



Life-Threatening Effects of Bronchiolitis Related to Electronic Cigarette Use

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ABSTRACT

Bronchiolitis, characterized by inflammation of the bronchioles, presents significant health risks, particularly to infants, the elderly, and those with preexisting respiratory conditions. Traditionally associated with viral infections, bronchiolitis has recently been linked to electronic cigarette (e-cigarette) use, a trend that has surged in popularity over the past decade. While e-cigarettes are often marketed as safer alternatives to traditional smoking and are seen as viable tools for smoking cessation, emerging evidence suggests they may contribute to the onset or exacerbation of bronchiolitis and other respiratory conditions. To address these concerns, we recommend a prescription model for e-cigarettes, particularly in the context of smoking cessation. This model would involve prescribing the minimum effective dose of e-liquid, tailored to individual factors such as age, gender, and health status, to reduce the risk of adverse effects. Additionally, developing a screening tool to assess the risk of e-cigarette or vaping-associated lung injury (EVALI) is crucial before recommending e-cigarettes as a cessation aid. Furthermore, we propose the implementation of a physical alert system, similar to those used for steroid or anticoagulant medications, to track the specific substances in e-liquids. This would aid clinicians in swift diagnosis and management. As the e-cigarette market continues to grow, careful regulation and further research are essential to prevent the public health consequences seen in the tobacco industry.

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Bronchiolitis refers to the inflammation of the small airways in the lungs, known as the bronchioles. Bronchiolitis poses significant health risks particularly in vulnerable populations such as infants, the elderly and individuals with pre-existing respiratory conditions. Traditionally associated with viral infections, bronchiolitis has recently garnered attention in the context of electronic cigarette (e-cigarette) use. E-cigarettes, initially marketed as a safer alternative to traditional tobacco smoking, have seen a dramatic rise in popularity over the past decade. This increase in usage coincides with a growing body of evidence linking e-cigarette

use to various respiratory issues, including the exacerbation and potential initiation of bronchiolitis [1]. The regulation of recreational e-cigarette usage is beyond the scope of this commentary, and instead, this commentary will discuss the use of e-cigarettes concerning smoking cessation.

It is known that e-cigarettes are a feasible substitute for tobacco smoking as e-cigarettes can mimic the somatic, psychosocial, and personality-centric aspects that were formerly experienced through tobacco smoking and may, therefore, support long-term smoking cessation [2]. Despite these benefits, regulations need to be implemented by health policymakers to prevent or limit the deleterious side effects of e-liquids within e-cigarettes such as diffuse alveolar haemorrhage and hypersensitivity pneumonitis [1]. One such regulation may involve the use of an e-cigarette prescription model for individuals who wish to cease tobacco smoking. Healthcare professionals prescribe certain medications to patients to avoid overdose and simultaneously avoid under-treatment, which is reflected in the drug dose, frequency, route of administration and drug interactions. As e-cigarettes contain bioactive compounds, such as nicotine, aldehydes and volatile organic compounds, it is essential to prescribe the minimum effective dose of e-liquid within an e-cigarette to facilitate weaning from tobacco. The challenge, therefore, is to ascertain what prescription regime will provide clinical benefit with minimal toxicity depending on key pharmacokinetic factors such as age, gender, body weight, renal function and so forth. We recommend that researchers should conduct randomised clinical trials with adequate statistical power to improve our understanding of the minimum effective dose in e-liquids specifically for individuals on a smoking cessation regimen.

Numerous reports from 2019 to 2022 have highlighted growing evidence of cardiovascular harm from e-cigarette use. Specifically, e-cigarette use has been linked to increased arterial stiffness, elevated blood pressure, oxidative stress, myocardial fibrosis and coronary vascular disease. Additionally, e-cigarettes reduce myocardial blood flow during exertion, impair endothelial function and decrease nitric oxide production [3-5]. Additionally, e-cigarette use has been associated with a statistically significant higher incidence of asthma, respiratory disease, COVID-19 infection, wheezing and myocardial infarction [6].

