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Review Article

Emerging Perspectives of Endotracheal Intubation in Patients with Severe COVID- 19 Pneumonia: A Narrative Review

Dheeraj Kapoor*, Pradeep Atter, Amanat Kang, Manpreet Singh

Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Chandigarh, India.

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ABSTRACT

The coronavirus disease 2019 (COVID -19) pandemic that has engulfed the world has put an immense strain on the existing healthcare systems. The rapid, insidious and often dramatic deterioration of the respiratory function of an infected patient, has led to an increased need for effective and rapid airway control. However, such airway control techniques put the healthcare workers to an increased risk of exposure to the virus. Therefore, interventions aimed at minimising such risks, while preventing the complications inherent to securing an airway are imperative to the management of a COVID-19 patient in acute respiratory failure (ARF). Personal protective equipment (PPE) is sine qua non to keep the intubator safe, however some barrier equipment's have been employed with limited success. There are varied schools of thought on whether to intubate early or late, and the use of non-invasive methods for management of respiratory failure, however, most consensus statements reinforce the need for rapid sequence induction (RSI), which provides ideal intubating environment for an experienced intubator. Techniques, which decrease the number of required personnel as well as time, to secure the airway and increase the distance of the intubating physician from the patient, are recommended. Routine use of, videolaryngoscope, if available, is recommended. While intubation with an endotracheal tube is the gold standard airway technique, second generation supraglottic airway devices (SAD) are increasingly being recommended, particularly in cases of failure to intubate or in an unanticipated difficult airway. Awake intubation techniques are contraindicated due to increased risk of cough and subsequent aerosolization; however, few modifications were innovated when if it all required. In this review, we summarise the existing data with respect to the modifications and guidelines in severe COVID-19 patients who requires endotracheal intubation for invasive mechanical ventilatory support.

The term Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) commonly known as coronavirus disease 2019 (COVID-19) pandemic presents unprecedented challenges in management and containment of spread [1]. Human to human transmission is the chief mode of the virus dissemination with the highest viral load being present in the upper airway tract and its secretions [2]. It has anthropological transmission via droplets or aerosol route predominantly, however, direct transfer via fomites and self-inoculation are also postulated [1,3]. Depending on the disease severity, COVID-19 associated acute respiratory distress syndrome (CARDS) is seen in about 14-17% of infected patients [4]. The symptom onset occurs over a span of seven days but the progression to ARDS after development of

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: kapoor.dheeraj72@gmail.com

respiratory distress occurs dramatically with an average span of mere 2.5 days [5]. About 15% of in-hospital patients were observed to require endotracheal intubation followed by mechanical ventilation [5]. There are definite lacunae regarding airway management of novel COVID-19 disease, which in addition to the usual challenges of airway management carries additional risk of exposure to the clinician. The review highlights the emerging perspectives in airway management of COVID-19 patients, with specific focus on endotracheal intubation (ETI) management, which is incorporated in the antecedent clinical practice.

1.1 Factors Determining Endotracheal Intubation and Invasive Mechanical Ventilation.

The primary factors associated with the requirement of ETI in COVID-19 patients were severe shortness of breath, low oxygen saturation (> 90% on room air), and high respiratory rate (>30/min). Increased risk of intubation is prevalent in patients with higher body mass index (BMI). [6] This can be linked with the deprecation of pulmonary function superimposed with inflammatory cytokine release leading to deleterious consequences in terms of disease progression and severity. Obesity, hypertension, chronic obstructive pulmonary disease (COPD), cardiovascular diseases and type-2 diabetes mellitus were associated with elevated risk for intubation. Diabetes mellitus confers independent risk for intubation as metabolic disorders impair function of macrophages and lymphocytes, which are pertinent to the body's immune response [6]. Elderly patients have depleted angiotensin-converting (ACE-2) stores. ACE-2 is an important anti-inflammatory substance, the reduction of which causes the setting in of pro-inflammatory cytokines easily and their sequelae are severe [6]. ACE-2 receptors are the purported binding site for the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus. These are present on respiratory epithelium and pneumocytes, hence tracheal smooth muscle relaxation is hampered and airway becomes hypersensitive [7]. In addition, they are also present in the Leydig cells of male testis. Therefore, these Leydig cells may function as a potential site of viral harbour, hence, underlining the presence of male preponderance seen amid the patient population [6].

