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Practice recommendations for the management of children with suspected or proven COVID-19 infections from the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC) and the section Respiratory Failure from the European Society for Paediatric and Neonatal Intensive Care (ESPNIC)

A consensus statement

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Introduction

The spectrum of respiratory illness from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Coronavirus Disease 2019 (COVID-19) varies from mild upper respiratory tract symptoms to severe acute respiratory distress syndrome (ARDS). COVID-19 induced ARDS in adults is characterised by hypoxaemia without increased work of breathing (likely representative of ventilation-perfusion mismatching), unusually spared lung compliance, a heterogeneous degree of lung recruitability and usually a good response to prone positioning[1]. The clinical manifestations of severe COVID-19 disease in children have not been studied but it cannot be ruled out that a proportion of patients may present with clinical features like bronchiolitis, bronchopneumonia, and pneumonitis seen in other viral respiratory illnesses or with extra-pulmonary symptoms. Preliminary paediatric data shows that severe COVID-19 disease appears uncommon in young children although those < 1 years of age may experience greater disease severity[2-4].

The Paediatric Mechanical Ventilation Consensus Conference (PEMVECC) published recommendations for paediatric mechanical ventilation in 2017[5]. The panel and new invited members gathered online to evaluate if the published recommendations needed revising to address specific issues related to COVID-19 disease. The panel recommends adhering in general to the recommendations on mechanical ventilation in children published by PEMVECC and the practice recommendations from the Pediatric Acute Lung

Injury Consensus Conference (PALICC) published in 2015[5,6]. Given the lack of paediatric data, specific recommendations on managing paediatric COVID-19 cases cannot be made. The Panel recommends critically appraising data coming from adults with COVID-19 and published recommendations on managing COVID-19 in adults before making use of these in daily clinical paediatric practice.

Assessing disease severity

According to PEMVECC and PALICC, the panel recommends monitoring SpO_2/FiO_2 ratio in patients on non-invasive respiratory and the oxygenation saturation index (OSI) or the oxygenation index (OI) in invasively ventilated children for severity grading[6]. The level of FiO_2 should be guided by targeting $SpO_2 \leq 97\%$ to allow for valid measurement of the SpO_2/FiO_2 ratio and the OSI.

Practice recommendations for children at risk for paediatric ARDS (PARDS) as defined by a) chest imaging findings of new infiltrate(s) consistent with acute pulmonary parenchymal disease and b) oxygen supplementation to maintain $SpO_2 \geq 88\%$ and oxygenation index (OI) < 4 or oxygen saturation index (OSI) < 5.

If available, CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) or BI-LEVEL NON-INVASIVE VENTILATION (NIV) as a first-line approach is recommended rather than high-flow nasal cannula (HFNC), certainly in patients with $SpO_2/FiO_2 > 221$ and < 264. The rationale for this is that a higher pressure level might be obtained when using CPAP/NIV[7]. Intubation should not be further delayed if $SpO_2/FiO_2 < 221$.

For NIV, preference should be given to the use of a certified helmet because leaks are minimised; if not available then a non-vented oro-nasal or full-face mask, a double limb circuit (or a single limb with filter before the leak site) and appropriate bacterial/viral filters should be used. The panel recommends titrating pressures according to the patient's response (i.e. oxygenation and work of breathing). CPAP/NIV bears increased risk of aerosol contamination, certainly if there is a leak[8]. Strict personal protection equipment (PPE) is mandated with managing patients with suspected or confirmed COVID-19. Intubation must be recommended if there is no improvement in oxygenation (target SpO_2 92 – 97% and $FiO_2 < 0.6$) within 60 – 90 minutes. One adult report suggests considering adding the ROX index (SpO_2/FiO_2 divided by the respiratory rate) in the decision-making for intubation (i.e. ROX < 5). However, with $SpO_2/FiO_2 < 221$ intubation should not be further delayed.

HIGH-FLOW NASAL CANNULA (HFNC) might be considered as an option if CPAP/NIV is unavailable for patients with $SpO_2/FiO_2 > 264$ ($FiO_2 < .35 – .40$). Like CPAP/NIV, with interfaces others than helmets, HFNC bears increased risk of aerosol contamination, personal protection equipment (PPE) is therefore mandated, and this also while awaiting COVID-19 testing results[8]. Careful monitoring of patients on HFNC is essential. Escalation of therapy (i.e. non-invasive ventilation or intubation) should not be delayed, if there is no improvement in oxygenation within 30 – 60 minutes (target for HFNC treatment success: SpO_2 92 – 97% with $FiO_2 < 0.4$).

The panel recommends that INTUBATION is performed by an expert in airway management in a closed environment with a minimal amount of staff. Video laryngoscopy (if available) should be used. All personnel should have PPE. The panel recommends pre-oxygenating the patient with a bag/mask that is equipped with a bacterial/viral filter. If bag/mask ventilation is necessary, the panel recommends the "two-person technique" to ensure a better seal of the mask around the mouth. The panel recommends rapid sequence induction. The panel recommends the use of cuffed endotracheal tubes, inflating the cuff immediately after intubation before verification of the position of the tube by end-tidal CO_2, chest X-ray, auscultation or ultrasound exam.

The panel recommends assessing the quasi-static compliance (with spontaneous breathing absent) after intubation under zero flow conditions.

