



### Case Report

## Popcorn Lung and E-Cigarettes the Risk of Post OP Anesthesia Complications

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### Abstract

Popcorn lung, also known as occupational bronchiolitis obliterans, is believed to be caused by chemicals that are found in many flavoring agents. Bronchiolitis obliterans is a disease of inflammatory obstruction of the bronchioles leading to scarring and fibrosis. The flavoring agents which are known as diacetyl (2,3-butanedione) diketone and 2,3-pentanedione have been used in the manufacturing of popcorn to increase the aroma and intensity. Similarly, these agents have been used in the flavoring of e-cigarettes. Given the link between exposure to these flavoring agents and an increase risk of bronchiolitis obliterans coupled with the increased prevalence of e-cigarette use, the current study examines post-operative anesthesia risk associated with the use of e-cigarettes.

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**Citation:** Mulligan J, Deitrick P, Weaver S, Valei F, Fielding AF (2018) Popcorn Lung and E-Cigarettes the Risk of Post OP Anesthesia Complications. J Pulm Med Respir Res 4: 019.

**Received:** June 15, 2018; **Accepted:** December 12, 2018; **Published:** December 20, 2018

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### Introduction

Bronchiolitis obliterans is a disease of inflammatory obstruction of the bronchioles leading to scarring and fibrosis. In 2000, the first cases of bronchiolitis obliterans were identified at a microwave popcorn production facility; after that time electronic cigarettes (e-cigarettes) were developed and have been shown to contain similar flavoring agents. These flavors have been identified by “Vapers” to contribute to their efforts to quit smoking or at least to reduce cigarette consumption and still maintain pleasure perception. Vapers usually switch between flavored products. Surveys show sweet flavors are the most popular among vapers [1].

The Chinese firm Hon Lik made the first modern electronic cigarettes in the mid-2000s [2], as a substitute for the conventional smoker, marketed as a healthier alternative. Since the emergence of new generations of e-cigarettes, they have increased in popularity especially among the younger smokers. Presently there are over 7000 different flavoring agents used in e-cigarettes. E-cigarettes are unfortunately not currently regulated by the US Food and Drug Administration. Under the Family Smoking Prevention and Tobacco Control Act (2009) the FDA has issued a proposed rule to include e-cigarettes [3]. Liquid flavoring agents seen in e-cigarettes have been shown to contain diacetyl (2,3-butanedione), diketone and 2,3-pentanedione. Levels of diacetyl and 2,3-pentanedione were found in a large proportion of sweet flavored e-cigarette liquids in concentrations greater than considered conventionally safe. Interestingly, these chemicals were even found in products which are coming from manufacturers who clearly made claim their products didn't contain them [4]. When used e-cigarettes have been shown to even have levels of these compounds that exceed the exposure levels of factory workers who had reported as having been exposed. The exposure pathways for these flavoring chemicals is through inhalation which is similar for both the users of the e-cigarettes and popcorn factory workers. E-liquids which contain nicotine, propylene glycol, and flavoring agents are heated, vaporized, and then inhaled. Once heated the (2,3-butanedione), diketone and 2,3-pentanedione are released for inhalation [3,5].

### Discussion

In 2000 there were 8 cases of severe bronchiolitis obliterans recorded in people who had worked in microwave-popcorn production factory [6]. Subsequently spirometry evaluation of 87% of workers in this factory showed higher rates of cough and shortness of breath and with higher rates of airway obstruction. Higher occurrences of lung function abnormalities in this group reflected an occupational bronchiolitis obliterans caused by inhalation of the volatile flavoring agents [7].

Bronchiolitis obliterans is the inflammatory and fibrotic process in which partial or complete obstruction of the bronchioles occurs [8]. In bronchiolitis obliterans, the proliferation of granulation tissue in the bronchiolar epithelium leads to obstruction of the small airways. It is believed generation of reactive oxidative agents also plays a significant role in pathology of diacetyl toxicity producing a

reactive oxygen species [9]. The disease can manifest as an obstructive, restrictive, or mixed pattern of a pulmonary dysfunction [10].

Prolonged exposure to diacetyl (2,3-butanedione), diketone and 2,3-pentanedione can lead to fixed airflow obstruction, gas exchange impairment, obstructive lung disease. Bronchiolitis obliterans is an irreversible loss of pulmonary function. The disease process can become so severe that the only treatment may be a lung transplant [5]. Exposure has been shown to decrease the Forced Expiratory Reserve Volume (FEV1) and Functional Vital Capacity (FVC). Studies by Fedan et al., suggested the epithelial cell is adversely affected by flavoring in e-cigarettes.

