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CASE REPORT



Danger in the vapor? ECMO for adolescents with status asthmaticus after vaping

Lauren E. Bradford, MD^{a,b}, Meghan E. Rebuli, PhD^a, Brian J. Ring, MSRC^a, Ilona Jaspers, PhD^a, Katherine C. Clement, MD^{a,b}, and Ceila E. Loughlin, MD^{a,b}

^aDepartment of Pediatric Pulmonology, University of North Carolina School of Medicine, Chapel Hill, NC, USA; ^bUniversity of North Carolina Children's Hospital, Chapel Hill, NC, USA

ABSTRACT

Introduction: Electronic nicotine delivery systems (ENDS) use is on the rise in the adolescent and young adult populations, especially in the wake of sweet flavored ENDS solutions and youth-targeted marketing. While the extent of effect of ENDS use and aerosolized flavorings on airway epithelium is not known, there remains significant concern that use of ENDS adversely affects airway epithelial function, particularly in populations with asthma.

Case Study: In this case series, we review two cases of adolescents with history of recent and past ENDS use and asthma who required veno-venous extracorporeal membrane oxygenation (VV-ECMO) for status asthmaticus in the year 2018.

Results: Both patients experienced hypercarbic respiratory failure requiring VV-ECMO secondary to their status asthmaticus, with slow recovery on extensive bronchodilator and steroid regimens. They both recovered back to respiratory baseline and were counseled extensively on cessation of ENDS use.

Conclusion: While direct causation by exposure to ENDS cannot be determined, exposure likely contributed to symptoms. Based on the severity of these cases and their potential relationship with ENDS use, we advocate for increased physician screening of adolescents for ENDS use, patient and parent education on the risks of use, and family cessation counseling.

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Introduction

Electronic nicotine delivery systems (ENDS) were introduced to the consumer market in 2006–2007 (1). Since that time, the popularity of ENDS use has increased, while the use of combustible cigarettes has declined between 2011 and 2018; this trend is also evident amongst adolescents, though the decrease in use of combustible cigarettes has become stagnant between 2017 and 2018 (2,3). A plethora of appealing flavors (4,5) and targeted youth marketing are thought to contribute to increased adolescent use of ENDS (6,7). Of major concern, data from the 2018 National Youth Tobacco Survey indicated a 78% and 48% increase in ENDS use from 2017 use rates in high school and middle school students, respectively (8), with adolescents who have asthma being more likely to use ENDS as compared to their peers without asthma (9).

Many long-term effects of ENDS use and effects on people with respiratory disease, such as asthma, are still unknown (10–11). However, there is emerging

evidence that components of ENDS liquids have the ability to alter airway inflammation and cellular function (12–14). Interestingly, Bayly et al. (15) found that youth with asthma exposed to secondhand ENDS were at increased risk of reporting an asthma attack.

To expand awareness of the potential effects of ENDS in adolescent with asthma, we present two case reports of adolescents with known asthma and ENDS use history who presented with life-threatening asthma exacerbations necessitating veno-venous extracorporeal membrane oxygenation (VV-ECMO).

Case study 1

A 16-year-old male with known history of severe persistent asthma, obesity, and allergic rhinitis presented in respiratory arrest to an outside hospital (OSH). He had had no previous hospitalizations for asthma. His mother was known to use ENDS in the home. He also had a significant personal history of ENDS use,

however he did not specify how frequently. Before presentation, he was prescribed fluticasone-salmeterol 500–50 mcg diskus one puff twice daily, montelukast 10 mg daily, and cetirizine 10 mg daily for his severe asthma. The patient had a history of malaise for three days before presentation and had been using ENDS with friends, who were also using ENDS, before onset of symptoms. Respiratory distress began abruptly one hour before arrival to an OSH emergency room. He quickly decompensated and required intubation for hypercarbic respiratory failure upon presentation. The patient vomited during the procedure, resulting in possible aspiration. He continued to have worsening hypercarbic respiratory failure and required VV-ECMO cannulation upon arrival to the pediatric intensive care unit (PICU).