1.2 Risks to health care workers (HCW) managing airway.

The healthcare workers managing airway of COVID-19 are at immense risk as the highest viral load is present in upper airway secretions. Airway management is a time sensitive task and is vulnerable to aerosol transmission and the same may be accentuated by aerosol generating events (AGE) like coughing or suctioning [8, 4]. Furthermore, the patients may be agitated; hence, safety in terms of barrier protection and maintaining safe distance may be compromised. The group at the maximum risk comprises intubation providers, respiratory therapists and bedside nurses [9]. Therefore, it is imperative that the strategies put forth to manage the airway offer adequate protection and at the same time do not cause kinaesthetic limitations that increase the time required to secure an airway.

1.3 Indications for endotracheal intubation.

Meng et al with there initial experience in Wuhan, developed an algorithmic approach for ETI in hypoxemic patients or patients who were at risk of developing respiratory failure [10]. High-risk symptoms clubbed with respiratory parameters (respiratory rate more than 30/min, oxygen saturation less than 93% on room air and PaO2/FiO2 ratio less than 300) were kept under evaluation and high flow oxygen therapy was administered for few hours and if the condition worsened or no objective benefits were seen, then a decision for intubation was made. In addition to impending respiratory failure, intubation is considered for patients who cannot maintain their airway or who underwent cardiac arrest and cardiopulmonary resuscitation [10].

1.4 Phenotype variations: H and L form.

In patients with COVID-19, it was observed and documented by various authors that a high respiratory drive is present along with high compliance [11]. This is supported by the formation of phenotypically categorized patient subset where L- form has good lung volume and compliance but low recruitable alveoli in lungs and H-form are the ones who have progressed to an ARDS like condition and have low volume and compliance and highly recruitable alveoli based on differential atelectasis. Also, interstitial oedema occurs which increases the lung weight superimposed with large transpulmonary pressure flux, may lead to lung injury [12-13]. The high compliance and drive help the patients to draw in more tidal volumes by increasing the negative intrathoracic pressure. The physiological response to hypoxemia is dampened by increased minute ventilation causing reduction in PaCO2; hence the threshold to increase motor output to involve accessory muscles is not reached. Therefore, an apparent well looking appearance stands in stark opposition to the picture in clinical investigations and radiograph pointing towards the presence of hypoxemia. This helped in formulation of the notion of silent or 'happy hypoxemia' in COVID-19 patients, where delaying intubation causes accumulation of oxygen debt in the face of feigned wellness [12].

1.5 Controversies: early versus late intubation!

Zealous arguments have been made as far as early intubation in COVID-19 patients is concerned. One school of thought advocates while another fervently abolishes the concept citing risk of increased mortality in patients who were intubated early. Gattinoni et al came forward with the concept of patient self-inflicted lung injury (P-SILI). It was postulated that the high variation in transpulmonary pressure across the lung units due to high drive present in the patients causes lung injury similar to the injury that occurs in mechanically ventilated patients and to pre-empt this lung injury advised early intubation [11]. Moving further, emergency procedures are associated with higher risk of transmission due to less preparation and less safety measures that can be put in place [4].

