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Use of high flow nasal cannula as a modality of acute respiratory failure due to COVID-19

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ABSTRACT

Oxygen (O_2) therapy is the first-line therapy for acute respiratory distress with hypoxemia due to Coronavirus disease-2019 (COVID-19). High-flow nasal cannula (HFNC) therapy represents one of the O_2 therapy alternative modalities. HFNC is a supportive O_2 therapy device using a specially designed HFNC warmed and moisturizer, resulting in a stable flow rate. The physiological mechanisms of HFNC make its efficacy better than other O_2 therapy applications. Management of COVID-19 focuses on preventing disease worsening, and HFNC can optimize the outcome of therapy. Further studies are necessary to evaluate the benefits of HFNC in hypoxemia management. It is also important to clarify its contraindications and factors associated with HFNC failure.

Introduction

Coronavirus disease-2019 (COVID-19) is an infectious disease caused by Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2). SARS-CoV-2 is a new type of coronavirus identified in humans, first reported in Wuhan, China, on December 31st, 2019. COVID-19 has spread to various parts of the world, and on March 11th, 2020, WHO declared a COVID-19 pandemic (1,2).

A preliminary report from the Chinese Centers for Disease Control and Prevention estimated that most confirmed cases of SARS-CoV-2 infection were 81% mild-moderate, 14% severe, and 5% in critical condition (3). Severe SARS-CoV-2 infection is a critical condition for the occurrence of acute respiratory distress syndrome (ARDS), and even respiratory failure (4).

Patients with COVID-19 who are accompanied by pneumonia have respiratory problems hindering the maintenance of O_2 needs. Respiratory disorders can range from respiratory distress to respiratory failure. Respiratory distress is the increase and worsening of breathing effort. Respiratory failure is a disorder of one or more respiratory functions and is a life-threatening condition. COVID-19 patients will experience respiratory failure in severe and critical conditions (2).

O_2 therapy is the first-line therapy for respiratory distress with hypoxemia due to COVID-19. The method for providing O_2 therapy varies and must follow the severity of the disease (2). The goal of O_2 therapy is to maintain O_2 (SpO_2) saturation >90% (2). High flow nasal cannula (HFNC) is a modality for O_2 therapy in COVID-19 with mild to moderate ARDS. HFNC is an option to treat hypoxia (2). The most important rational approach to O_2 therapy with HFNC in respiratory distress patients with hypoxemia is to treat hypoxia as soon as possible to reduce the risk of intubation. However, HFNC therapy requires close monitoring, and if there is no improvement, an immediate switch to another therapeutic modality is needed, such as intubation with mechanical ventilation.

Differences between O_2 support with low flow and high flow nasal cannulas

O_2 support therapy is an intervention used by clinicians in acute hypoxia treatment. One of the supportive O_2 therapies is the use of a conventional low flow nasal cannula (LFNC). However, LFNC is only effective in providing O_2 support with a flow rate of 4-6 liters/minute or equivalent to the inspired oxygen fraction (FiO_2) of 37-45% (5). Furthermore, LFNC can cause dryness and irritation in the nasal mucosa, increasing the potential for bleeding during long-term use (5). Additionally, there are limitations to O_2 support with LFNC as it depends on the diameter of the nasal cannula used and the adult size is 6.1 mm (5). Furthermore, LFNC is an open O_2 supplementation approach with a high rate of gas leakage and delusions of O_2, limiting its efficacy (6).

Respiratory disorders require external support to provide O_2 and excrete CO_2 effectively. Additionally, a device that allows comfort, long-term tolerability, and oral nutrition while providing effective oxygenation and reducing the breathing work. This need has enabled experts to find a device named HFNC (7). HFNC therapy is an O_2 supplementation that can deliver O_2 warmed and humidified up to 100% with a flow rate of up to 60 liters/minute (7). The flow control ability of FiO_2 is greater than that of LFNC (5,6)

High flow nasal cannula structure and settings

The high flow O_2 therapy requires a specially designed cannula that is warmed and moisturized, resulting in a stable flow rate (8). HFNC fulfills inspiration needs by providing an air-O_2 mixture warmed to 37 °C with a relative humidity of 100% and can deliver 21-100% FiO_2 with a flow rate of up to 60-70 liters/minute (9). The flow rate and FiO_2 can be titrated independently based on patient needs (9).

