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Abstract

□ NON-INVASIVE VENTILATION VERSUS HIGH-FLOW NASAL CANNULA OXYGEN THERAPY WITH APNOEIC OXYGENATION FOR PREOXYGENATION BEFORE INTUBATION OF PATIENTS WITH ACUTE HYPOXAEMIC RESPIRATORY FAILURE: A RANDOMISED, MULTICENTRE, OPEN-LABEL TRIAL.

Frat JP, Ricard JD, Quenot JP, et al. *Lancet Respir Med*. 2019;7:303-312

Endotracheal intubation is a commonly performed procedure in the critically ill patient and is associated with the risk of peri-intubation hypoxemia. These authors attempted to determine if there is an advantage to preoxygenation with non-invasive ventilation versus highflow nasal cannula, which has not previously been studied.

Investigators conducted a randomized, parallel group, non-blinded, open-label multicenter trial across 28 intensive care units in France. Statistical analysis was performed under an intention to treat protocol. Study participants were patients with hypoxemic respiratory failure that required intubation via rapid sequence induction. Eligible patients were over 18 years of age and had a respiratory rate >25, signs of distress, or a PaO2/FiO2 ratio of <300. The main exclusion criteria included cardiac arrest, declining mental status with GCS <8, pregnancy, intubation prior to arrival in ICU, recent airway or gastrointestinal surgery, or significant facial fractures. Once patients met inclusion criteria they were randomized and categorized as mild or moderate to severe hypoxemia using a cut off of PaO2/FiO2 ratio of >200mmHg and <200mmHg respectively. In the patients receiving non-invasive ventilation, the ventilator was set to pressure support with a tidal volume between 6ml/kg and 8ml/kg based on ideal body weight, PEEP 5cm H20 and FIO2 of 1.0. These patients received non-invasive ventilation throughout pre-oxygenation and induction until larygoscopy. In the patients receiving high flow nasal cannula it was set at 60 L/min with an FiO2 1.0 and a jaw thrust was performed to ensure airway patency. In the nasal cannula group, the patient received high flow throughout intubation until tube placement was confirmed. Both groups were preoxygenated for 5 minutes. The primary outcome investigated was severe peri-intubation hypoxemia, defined as pulse oximetry < 80% for five seconds or more during the period between rapid sequence intubation and 5 minutes after endotracheal tube placement was confirmed. Multiple secondary safety and efficacy outcomes were recorded, including lowest peri-intubation Sp02 duration of laryngoscopy, number of laryngoscopy attempts, episodes of a systolic pressure <90mmHg, feasibility of the pre-oxygenation method, and others.

Over the course of eight months, 2079 patients were intubated, of which 745 patients met eligibility criteria and 322 patients were randomized. In the non-invasive ventilation group, 23% of patients had severe hypoxia compared to 27% in the high flow group (absolute difference -4.2, 95% CI [-13.7-5.5]). In the sub-group of moderate to severe hypoxemia, severe hypoxia occurred at 24% with non-invasive ventilation and 35% with high-flow (absolute difference -11.3, 95% CI [-22.3-0.3]). In the mild to moderate hypoxemia sub-group there was no difference between non-invasive ventilation and high flow oxygen. Overall and in analyses of the sub-groups, there were no differences for any of the secondary outcomes.

The authors concluded that when choosing a preoxygenation strategy between high-flow nasal cannula or non-invasive ventilation, overall there were no differences in the rates of peri-intubation hypoxia or late complications.

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Comments: These results show no difference overall between HFNC and non-invasive ventilation, but in severely hypoxemic patients, this trial appeared to favor non-invasive ventilation over high flow. This makes sense physiologically, understanding that in the critically ill patients there is an element of shunt physiology that is mitigated with alveolar recruitment measures, which non-invasive ventilation provides. While the authors state there is no difference, we should interpret these negative findings with caution, as confidence intervals are wide. Additionally, there were more cardiac arrest events in the HFNC group than in the non-invasive group and since this was still a rare occurence, the difference was not significant but likely underpowered. Knowing the above limitations, we do not feel this changes current practice, but would tend to choose non-invasive ventilation based on these findings.

□ OUTCOMES OF CHILDREN WITH BRONCHIOLITIS TREATED WITH HIGH-FLOW NASAL CANNULA OR NONINVASIVE POSITIVE PRESSURE VENTILATION.

Clayton JA, McKee B, Slain K, et al. *Pediatr Crit Care Med*. 2019;20(2):128-135

Bronchiolitis is the leading cause of hospital admissions for infants in the United States. 15-25% of these patients are admitted to the pediatric intensive care unit (PICU), where 25-40% require intubation and invasive mechanical ventilation (IMV). IMV carries substantial risk of complications including vocal cord dysfunction, ventilator-induced lung injury and infection. Methods of respiratory support such as noninvasive positive pressure ventilation (NPPV) with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) and high-flow nasal cannula (HFNC) have been shown to reduce eventual conversion to IMV. It is unclear, however, whether there is an initial modality of airway support that reduces risk of eventual IMV use.

