive ventilation causes failure of therapy and that's why more carbon dioxide rebreathing is seen. Studies have shown that mask volume is related to carbon dioxide rebreathing. Failure is due to leak of air reduces positive airway pressure. Mechanism behind dual oxygen therapy is reduction of anatomical dead space, mixing of gas, reduction of mask volume and more amount of oxygen concentration. There might be possibility in spontaneously breathing patient that hypoxic respiration may be reduced which make therapy successful [7].

Prone ventilation

When mechanical ventilation is given to the patient lying in prone position said to be prone ventilation. This method has proven to increase oxygen concentration. It helps by reducing lung compression which ultimately leads to increase in lung perfusion. Ventilation becomes more homogeneous as difference between dorsal and ventral transfusion pressure decreases. Because of this ventilator associated lung injury decreases and improves ventilation and oxygenation. Improvement of oxygenation by proning is seen in other non-infectious studies and even in healthy lungs. One study suggested that increase positive end expiratory pressure by prone positioning. Recruitment of collapsed lung unit is possible if initiation is done in early phase of disease. Additional monitoring in case of proning is not required but endotracheal suctioning is required. Some study shows faster nutrition achieved when the patient put in reverse Trendelenburg position in prone position. Sedation is must for these procedures. Six to eight hours per day is required to achieve maximum benefit. When signs of improved oxygenation are seen then cessation of proning is done. There are certain contraindications like spinal instability, shock and increase [8].

Prone positioning in pregnancy

From certain study it is suggested that prematurity can be avoided if proper use of alternating prone position and lateralization with high flow nasal cannula in COVID-19 positive pregnant patient. One study conducted in 2014 shows that prone position ventilation has satisfactory effect in pregnant women suffering from severe H₁N₁ associated ARDS. According to WHO there are not so many studies to prove effectiveness of prone ventilation in pregnancy. There may be beneficial effect

being in lateralized position. Complications-As arms are in extended position which may lead to brachial plexus neuropathy. It also includes facial and ocular oedema. Skin protection should be done in the patient and redistribution of pressure point should be carried out as preventive strategy [9].

Oxygen therapy in children having COVID-19 infection

Mainly children who are asymptomatic have been advised to isolate for 1-2 weeks as per protocol. In mild case of pediatric age group who are showing symptoms related to respiratory tract infection there is no need of antiviral therapy. In children who are experiencing mild to severe symptoms should be considered for oxygen therapy which includes oxygen mask or nasal catheter. If children not respond in to these then high oxygen flow catheter inhalation or non-invasive ventilation should be used. But these techniques increase the incidences of aerosol production. Because of these reason health care professionals should wear Personal Protection Equipment (PPE) and negative pressure isolation room may be required for protection from transmission. Frequent monitoring is enquiry for escalation to mechanical ventilation if the patient is deteriorating [10].

Nocturnal oxygen therapy

It has been seen that cytokine storm is the main cause for exacerbation of COVID-19 infection. If early intervention is done then progression can be halted. Diurnal rhythmicity is seen in human whole blood. Peak of pro inflammatory cytokine is at night and early morning due to low level of cortisol. Lipopolysaccharide (LPS) with whole blood stimulation increases cytokine and chemokine levels during night and early morning time. It is expected to decrease in production of inflammatory factors when there will be reduction in nocturnal pathogen exposure. Some recent studies suggest that virus can be aspirated from lung (deep), so nocturnal oxygen therapy has therapeutic importance as entry of virus into lungs occur mostly during this time. This therapy can be therapeutic option that is home quarantine [11].

Home oxygen therapy

This was mainly used for chronic pulmonary lung disease and cardiac disease patients but due to outbreak of COVID-19 this therapy is used in the patient who are recovering and out of danger and can sustain on low level of oxygen given as external support.

Supplementation comprises

- **Long term oxygen therapy:** oxygen is given for 15 hrs. daily.
- **Ambulatory oxygen therapy:** This is given to those who are non-hypoxemic at rest but they may have hypoxemia while doing exercise.

- **Short burst oxygen therapy:** Brief and intermittent oxygen therapy when they don't have symptoms and signs of hypoxia
- Palliative oxygen therapy
- Delivery system includes
- **Low flow nasal cannula:** One to six litres per minute of oxygen can be delivered by this system.
- **Simple oxygen mask:** Six to ten litres per minute can be delivered. Simple bore tube can be used which is connected to mask.

Venturi mask

This is mainly used in the patient who are hypercapnic and in respiratory failure. Indications for home therapy are as follows.

- Chronic lung disease
- SARS-CoV
- Cystic fibrosis
- Pulmonary hypertension
- Interstitial pulmonary disease

Preparation for therapy

For home therapy oximeter is must for monitoring. This device is mainly used in long term oxygen therapy. This therapy is boon but comes with certain complications. Excessive oxygen *i.e.* concentration more than 50 percentage which may lead to atelectasis and oxidative stress [12].

DISCUSSION

COVID-19 is extremely serious disease which ultimately damage to lung leading to hypoxia and to tackle this various oxygen therapy and equipment have been tried. Oxygen nasal cannula and face mask used for mild hypoxia but not that efficient [1]. High flow nasal is more efficient than non-invasive ventilation. Pathological lung requires high flow rate which provided by high flow nasal cannula and leads to decrease incidence of intubation [4]. Other method tried is dual oxygen therapy which decreases anatomical dead space, mixing of gas and increases amount of oxygen concentration [7]. Prone ventilation has shown promising result as it increases perfusion of lung and makes ventilation more homogeneous [8]. Nocturnal oxygen therapy mainly based on fact that peak of pro inflammatory cytokine is at night and early morning [11]. Once patient come out of danger home based oxygen therapy is tried [12]. So these are the different modes which are used in COVID-19 patient for oxygen therapy.

CONCLUSION

At last in COVID-19 patients oxygen therapy is must to correct hypoxia. We have summarised benefits and risk of different mode. From the above data HFNO is considered better option along with SJOV. Along with the risk to benefit ratio combine therapy in the form of dual oxygen therapy has also shown improvement in patients. We tried to discuss oxygen therapy in children and

pregnant women and in pregnancy lateralized position along with other methods of oxygen therapy. Prone ventilation can make ventilation homogeneous and shows satisfactory improvement in oxygen level in acute respiratory distress syndrome. We tried to sum up different modes of oxygen therapy and how to use this oxygen therapy in home based management after recovery which has proven to be effective and decreases long stay in hospital. Overall high flow nasal cannula and non-invasive ventilation are preferable over other methods in oxygen therapy as it improves oxygen level if used at early phase of disease which will halt the further progression of infection.

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