HFNC has three essential components (7). First, an airflow generator produces flow rates of up to 60-70 liters/minute. Second, the O_2-air blender increases the control of FiO_2 regulation from 21 to 100%. Third, the humidifier sets an absolute humidity of 44 mmH_2O/liter and a heater sets the temperature between 35-37 °C (Figure 1). Also, the system includes a non-condensing water reservoir, a circuit system, and a special nasal cannula. The adult-sized cannula is 7.2 mm (8,10).

There are two main settings in HFNC, flow rates, and FiO_2. Flow rates can be set between 30 and 70 liters/minute (7). HFNC can provide air-O_2 mixtures with FiO_2 from 21% to almost 100% (7). Renda et al. (11), recommend the following practical settings for HFNC in Table 1.

Physiological effects of high flow nasal cannula

HFNC has several advantages over conventional O_2 treatments (12). O_2 therapy with HFNC has five physiological mechanisms that make the efficacy of HFNC better than other O_2 therapy supports, including;

1. CO_2 washout in the physiological death space,
2. Lowering the respiratory rate,
3. There is a positive final expiratory pressure (PEEP),
4. Increase tidal volume,
5. Increase the final expiratory lung volume (EELV) (8).

Anatomical dead space accounts for about one-third of the tidal volume of the breath (2). When ventilation is ineffective, there is CO_2 accumulation and retention in the anatomical dead space during inspiration. So that this condition can decrease O_2 diffusion in the alveoli (2).

High FiO_2 in HFNC increases the volume of gas in the alveoli more than the patient's volume ventilated physiologically (10). Increased ventilation allows washout or elimination of CO_2 with excess O_2 and can also increase mucus clearance in the airways (8). This results in creating a more significant O_2 diffusion gradient, potentially increasing oxygenation (8). HFNC could eliminate the residual volume of CO_2 in the upper airway and replace it with O_2-rich gas quickly and effectively (13).

HFNC reduces airway resistance in the nasopharynx and improves ventilation and oxygenation through positive pressure (7). Physiologically, the nasopharynx is a dynamic area that allows expansion or constriction of the airway. HFNC creates a positive pressure area, pressing the interior of the nasopharynx outward, thus causing dilation of the nasopharyngeal diameter and reducing airway resistance (7). Reduced airway resistance increases the potential for ventilation and oxygenation.

Additionally, HFNC creates positive alveolar pressure at the end of expiration to reduce the respiratory rate and the distribution of alveolar ventilation to be homogeneous throughout the lung region and improve tidal volume (11).

HFNC can also increase EELV (14). An increase in EELV indicates a positive alveolar PEEP. As a result, the PEEP in the lower airway increases (14). Positive pressure causes an increase in the alveolar surface area, so it does not collapse because of the increased pressure on the surface during expiration (14). Therefore, the ventilation process is improved and gas diffusion becomes more effective, resulting in better oxygenation. However, one thing that must be considered when using HFNC is that mouth must be closed to get optimal PEEP (15). The estimated amount of PEEP produced with the mouth closed at 1 cm H_2O at a 10 liters flow (15,16). It is a difficult challenge for patients to cover their mouths when experiencing respiratory distress (15).

The high flow nasal cannula mechanism in the treatment of respiratory distress

Administration of O_2 therapy with HFNC has a favorable mechanism for overcoming respiratory distress with hypoxemia (17);