Zhang et al also observed that intubating patients early, especially the ones who had impending respiratory failure or had poor prognosis, might help in providing better outcomes by reducing oxygen debt [14]. Meng et al also recommended early intubation in patients with increased oxygen debt hence, increased oxygen requirements and elevated work of breathing, where PaO2/FiO2 is declining or where noninvasive ventilation (NIV) or high-flow nasal oxygen (HFNO) therapy is considered [10]. Tobin et al, however, refuted the doctrine of early intubation based on the facts that P-SILI has not been established enough to be considered as a strong cause for intubation [15]. Also, high mortality rates were associated with early intubation across various hospitals and NIV and other conservative oxygen therapies were advised early on in the disease to delay intubation [15]. Here it can be argued that intubation might not be the sole risk factor for the high mortality as patients who require intubation are already in the penumbra of deteriorated haemodynamics and there will be other confounding factors at play for the increased risk of mortality.

Intubation also comes with inherent risks such as hemodynamic compromise due to hypotension caused by sympatholysis during induction or sudden desaturation because of hypoxemia [5]. It was also seen that if intubation was delayed and administered as a rescue measure then it resulted in higher early mortality [9]. However, logistical problems plague care for COVID-19 patients, causing unprecedented strain on the healthcare systems particularly in developing nations, resulting in unfavourable nurse: patient ratios and disproportionate number of ICU beds, making early intubation a gamble with unfavourable odds.

1.6 Preparation for endotracheal intubation

Numerous guidelines and recommendations have come up since the emergence of the epidemic, all however, underline the importance of being prepared and keeping all the airway management paraphernalia ready before entering the room with COVID-19 patients. Safe airway society (SAS) advocates a '6P' regime including planning, preparation, personal protective equipment (PPE), pre-oxygenation, performing the procedure and post- endotracheal intubation considerations [4]. It also advises to put in place an airway response team that should comprise the least functional number of people possible and should be cognizant about their individual roles so as to keep the duration of exposure minimum [4]. There should be no person apart from the chief airway manager, assistant and runner, who should be within six feet of the patient. Runners can relay equipment or drugs as per need of the airway manager. Airway manager should have an established hierarchy to perform the procedure including a backup assistant for difficult airway or front of neck access rescue [9]. Any invasive lines like central lines or nasogastric tube may be placed at the time of endotracheal intubation, to prevent viral exposure [16].

The airway response team should conduct rounds on suspects or confirmed patients to keep a watch on the clinical course of the patients, in order to prevent unpreparedness, if need for intubation arises. The members should be trained for handling difficult airways and it is prudent that the most experienced clinician should intubate. It is important to clearly inform the team of the patient's COVID-19 status to ascertain safety. The consultation should include the medical history and clinical investigations as well as the treatment received in the hospital thus far [9].

Meng et al proposed an acronym; 'OH MS MAID', so that the clinicians are mindful of adequate safety measures to be taken before airway management of COVID-19 patients. It stands for oxygen, helper, monitor, suction, machine, airway supplies, intravenous access and drugs, all of which should be checked and ready before undertaking the procedure of intubation per se [10].

To be prepared in advance, an intubation bag and code box can be prepared. The intubation bag may contain all the necessary equipment's for intubation and code box with resuscitation medications during intubation [5]. A Boston-based hospital also made 'COVID-19 bags' with inclusion of two PPE kits [17]. The inside bag contains all necessary equipment for intubation, outside bag contains backup and difficult airway equipment and vent back contains all the equipment necessary for fixation and confirmation of endotracheal tube placement [17].