Case study 1 results

The initial chest radiography demonstrated bilateral hypoinflation, pneumomediastinum, without focal consolidation or opacification. His initial arterial blood gas showed respiratory acidosis with a pH of 6.85 and a partial pressure of carbon dioxide (pCO₂) of >100 mm Hg. He continued to receive 20 mg/h of continuous albuterol treatment, intermittent inhaled ipratropium, and intravenous (IV) methylprednisolone 60 mg every 12 h. He required ECMO support for five days.

Following removal of ECMO support, the patient continued to require mechanical ventilation, continuous albuterol treatment, intermittent ipratropium, and IV methylprednisolone. He was then extubated to a non-rebreather on hospital day 9. He was then spaced to intermittent albuterol dosing and corticosteroids by mouth and was discharged on hospital day 18. He was discharged on his previous asthma controller medication regimen. Before discharge, a certified asthma nurse educator counseled him extensively on the dangers of vaping and cigarette smoke exposure. He was encouraged to quit and avoid exposure. Following discharge, he has continued to use ENDS, and has had six hospital encounters for asthma exacerbations despite adherence to asthma control regimen, as documented by patient and parental report as well as pharmacy medication refill history.

Case study 2

A 14-year-old female with history of severe, persistent, uncontrolled asthma presented to an OSH emergency room in respiratory distress. In the past, she had been

treated with fluticasone-salmeterol 230–21 mcg metered dose inhaler (MDI) with spacer two puffs twice daily. She had not taken fluticasone-salmeterol MDI for two years. She had a history of ENDS use, the extent of which was not documented. She also had secondary exposure to cigarette smoke at home. Leading up to her hospitalization, she had a one to two week history of increasing shortness of breath and cough. During that time, she was taking albuterol MDI for rescue, frequently. Her symptoms worsened and she presented to an OSH emergency room in respiratory distress with significant accessory muscle use, tachypnea, and hypoxemia to 89%. Her hypoxemia improved with three nebulized treatments of albuterol and ipratropium, however her respiratory distress persisted. She continued to have significant respiratory distress despite treatment with continuous albuterol, IV magnesium, IV methylprednisolone, IV terbutaline, IV aminophylline, inhaled helium, and noninvasive ventilation. The patient was transferred to an OSH PICU where she was intubated for hypercarbic respiratory failure and then transferred to our PICU for further care.

Case study 2 results

Her initial chest radiography demonstrated pneumomediastinum and a left lower lobe opacity, thought to represent atelectasis. Her initial arterial blood gas demonstrated severe respiratory acidosis with a pH of 6.97 and a pCO₂ of 105 mm Hg. Despite the administration of inhaled sevoflurane, she continued to have hypercarbic respiratory failure and was initiated on VV-ECMO.

She remained on ECMO for six days and was continued on intermittent albuterol dosing. Following removal of ECMO support, she continued to require mechanical ventilation. Work of breathing and wheezing worsened and she again required continuous albuterol treatment. Continuous albuterol treatment was then spaced to intermittent albuterol dosing. She was extubated on hospital day 8 to 15 liters per minute of supplemental oxygen via high flow nasal cannula. She was then weaned off of supplemental oxygen and completed 12 days of corticosteroids. Before discharge, she began treatment with budesonide-formoterol 160 mcg–4.5 mcg MDI two puffs twice daily. Before discharge she received formal asthma education from a certified asthma nurse educator and was counseled on the dangers of ENDS use. She has been hospitalized for asthma once at an OSH since discharge. It is unclear if she has had further ENDS use exposure.