1. High FiO_2 gas flow encourages the release of CO_2 gas in the anatomical dead space,

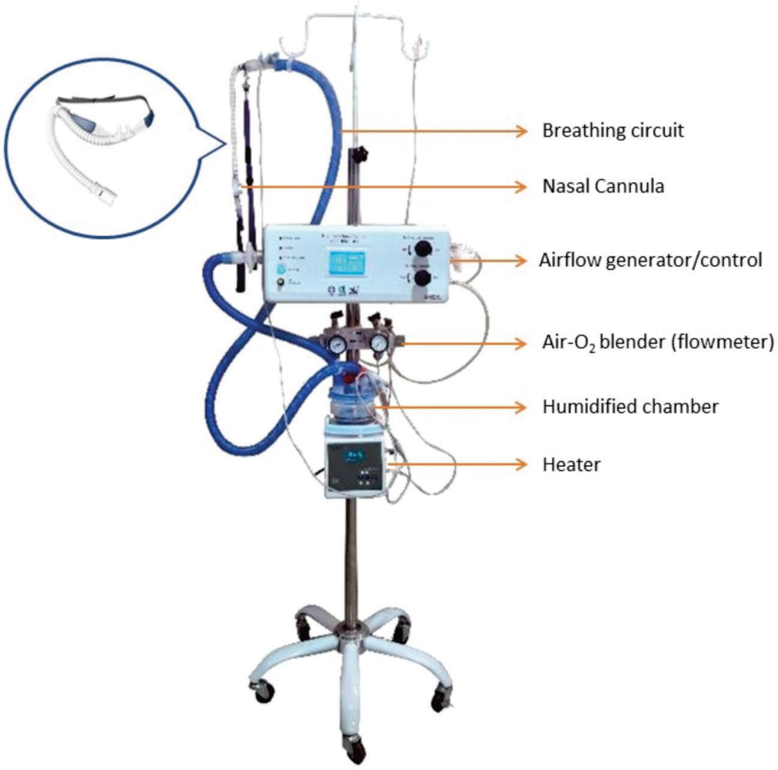

Figure 1. High flow nasal cannula components

Table 1. Recommended HFNC settings (11)

Prongs	Prongs should not totally occlude nostrils
Flow rate	Start at 30-40 liters min-1 and increase to meet the patient's demand
Temperature	Set at 37 °C
FiO_2	Increase the FiO_2 until satisfactory SaO_2 is achieved
Flow	Increase the delivered flow until a reduction in respiratory rate and stable SaO_2 are achieved
Water reservoir	Place as high as possible above the humidifier
Monitoring	Continuous monitoring of heart rate, respiratory rate, SaO_2
Positive response and weaning	Gas flow rate and FiO_2 adjusted according to the clinical response (expected within 1 h). Reduce FiO_2 by 5-10% and reassess after 1-2 h. Reduce the flow rate by 5 liters min-1 and reassess after 1-2 h. Consider weaning from HFNC with flow rates of 25 liters min-1 and FiO_2 <0.40.
Ineffective response	If there is no improvement after 60-120 min, treatment escalation must be considered.

HFNC: High flow nasal cannula, FiO_2: Inspired oxygen fraction

2. The high flow of FiO_2 gas in the alveolar increases lung volume,

3. Gas flow warmed to 37 °C and humidified by 100% can maintain mucociliary function for a good cleaning function,

4. The use of HFNC can reduce the airway resistance,

5. HFNC, in general, increases patient comfort compared to conventional O_2 or non-invasive positive pressure ventilation.

Clinical applications and indications for O_2 therapy with HFNC

The following are some clinical conditions and indications for the use O_2 therapy with HFNC (7,10);

1. Acute hypoxemic respiratory failure,
2. Hypercapnic respiratory failure (e.g., chronic obstructive pulmonary disease),
3. Impaired respiration due to acute heart failure/pulmonary edema,
4. Impaired respiration due to immune disorders,
5. Impaired pre-intubation and post-extubation respiration,
6. ARDS in COVID-19,
7. Patients who cannot be intubated,
8. Reducing suffering in patients at the end of life.

HFNC can be used effectively in moderate hypoxemic acute respiratory failure. Hypoxemic acute respiratory failure results from intrapulmonary shunt due to collapsed alveoli (7). It is refractory to O_2 supplementation (18). Increased alveolar-capillary hydrostatic pressure and permeability cause the alveoli to fill with blood due to bleeding and/or fluid in inflammatory conditions such as pneumonia (18).

O_2 therapy is essential, but it has maximum-positive benefits and potentially toxic effects. Increased levels of hyperoxia-induced reactive O_2 species (ROS) have an impact on the surrounding biological tissues. Increased levels of ROS cause hyperpermeability, coagulopathy, and collagen deposition within the alveolar space (19). In hyperoxia, multiple signaling pathways determine the pulmonary cellular response, including apoptosis, necrosis, and repair (19). Therefore, it is crucial to prevent alveolar damage caused by hyperoxia in patients requiring HFNC (19).

Contraindications to using O_2 therapy with HFNC

Contraindications to O_2 therapy with HFNC are divided into absolute and relative contraindications (2,10);

A. Absolute contraindications

1. Decrease in consciousness,
2. Cardiac arrest,
3. Respiratory arrest,
4. Conditions requiring emergency actions.

B. Relative contraindications

1. Cardiogenic shock,
2. Gastrointestinal bleeding,
3. Status epilepticus,
4. Airway obstruction (e.g., a large tumor pressing the airway),
5. Anaphylaxis that causes airway disorders.