1.7 Protective equipment during intubation

New equipment has been designed which can be implemented as a safety measure. Inadequate access to standard personal protective equipment (PPE) has occurred during this pandemic and clinicians have been compelled to improvise protective barrier enclosures for use during endotracheal intubation. On the same lines, a protective device, known as 'aerosol box' was made, which prevents dispersion of aerosols during intubation procedure. It is a transparent box, which incorporates two circular side portholes and covers the head of the patient [18]. Canelli et al advocate that this ad hoc barrier provides a modicum of protection against a simulated forceful cough and can be considered only as an adjunct to a standard PPE [18]. It however, comes with certain drawbacks, which include hindrance in movements during manipulation of the airway and prolongation of intubation times [19]. Also, redirection of droplets towards the foot end of the bed can occur. Introduction of new contaminated equipment that requires safe disinfection before reuse may become cumbersome and the PPE can be breached from putting the hands inside from the side portholes and hence warrants for some modifications in aerosol boxes [19]. Additional holes can be provided for passing of accessory airway equipment as well as for the assistant. The shape of the side portholes can be change from circular to elliptical allowing more space for manipulation [20]. Transparent plastic sheets that can be clipped to poles or placed over a stand, with an a high volume suction to remove aerosols, offers versatility and flexibility and therefore increasing manoeuvrability, visualization, and access while also protecting staff [21]. In France, neonatal ICU incubators were refurbished into aerosol boxes with more space and additional holes for passing accessory airway equipment and help assistant in manoeuvres such as Sellick's in rapid sequence induction (RSI) [22]. Anti-aerosol 'Igloo' was introduced, which sits over the head of the patient as a hood and allows for more space of manipulation and does away with the seams of the aerosol box where the virus may be trapped. It is lighter, more ergonomic and cost efficient than aerosol boxes [23]. In addition, to the aforementioned adaptations, a protection sleeve can also be used which is closely juxtaposed to the patient's face and has space for passing the laryngoscope, mask and the endotracheal tube [24].

1.8 Checklists for Endotracheal Intubation

Checklists for airway management have been proposed in various consensus guidelines, which can be placed in the setting where emergency endotracheal intubation may be undertaken so that the clinicians are aware of the adequate preparation required before undertaking the airway management of COVID-19 patients. [4, 25-26] Further, a modified integrated checklist in obstetric patient population was also proposed on the same line as in other COVID-19 adults patients [25].

1.9 Stepwise Approach for endotracheal intubation

We summarise the following stepwise approach followed for ETI with an acronym 'POLICE', so that the carer remain aware of the essential precautions and subsequent actions chronologically taken in COVID-19 patients.

1.9.1 Position

The intubating position should be 45° head up or ramped position, as it allows more efficient preoxygenation and ventilation especially in high-risk groups, allowing more safe apnoea time. It also reduces the airway pressure if facemask ventilation is required. On the flip side, this inclined position does have certain shortcomings, such as more technical skills requirement for intubation with created slope and adjustment and further secure placement of aerosol box over the head [7,25].

1.9.2 Preoxygenation

While proficient pre-oxygenation in COVID-19 patients is important, an emphasis has been laid on appropriate equipment selection of tight fitted masks along-with ambient pressure oxygenation or closed systems, if positive pressure ventilation (PPV) is indicated, to prevent viral transmission [27-28] Despite this, non-rebreather mask has been routinely used and might be the only feasible option in clinical setting, however it is one of the worst offending methods with maximum aerosol generation [29]. Preoxygenation may also alternatively be accomplished with a bag valve mask (BVM) and viral exhalation filter assembly. The airway operator should ensure a tight BVM seal using a two handed "V-E" or vice grip, while applying 10–15 cm of PEEP for prevention of de-recruitment and hypoxia [4, 7]. A closed circuit, like Waters' circuit can be used to minimise the virus leak. End tidal oxygen monitoring to obtain maximum preoxygenation should be used [7,25]. Apnoeic oxygenation can be done using low flow nasal oxygen in case of suspected hypoxia [30]. Awake fiberoptic intubation should be avoided wherever possible to minimise aerosol generation [7,25].