Discussion

Cigarette use has long been known to worsen asthma and cause respiratory distress (16). The use of ENDS and their effects on asthma status has not yet been extensively studied. These two cases of adolescents with known asthma and ENDS exposure demonstrate the possibility that ENDS use may affect asthma exacerbations and complicate clinical care. In the first case, the patient had previously never been admitted for asthma exacerbations. In the second case, which occurred within two months of the first case in the year 2018, the patient had several admissions for asthma in the past, including in the PICU, but had not been admitted for asthma for several years. Neither had ever required intubation secondary to status asthmaticus. Both patients had known personal ENDS use histories and both had sudden hypercarbic respiratory failure requiring ECMO cannulation. Unfortunately, as this was a retrospective case study, the exact frequency and particulars of ENDS use by each patient were unavailable in the chart documentation.

While there are several confounding factors including lack of asthma control, poor medication compliance, and other possible contributory factors, ECMO cannulation for asthma is a rare occurrence and notable in these cases. Interestingly, in both of these cases, primary and secondary exposure to ENDS use occurred before hospitalization. While direct causation of these incidents to ENDS cannot be determined, the role of ENDS in complicating asthma control, exacerbations, and treatment cannot be ruled out. It is very possible that ENDS use exposure, at a minimum, contributed to more complicated clinical course and patient presentation.

While we cannot attribute ENDS exposure as a direct factor in VV-ECMO cannulation in these cases, it raises the issue of ENDS use affecting asthma control and exacerbation severity. These cases, in combination with recent ENDS use trends, indicate that ENDS use could significantly impact people with asthma. Alarming, adolescents and young adults with asthma are actually more likely to use ENDS than their age-matched peers (17). It has also been shown that adolescents with asthma exposed to secondhand ENDS are at increased odds of reporting an asthma attack (14). While the similar ENDS exposures and hypercarbic respiratory failure requiring VV-ECMO in the cases presented here is an important association to note, it is unknown if ENDS use was a direct contributor to respiratory failure. The combination of these unique case associations with ENDS use and

asthma together with recent increases in ENDS use trends among adolescents may suggest that ENDS use may significantly impact people with asthma.

A major driver of ENDS popularity with adolescents may be ENDS flavorings. In one study, the amount of unique ENDS flavoring increased from 466 types in August 2012, 7764 types in January 2014 (4), to over 15,000 by 2016 (18). A significant portion of these flavorings use known airway irritants and toxicants. Flavors such as benzaldehyde, cinnamaldehyde, diacetyl, and camphor, have been identified as potential respiratory hazards by the Flavor and Extract Manufacturers Association (FEMA) of the USA (19). Diacetyl, typically used for creamy or sweet flavors, has been shown to cause bronchiolitis obliterans after occupational exposure, which is an irreversible, obstructive pulmonary disease affecting the small airways of the lungs (20). One study showed the presence of diacetyl in 110 (69%) of 159 sweet-flavored ENDS liquid products (21). This same study estimated that at daily use of 3 ml ENDS solution would expose them to doses of diacetyl far above the recommended dose by the National Institute for Occupational Safety and Health (NIOSH) and the Centers for Disease Control (CDC). These data are of particular concern as sweet flavorings in ENDS are more popular in adolescent and young adult populations (22,23). Beyond flavorings, one of the main components of ENDS solution, propylene glycol, has also been shown to be a possible irritant to airways, particularly when heated to temperatures greater than 270 °C (19). ENDS flavorings may drive some of the adverse events which lead to increased asthma exacerbation rates, making adolescents with asthma potentially more vulnerable to the effects of ENDS on the airway.

Conclusion

Here, we present two cases of adolescents with asthma and a history of ENDS use who presented with hypercarbic respiratory failure necessitating treatment with VV-ECMO. While direct causation by exposure to ENDS cannot be determined, exposure likely contributed to symptoms. Based on the severity of these cases and their potential relationship with ENDS use, we advocate for increased physician screening of adolescents for ENDS use, patient and parent education on the risks of use, and family cessation counseling. This concern for the potential adverse health effects caused by ENDS use is further highlighted by the recent federal court ruling enforcing the FDA to have tobacco manufacturers comply with required FDA approval of

their products, particularly flavored ENDS solutions, before they are able to sell said products on the market any further (24).

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Declaration of Interest

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