Evaluation of therapy with HFNC

HFNC requires periodic evaluations to determine whether the patient is experiencing improvement or worsening. If HFNC is not closely monitored, it can result in delayed intubation. The criteria of HFNC evaluation (20):

1. PaO_2 <60 mmHg and O_2 saturation <90%, with an HFNC flow rate of 30 liters/minute and FiO_2 of 1.0,
2. Respiratory acidosis with a pH <7.25 and pCO_2> 50 mmHg,
3. Respiratory rate >30 times/minute (tachypnea) or unable to produce phlegm,
4. Increased thoraco-abdominal breathing occurring 15-30 minutes after the start of HFNC.

If there are two of the four criteria above, the respiratory condition is expected to worsen (20). The doctor must immediately switch HFNC to intubation with mechanical ventilation.

Respiratory rate and oxygenation (ROX) index

The ROX index, defined as the ratio of SpO_2/FIO_2 to respiratory rate is used to assess as a predictor of the need to intubate in patients who received HFNC O_2 therapy (21,22). ROX index can assess the success of using HFNC in COVID-19 patients with ARDS. The ROX index is used, with the following formula (23);

$$\text{ROX Index} = \frac{(SpO_2 / FiO_2)}{(\text{Respiration Rate})}$$

HFNC therapy is started at O_2 30-40 liters/minute, which can be increased according to the patient's need (4). The flow of O_2 increases until the inhalation rate decreases and a stable SaO_2 reach. In acute respiratory failure, up to 100% FiO_2 can be administered (21,22). The flow rate and FiO_2 can be adjusted according to the patient's clinical response (4).

After 1 h of HFNC, an evaluation should be performed if the patient shows clinical improvement and meets good ventilation criteria (24). Ventilation is accepted sufficient if the ROX index is ≥4.88 at 2, 6, and 12 h (25,26). This indicates that the patient does not need invasive ventilation. However, ROX index <3.85 indicates a failure to use HFNC and the patient is considered at high risk of immediate intubation (25,26). If the ROX index is between 3.85 and <4.88, scoring must be repeated every 1 to 2 h (Figure 2) (4,25,26).

Weaning off HFNC therapy

Weaning off HFNC can be started when the patient's condition is improved. Weaning is started by lowering the FiO_2 by 5-10% and re-evaluating it every 1-2 hours (11). If FiO_2 <0.4, the flow rate can be reduced by 5 liters/minute. HFNC can be removed when the flow rate reaches ≤25 liters/minute and FiO_2 <0.4 (11).

HFNC therapy in COVID-19

COVID-19 in critical condition with ARDS requires treatment in the intensive care unit (ICU). There are two types of respiratory failure; hypoxemic respiratory failure (type 1) and hypercapnic respiratory failure (type 2) (27). Type 1 respiratory failure occurs if the partial arterial O_2 pressure (PaO_2) is ≤60 mmHg in room air, and type 2 respiratory failure occurs when the partial arterial CO_2 pressure ($PaCO_2$) is ≥50 mmHg. COVID-19 cases with respiratory failure using a ventilator have a mortality of up to 80% (2,25).

COVID-19 with ARDS or respiratory failure requires supportive O_2 therapy. In this modern era, the choice of non-invasive O_2 support is the modality of choice using HFNC (17). O_2 support with HFNC can be administered to treat mild to moderate ARDS. The management of COVID-19 focuses on efforts to prevent the disease from worsening. Therefore, treatment management needs to be planned immediately to optimize the outcome of therapy. There are three essential steps in preventing disease worsening (2,25);

1. HFNC is preferred over non-invasive mechanical ventilation (NIV) in patients with ARDS,

2. Restricted fluid resuscitation, especially in patients with pulmonary edema,

3. Positioning the conscious patient in the prone position,

The European Respiratory Society provides recommendations for the use of HFNC in COVID-19 patients as follows (25,27):

1. In adults with COVID-19 and acute hypoxemic respiratory failure, HFNC is superior to conventional O_2 therapy (weak recommendation, low-quality evidence).

2. In adults with COVID-19 and acute hypoxemic respiratory failure, HFNC is superior to NIPPV (weak recommendation, low-quality evidence).