1.9.3 Induction

Rapid sequence induction (RSI) is the universally recommended dictum and can be achieved by using rocuronium or succinylcholine as muscle relaxants. Rocuronium, confers a longer muscular blockade hence coughing can be delayed whilst undertaking the intubation. Succinylcholine (1mg/kg) can be used if not contraindicated and gives the safety of quick return of spontaneous ventilation in case of difficult airway. [7,25] The application of cricoid pressure is contested and should be reserved for cases where aspiration is anticipated as it may occlude the glottis view and hinder efficient ventilation and first-pass intubation success [30]. Full neuromuscular blockade is advocated as it optimises the conditions for intubation. The laryngeal reflexes are abolished reducing the incidence of coughing or bucking [7]. Intravenous lidocaine can be used in lieu of opioids, which may precipitate coughing. However, it should not be used in patients who are at risk or have haemodynamic instability [9].

Induction agents are not devoid of side effects especially thiopental and propofol which cause hypotension and can be minimized by using a crystalloid bolus, reducing the induction agent dose or concomitant use of vasopressors. Midazolam has a slow onset of action and etomidate is associated with suboptimal intubating conditions than propofol and may lead to adrenocortical suppression. Ketamine can be used in patients with an increased risk of cardiovascular instability. If more than one attempt is taken, then repeat boluses of the inducing drug can be given to avoid emergence [7].

1.9.4 Laryngoscopy

Video laryngoscopy has seen a near universal acceptance as a more preferred method of laryngoscopy in COVID-19 patients, as it is safer in terms of decreasing the time to intubation and increasing the success rate of first attempt of intubation as well as increasing the distance between the clinician and the patient's airway provides more safety. Further, it can be done while the patient's head is in a neutral position and does not require sniffing position. However, airflows should be compulsorily switched off during laryngoscopy [31]. A channel videolaryngoscope can be used, with a pre-assembled endotracheal tube avoiding the requirement of stylet, as reverse outflow during the removal may cause aerosol spread. Arulkumaran et al have documented benefits of using video laryngoscopy instead of direct laryngoscopy not only in terms of expediting the process of successful intubation but also reducing the risk of oesophageal intubation and airway trauma and causing hypotension [32].

Heat moisture exchanger (HME) filter followed by the circuit is connected, as soon as trachea is intubated, making a closed loop, therefore restricting the virus leak [33]. If required, in-line tracheal suction can be done, and open suction is to be avoided altogether. Also, if disconnecting the circuit is unavoidable, cautious clamping of the endotracheal tube should be in deep anaesthesia, so that coughing can be avoided [34].

1.9.5 Confirmation of endotracheal tube placement

Ascertaining endotracheal tube placement can be undertaken using end tidal carbon dioxide (ETCO2) monitoring. Oxygen saturation of these patients is not a reliable indicator because of the limited oxygen reserve and bilateral chest rise should be used instead of auscultation, as it is difficult to use stethoscope with PPE wears [2,35]. Post-intubation considerations include safe disposal of the equipment and PPE after securing the airway. If repeat instrumentation is to be done, it is prudent to limit consumption, hence, reusable equipment are preferred. Adequate sedation must be ensured to limit the ventilator patient asynchrony and haemodynamic instability [9]. As soon as the airway is secured a HME or High Efficiency Particulate Air (HEPA) filter should be placed before connecting the circuit, and cuff should be inflated, in the minimum time possible, to at least 20-30 cm water pressure and if high airway pressures are anticipated then a surplus of 5 cm water pressure more than the peak inspiratory pressure should be used [7]. A close suction device along with an endotracheal tube with subglottic suction is recommended [7].

1.9.6 Extubation of endotracheal tube

As airway management in these patients is associated with higher risk of virus aerosolization, hence opioids, lidocaine or dexmedetomidine is considered to reduce coughing and permit smooth emergence. The patients are not to be extubated on room air and always should be covered with a facemask immediately after removal of the airway [4]. In addition, covering the patient with a plastic sheet and a post extubation oxygen support should be in place and the airway team should be well versed with it. Metered dose inhaler (MDI) can be used instead of nebulisation and tube exchangers can also be considered [9]. Direct transfer without bypassing the post anaesthesia care unit (PACU) stay is encouraged. The Pediatric difficult intubation collaborative (PEDI-C) recommends, placing a suction device under the drape or a plastic sheet to scavenge the aerosols [36].