Practice recommendations for invasively ventilated children

Initial ventilator settings and targets

The panel cannot recommend about the mode of ventilation that should be used; institutional guidelines should be applied. The panel recommends applying lung protective ventilation according todays recommendation (Vt-exp 5 – 7 mL/kg ideal bodyweight, (Pplat) < 28 – 32 cmH_2O, driving pressure ≤ 15 cmH_2O) per PALICC recommendation[6]. Lower Vt ranges might become necessary with poorly compliant respiratory system conditions, i.e. with severe restrictive lung disease. There is no data from paediatric COVID-19 cases suggesting other directions.

Initial PEEP should be around 10 cmH_2O and might need for further increase, for which best but limited paediatric evidence based guidance can be given by the ARDS Network PEEP/FiO_2 grid[9]. The panel considers it reasonable to titrate FiO_2 to maintain SpO2 92 – 96% in the lack of any specific paediatric data. For patients with severe disease the minimal acceptable SpO_2 should be 88 %[10,11]. The panel recommends allowing for permissive hypercapnia, thereby accepting pH > 7.20 unless specific clinical indications dictate otherwise.

Neuromuscular blockade

The panel recommends considering early use of neuromuscular blocking agents (NMBA) for 24 – 48 hours in moderate-to-severe PARDS (i.e. PaO_2/FiO_2 < 150; OI ≥ 12; OSI ≥ 10). The rationale for using NMBA includes avoiding spontaneous breathing at high transpulmonary pressures, minimising persistent ventilator dyssynchrony, need for ongoing deep sedation, prone positioning, or avoiding high plateau pressures. The panel cannot recommend on threshold plateau pressures when to start NMBA. NMBAs can be discontinued if PaO_2/FiO_2 ≥ 150; OI < 12; OSI < 10.

Prone positioning

The panel recommends considering early and prolonged prone positioning in moderate-to-severe PARDS (i.e. PaO_2/FiO_2 < 150; OI ≥ 12; OSI ≥ 10). Practices vary between 12 – 18 hrs per day with the patient in prone position. Prolonged prone positioning (>24 hrs) may be considered early in the disease trajectory. Prone positioning can be discontinued if PaO_2/FiO_2 ≥ 150; OI < 12; OSI < 10. Special care should be taken when prone positioning the patient to avoid circuit / ETT disconnec-

tion. A bolus of NMBA before turning the patient might be considered.

Escalating therapies for refractory hypoxaemia

The panel recommends considering escalating therapies when (refractory) hypoxaemia (defined by PaO_2/FiO_2 < 150; OI ≥ 12; OSI ≥ 10 and/or FiO_2 > 0.6) is present.

The panel recommends titrating PEEP when there is (refractory) hypoxaemia. The panel cannot recommend the best approach to titrating PEEP or a best recruitment manoeuvre. The only paediatric data available (not including COVID-19 patients) on best PEEP settings showed that not adhering to the ARDS Network low $PEEP/FiO_2$ grid was associated with increased mortality in all-cause PARDS[9]. However, balancing oxygenation and haemodynamics remains important when titrating PEEP.

The panel recommends a nitric oxide trial if an alteration in the hypoxic pulmonary vasoconstriction reflex is presumed (i.e. when there is no improvement in oxygenation despite all other measures). This may especially be the case in COVID-19 cases with normal lung compliance. The panel cannot recommend about the use of corticosteroids. However, based on recent findings from one adult study, the use of systemic corticosteroids may be considered to limit the pro-inflammatory state, especially in severe PARDS[12].

The panel finds it reasonable considering HFOV for refractory hypoxaemia in COVID-19 induced ARDS with reduced respiratory system / lung compliance using a staircase titration of the mean airway pressure (mPaw). The the timing of initiation is influenced by personal preferences, institutional experiences, risk assessment and availability of equipment. The panel emphasizes that HFOV should be considered with caution if there is little or no experience with this modality. The panel recommends adding a bacterial/viral filter system to the expiratory limb of the HFOV circuit to minimise the risk of aerosol contamination when devices with free leak (such as the SensorMedics) are used. Newer, mainly neonatal HFOV devices work with classical dual limb circuits, therefore same precautions have to be taken as during conventional ventilation.

The panel finds it reasonable to consider ECMO if refractory hypoxaemia persists despite all measures used. Limited availability of human resources and equipment may influence the decision-making[13].

The panel recommends a restrictive fluid strategy in paediatric COVID-19 cases.

Caring for the invasively ventilated child

The panel recommends that all staff entering room must ensure they have adequate PPE – do not risk exposure

The panel recommends minimizing ETT disconnections and the use of inline, closed suctioning. The panel cannot make specific recommendations about airway humidification, but preference to heat moisture exchangers with bacterial/viral filters (HMEFs) should be given for airway humidifation to reduce the risk of aerosol contamination, also there is no strong evidence for this. Active humidification may bear the risk of aerosol contamination, whereas passive humidification requires changing every 24 hrs.

The panel recommends the use of bacterial/viral filters on the expiratory limb of the patient circuit and to replace them every 24h, or earlier if they become wet to ensure full efficiency.

The panel recommends immediate clamping of the endotracheal tube in case of disconnection whether expected or unexpected. The panel recommends against routine chest physiotherapy in absence of any thick mucus or history of mucus plugs in the airways. The panel recommends against using cough-assist devices.

The panel recommends all personnel continue using PPE when extubating a patient because of the inherent risk of aerosol contamination with this procedure. Preventive measures to minimise aerosolization from devices or patient coughing should be taken.

In addition to these recommendations, the panel recommends adhering to the ESPNIC Nursing Section recommendations (available on www.espnic-online.org).

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