3. In adults with COVID-19 who receive NIPPV or HFNC, close monitoring of worsening respiratory status to make the decision of early intubation (best practice statement).

Combination of the prone and HFNC positions in COVID-19

A study by Xu et al. (28) reported COVID-19 patient with a P/F ratio ≤300 who was in the prone position early for more than 16 hours and combined with HFNC therapy have no worsening or received invasive ventilation and survived completely. This study also showed that HFNC could reduce the rate of endotracheal intubation in patients with respiratory failure. Additionally, the prone position can correct the ventilation-perfusion mismatch and open the airway, reducing pulmonary atelectasis with adequate sputum drainage (28).

The prone position combined with HFNC requires a patient with good mental status, communication, and stable hemodynamics (Figure 3). The patient should be briefed on the prone position maneuvers and ensure adequate HFNC placement. The vital and clinical signs are monitored during the prone position (28,29).

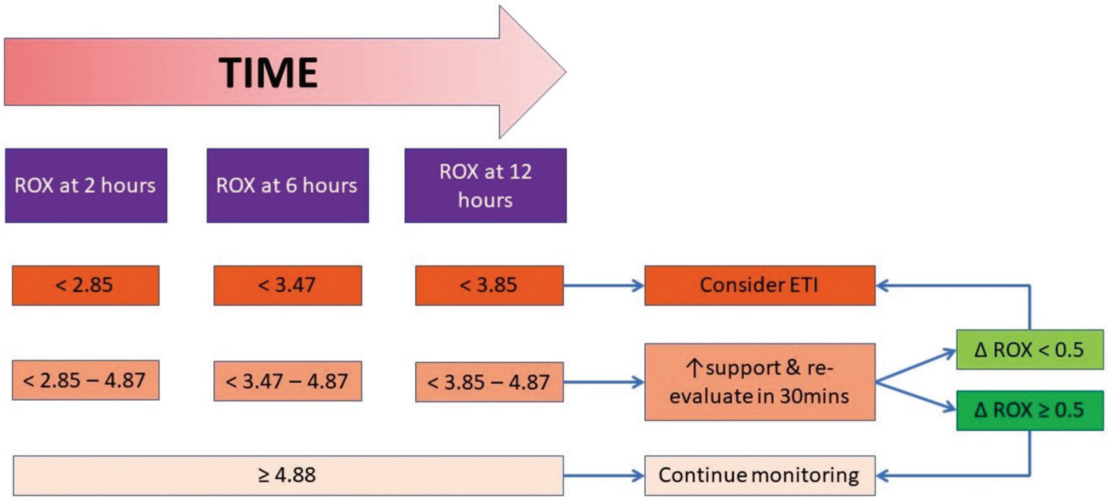

Figure 2. Evaluation of HFNC with the ROX index

HFNC: High flow nasal cannula, ROX: Respiratory rate and oxygenation

Advantages and limitations of HFNC in COVID-19 patients

The advantages of HFNC include ease of setup and use, such as the use of nasal prongs for patients. The low risk of skin irritation because of high O_2 flow makes the mucosa dry, but HFNC can keep nasal mucosa humidity. Patients can still eat, drink and communicate without removing the HFNC, facilitating the performance of medical personnel, and reducing the time spent on nasal tightness. Additionally, it is more stable and does not remove the equipment that triggers aerosols (30,31).

Like many other medical interventions, there are limitations and drawbacks to HFNC. One of the main drawbacks is the higher maintenance cost, the complexity of the HFNC device, training requirement, risk of gas leakage, and loss of positive pressure effects on the improper airway seal (7,10). Another limitation is the potential for delaying intubation and end-of-life decisions in patients with decreased consciousness, facial injuries, excessive secretions increasing the risk of aspiration, and hemodynamic instability (7,10). Additionally, the disadvantages of HFNC include that the sound of a loud instrument makes noise, patient's activities become limited, and complaints of altered smell in rare cases (20).