Endersby et al gave a modified tracheal extubation acronym, 'SNAP' algorithm, which helps in remembering the extubation plan for COVID-19 patients. It includes; attaching a new sampling line to the filter followed by connecting the new assembly to the circuit then trachea is extubated, followed by placement of the facemask with the new assembly and a transient uplifting of the facemask to pull up the surgical mask onto the nose and mouth and then re-application of the oxygen facemask [37].

1.10 Difficult intubation

Difficult or failed intubation is more frequently encountered in COVID-19 patients owing to the presence of inflamed or ulcerated epiglottis or subglottic oedema. Hence, more extensive 'MACOCHA' scoring system is encouraged to evaluate the presence of difficult airways [25]. Second-generation supraglottic airway (SGA) devices may be used as a rescue ventilation device after failed intubation in this subset of patients [25]. Their use is associated with quicker placement, safer distance than direct laryngoscopy, less precipitation of coughing hence, lesser aerosolization and also better oxygenation at emergence while allowing the inserter to maintain an even further distance from the patient. They can also be placed in the interim time between induction and placement of an endotracheal tube especially with difficult airways and to lower the risk of aerosolization. However, to limit or avoid aerosol spread with SGA devices, certain modifications were proposed. Yang et al introduced a device called 'Taipei Azalea', which is a modification of I-gel SGA preassembled with the HME filter and has plastic sheet affixed to it to cover the face of the patient while undertaking insertion as well as removal of the SGA [38]. Chua et al proposed closed SGA guided flexible bronchoscopic intubation to minimize aerosol spread [39].

In the event of complete failure of ventilation, it is recommended that a surgical cricothyroidotomy maybe done [7]. The PEDI-C suggests that in paediatric patients, after video laryngoscopy, the preferred method of securing the airway is fiberoptic intubation through SGA. Following that, free hand fiberoptic bronchoscopy can be done if required. Oral rather than nasal fiberoptic bronchoscopy can be done and an endoscopy mask is in situ while using the nasal bronchoscope [36].

In a 'cannot intubate, cannot oxygenate' (CICO) scenario, front of neck access (FONA) is taken, once all attempts at securing the airway are exhausted. As FONA is an aerosol generating procedure, since cannula cricothyroidotomy requires jet ventilation and tracheostomy may require suctioning, hence, 'scalpel-bougie' technique is recommended [7,25]. Complete neuromuscular blockade with 100% oxygen without application of positive pressure is advocated to optimize the condition for the procedure and in addition, prevents laryngospasm and subsequent aerosolization [7,25].

Conclusion

Airway management of severe COVID-19 patients pose a remarkable challenge to the airway managers, owing to the highly infectious spread of disease through aerosols and droplet route. Recently, several guidelines and recommendations in airway management have been formulated by leading airway societies across the globe to mitigate the spread of COVID-19 infection amongst the health care workers. Numerous modifications in airway techniques have also been suggested to ensure minimal viral exposure. Special emphases were on those posted specifically in critical areas in hospital such as intensive care unit, emergency room and operation suite, and are directly involve in airway control of this subset of patients. Airway managers should be cognizant with finer intricacies of the mechanism of viral spread and should be well-versed and proactive to deal with the same. Endotracheal intubation still remains the gold standard for providing controlled ventilation to severe COVID-19 patients presenting with acute respiratory failure. A pre-formulated stepwise approach for ETI should be considered and implemented strictly, based on updated existing data and need to be adapted according to the available resources in respective hospital setup. Various adjuncts for ETI such as SGA and fiberoptic bronchoscope need to be judiciously considered to minimise the production of aerosols. Nevertheless, one must not forget the basic fundamental principles of ETI and should adhere with them concurrently with modifications required to spread the viral infection.

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