This study compiled data using the Virtual Pediatric Systems (VPS) database, which includes over 135 PICUs, mostly in the US with a minority of centers in Canada and Saudi Arabia. Patients up to two years of age were included if they were both admitted to the PICU with a primary diagnosis of bronchiolitis and received HFNC or NPPV, but were excluded if they had a history of tracheostomy or received IMV prior to NPPV. The primary outcome was the use of IMV following initial treatment with HFNC or NPPV. Secondary outcomes were mortality and PICU length of stay (LOS). Additional variables collected for matching and analysis included but were not limited to demographics, PIM (Pediatric Index of Mortality) 2 scores, comorbidities, positive respiratory syncytial virus (RSV) testing, maximum heart rate and respiratory rate during the first twelve hours of PICU care.

6496 children admitted to 92 PICUs between 2009-2015 were included in the analysis. The median PIM 2 risk of mortality was 0.21% (IQR 0.18–0.31%), and the median PICU LOS was 2.9 days (IQR 1.8–4.9 d). IMV was used in 798 patients (12.3%), and 20 patients (0.31%) died prior to PICU discharge. IMV was more common in subjects initially supported with NPPV than in those supported with HFNC (20.1% vs 11.0%; $p < 0.001$). Also associated with higher rates of IMV were lower age, lower weight, comorbidities and higher PIM 2 risk of mortality. NPPV was also associated with a longer PICU length of stay and increased mortality. Regression indicated that not only was NPPV independently associated with increased odds of IMV (OR 1.53 [95% CI, 1.24–1.88]), but so was lower age, lower weight, presence of comorbidities, negative RSV test, and higher PIM 2 score.

The authors conclude that HFNC may be the preferred initial support modality for critically ill children with bronchiolitis, due to the lower association with subsequent IMV. They admit that there may be unmeasured confounders affecting the outcomes of each cohort and that a retrospective trial cannot establish causation. They recommend a prospective interventional trial to establish causality and confirm the superiority of a particular form of ventilatory support in reducing incidence of IMV, but point out that powering such a study would be extremely difficult due to the volume of enrollments required.

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Comment: To date, randomized controlled studies comparing NPPV with HFNC in pediatric bronchiolitis do not show significant differences in IMV rates. However, intubation rates are relatively low for bronchiolitis and thus detecting differences is difficult. This is the largest retrospective database review assessing the correlation of IMV in NPPV or HFNC for bronchiolitis. While there is significant risk of selection bias in this study, and there is no way to gauge baseline work of breathing in the database, the increased association of IMV after NPPV remains after controlling for severity of illness scores and comorbidities. HFNC already tends to be the modality of choice for infants, when available, due to ease of set up and titration. This study provides additional evidence that emergency physicians should strongly consider HFNC as first-line in the treatment of respiratory distress in pediatric bronchiolitis.

☐ NEUROPSYCHIATRIC SEQUELAE IN ADOLESCENTS WITH ACUTE SYNTHETIC CANNABINOID TOXICITY.

Anderson SA, Oprescu MA, Callelo D, et al. *Pediatrics*. 2019;144(2):e20182690

Amongst users of synthetic cannabinoids, adolescents make up the largest group that present to the Emergency Department. Compared to tetrahydrocannabinol (cannabinoids), synthetic cannabinoids (SC) have more adverse cardiotoxic and neurotoxic effects, especially in pediatric populations. Patients seek medical attention after SC abuse 30 times more than cannabis. The acute neuropsychiatric toxicities that adolescents experience after SC abuse are poorly understood. The goal of this study was to better characterize the neuropsychiatric toxicities of SC use compared to cannabis.

This retrospective cohort study was derived from the Toxicology Investigators Consortium (ToxIC), which is a multicenter registry that includes over 62,000 cases from 65 hospitals, from January 2010 to September 2018. Patients included were aged 13 to 19, had either self-reported or witness-reported use of SC or cannabis, and were all evaluated at bedside by a board certified medical toxicologist. Drug use was not routinely confirmed through bioanalytical testing. Patients were categorized into in one of four subgroups: SC-only exposure, SC and other drug exposure, cannabis only exposure and cannabis and other drug exposure. The primary outcome was the occurrence of neuropsychiatric signs and symptoms, as determined by the toxicologist, which were classified by 6 specific exam findings including agitation, coma and/or central nervous system depression, seizures, hallucinations, delirium and/or psychosis and extrapyramidal signs.

Of the 348 patients enrolled in this study, 107 were assigned to the SC-only group, 38 to the SC-polydrug group, 86 to the cannabis-only group, and 117 in the cannabis-polydrug group. Compared to the cannabis-only group, the SC-group had higher odds of CNS depression (OR 3.42; 95% CI 1.51-7.75) and seizures (OR 3.89, 95% CI 1.39-10.94), but lower odds of agitation (OR 0.18; 95% CI 0.10-0.34). The SC-polydrug group had higher odds of agitation (OR 3.11; 95% CI 1.56-7.44) and seizures (OR 4.8; 95% CI 1.80-12.74) compared to cannabis-polydrug exposures. The authors also note that in the SC-polydrug group, sympathomimetic were used in about 1.5 times the rate of cannabis group, while the cannabis-polydrug group use ethanol 3.8 times more than SC-polydrug group. This