Aerosol effects and safety of HFNC

HFNC might increase some concerns about the risk of virus transmission. A study by Whittle et al. (32), is measuring the spread of aerosols on various breathing devices. Aerosol dispersion distances for nasal cannula range 3-40 cm, simple mask at all flows ≈ 30 cm, ventury mask range 33-40 cm, NRM at all flows <10 cm, HFNC ranges 4.8-17 cm, NIPPV ranges 85-95 cm, and nebulizers <80 cm (32). However, recent practice recommendations for COVID-19 patients indicate using a medical mask over the HFNC device to limit the particle dispersion due to exhaled gas flow (33). Whittle et al. (32) recommended that the use of HFNC in COVID-19 should be applied cautiously and that adequate personal protective equipment (PPE) and protective measures for healthcare workers should be provided. The Australian and New Zealand Intensive Care Society (ANZICS) guidelines on COVID-19 state that HFNC therapy in the ICU is the recommended therapy for hypoxia associated with COVID-19, as long as the staff wears PPE (34). The risk of airborne transmission to healthcare workers is low with optimal use of PPE and good infection control precautions (34). The use of a negative pressure room is recommended for patients receiving HFNC therapy (34,35).

Conclusion

HFNC has many advantages in COVID-19 patients. It gives warm and moisturize O_2 to increase the patient's comfort. It also reduces the need for inspiration, increases the functional residual capacity, reduces the dilution of O_2-air, and can wash out CO_2 in the anatomical dead space. An initial assessment

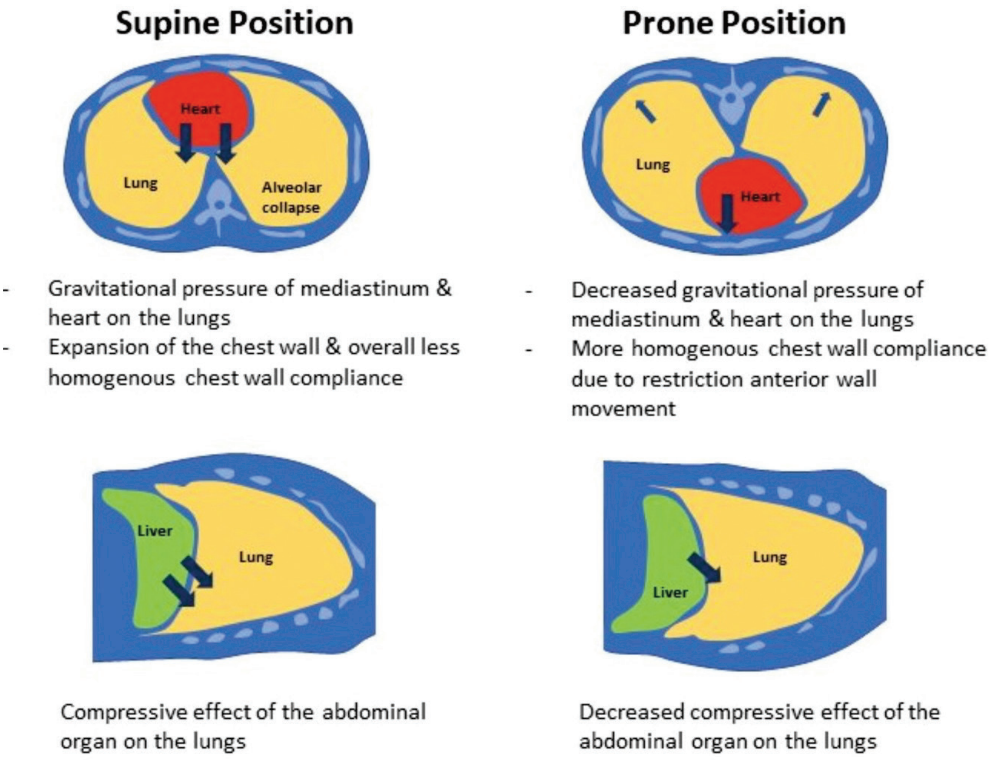

Figure 3. Comparison of the physiological effects of the supine and prone positions

is critical for the success of HFNC therapy. The ROX index can be used to predict the success or failure of HFNC therapy. Supportive O_2 therapy with HFNC is among the modalities for COVID-19 patients, having advantages over other conventional O_2 therapies. However, further studies are necessary to evaluate the benefit of HFNC in hypoxemia management. HFNC can be used in the ICU, operating room, emergency room, and ordinary wards. However, the use of HFNC in COVID-19 patients is recommended in rooms with negative pressure to minimize the risk of aerosol transmission.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.P.D., E.M., Concept: K.P.D., I.I., M.A., Design: K.P.D., E.M., Data Collection or Processing: K.P.D., Literature Search: K.P.D., I.P.D., Writing: K.P.D., I.P.D.

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