The pathophysiology of the popcorn lung is believed to be initiated by the epithelial damage caused by diacetyl (2,3-butanedione) diketone and 2,3-pentanedione [11,12]. The airway surface liquid and mucociliary clearance is regulated in epithelial cells through absorption of Na<sup>+</sup> and Cl<sup>-</sup> secretion in epithelial cells [13]. These chemicals cause disruption of the transepithelial Na<sup>+</sup> transporters which can eventually lead to pulmonary edema [14,15], and airway obstruction [16,17]. Fedan et al., revealed transepithelial depolarization and altered tight junction integrity was adversely affected in guinea-pigs after perfusing physiological salt solution containing diacetyl into the lumen [11].

It is believed diacetyl and 2,3-pentanedione are metabolized by the enzyme dicarbonyl/l-xylulose reductase to acetoin and 2-hydroxy-3-pentanone respectively [18,19], releasing their metabolites into the submucosal medium. These metabolites were able to change the Na<sup>+</sup> ion transporter function in much lower doses than needed to alter the morphologic shape of the epithelial cells that can be visible. It is important to recognize e-cigarettes have not been around in the market for long enough, so the health effect of the exposure to e-cigarettes aerosol has only been investigated in a few articles and the long term biological effects of e-cigarette aerosol exposure are not yet fully investigated.

As a rule, adequate preoperative evaluation of patients with pulmonary dysfunction by a pulmonologist is recommended before any anesthetic induction to avoid Postoperative Pulmonary Complications (PPCs). Smoking and lower FEV1 are identified as risk factors as PPCs. In patients with PPCs after non-cardiothoracic surgeries, the values of FEV1 and FVC were lower than those who had normal FEV1 and FVC rates suggesting FEV1 is an important factor for predicting postoperative complications after surgeries. Committed vapers may be at higher risk of PPCs after general anesthesia. Using neuromuscular blocking agents during GA may also exacerbate respiratory complications or post-operative hypoxemia [20].

Hypercapnia and desaturation can both happen because of “popcorn lung” as a result people should be screened for the possible effects of vaping to avoid these post-anesthesia pulmonary complications [21]. Studies by Hinrichs et al., demonstrated patients with bronchiolitis obliterans had a significant lower SO<sub>2</sub> venous saturation. Lower venous oxygen saturations can be further exacerbated due to anesthesia as general anesthesia disrupts central regulation of breathing, which can ultimately result in hypoventilation [22]. The majority anesthetic agents that we use like midazolam, Propofol, and fentanyl have depressive effect on the respiratory system, so careful attempt should be directed towards administering these drugs to the patients with these conditions.

E-cigarettes were thought to be a safe alternative to traditional tobacco smoking; however popcorn lung can be caused by inhaling the flavoring agents present in E-cigarettes. This condition can lead to patients being hypoxic and hypercapnic, and this can lead to a higher chance of having post anesthesia complications. In our study we would like to emphasize the importance of patient’s education on respiratory effects of e-cigarettes and investigate if there are any necessary actions that should be done in pre-op evaluations of the population of e-cigarettes smokers before providing anesthesia. In previous studies, Continuous Positive Airway Pressure (CPAP) has been suggested as one way of reducing post-operative anesthesia complications by improving respiratory failure. CPAP can improve respiratory failure by recruiting alveoli, reducing airway resistance, and improving lung expiration, leading to improved gas exchange and decreased hyperinflation [22]. We would like to investigate if spirometry tests or other available methods of preoperative screening would be efficient in the oral surgery settings for evaluation of long-term e-cigarettes smoker’s respiratory function, before determining if they are good candidates for sedations. We would also like to evaluate CPAP as a post-operative therapy in these patients to help reduce respiratory events. At this time there are no guidelines regarding e-cigarette smoking length and respiratory function depression during anesthesia, since e-cigarettes have not been available and in wide use for a long period of time. We think further studies need to be directed towards this important topic.

## Conclusion

Many individuals are under the impression that the use of e-cigarettes is considerably safer than the use of traditional cigarettes. However, it is well established that exposure to flavoring agents such as diacetyl (2,3-butanedione) diketone and 2,3-pentanedione may increase the risk of inflammatory pulmonary disease and ultimately bronchiolitis obliterans. Given the elevated levels of these compounds in e-cigarettes there is a need to further investigate the role of compound concentration in the development of inflammatory pulmonary disease. Also, due to the relative paucity of literature and the rapid increase in utilization of the e-cigarette it is imperative that we further investigate and develop pre-operative screening and post-operative management protocols for the safe and efficacious treatment of this patient population.

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