More recent updates on the cardiovascular and pulmonary effects of electronic cigarette use show there are many other toxicant exposures from smoking and vaping that can increase the risk of disease. However, it is likely that the reduced exposure to toxicants from vaping relative to smoking reduces the risk to health of those who use vaping products to quit smoking [7]. A recent systematic review found that among individuals who experienced side effects, the most commonly reported were throat irritation, coughing and mouth irritation [8]. Notably, there was no mention of cardiovascular or respiratory side effects. However, the level of side effects reported in this systematic review was generally lower than those observed in previous studies. This discrepancy may be attributed to differences in the reporting time window as the study utilised a shorter timeframe for capturing adverse effects. [Table 1](#) highlights a range of studies that discuss the cardiovascular and respiratory side effects of e-cigarettes.

Table 1. Showing research of electronic cigarette cardiovascular and respiratory harms including the title, study design, author and conclusion from the study (N = 10)

| Title | Authors | Study design | Study conclusion |
|--|-----------------------------|-------------------|--|
| E-Cigarettes and Cardiopulmonary Health: Review for Clinicians | Neczypor et al. (2022) [4] | Literature review | Clinicians should monitor the health risks of e-cigarette use, discourage nonsmokers and adolescents from using e-cigarettes, and discourage smokers from engaging in dual use without cigarette reduction or cessation |
| Impact of Electronic Cigarette Vaping on Cerebral Ischemia: What We Know So Far | Siegel et al. (2022) [9] | Literature review | The addictiveness of nicotine coupled with a myriad of micro- and macro-biological changes in the brain have made growing usage of EC a significant public health concern. Moreover, the other solutes in an e-liquid and metals of the EC coil comprise an additional concern that ECs may also be inducing novel neurotoxic effects compared to conventional tobacco products and cigarettes |
| Cardiopulmonary Consequences of Vaping in Adolescents: A Scientific Statement from the American Heart Association | Wold et al. (2022) [10] | Literature review | Thus far, the overall evidence suggests that acute cardiovascular effects of e-cigarettes may accrue over time with prolonged use, leading to cardiovascular disease in long-term e-cigarette users |
| Acute Effects of Electronic Cigarettes on Vascular Endothelial Function: A Systematic Review and Meta-analysis of Randomized Controlled Trials | Meng et al. (2022) [11] | Systematic review | Evidence from our pooled analyses indicated that acute inhalation of e-cigarettes leads to negative changes in vascular endothelial function. E-cigarettes cannot be used as an alternative to public health strategies for tobacco control and should not be considered cardiovascular safety products. More future research should be conducted to verify our findings. |
| Increased Vulnerability to Atrial and Ventricular Arrhythmias Caused by Different Types of Inhaled Tobacco or Marijuana Products | Qiu et al. (2023) [12] | Literature review | These pathophysiological results indicate that tobacco and marijuana products can induce arrhythmogenic substrates involved in cardiac electrical, structural, and neural remodeling, facilitating the development of arrhythmias. |
| Association Between E-Cigarettes and Asthma in Adolescents: A Systematic Review and Meta-Analysis | Li et al. (2022) [13] | Systematic review | This meta-analysis clearly establishes that both current use and ever use of E-cigarettes have significant associations with asthma in adolescents. |
| E-Cigarette Use: Device Market, Study Design, and Emerging Evidence of Biological Consequences | Snoderly et al. (2021) [14] | Literature review | Electronic cigarette use is associated with both acute lung injury and subclinical dysfunction to the lung and vasculature that may result in pathology following chronic use. |
| E-Cigarette Use, Small Airway Fibrosis, and Constrictive Bronchiolitis | Hariri et al. (2022) [15] | Literature review | The histopathologic pattern of small airway-centered fibrosis, including constrictive bronchiolitis, with vaping, potentially defining a clinical and pathologic entity associated with e-cigarette use. |
| Biomarkers of Airway Immune Homeostasis Differ Significantly with Generation of E-Cigarettes | Hickman et al. (2022) [16] | Literature review | Results indicate disrupted immune homeostasis in fourth-generation e-cigarette users. |
| Pulmonary Health Effects of Electronic Cigarettes: A Scoping Review | Gugala et al. (2022) [17] | Scoping review | Evidence indicates that e-cigarette use, especially dual use, leads to negative pulmonary effects and adverse outcomes. |

We currently know that aerosolisation reduces the dangers associated with smoke inhalation and ideally streamlines the composition of inhaled particles. Despite this, there are several gaps in the scientific community's collective knowledge of e-cigarette side effects. Firstly, the wide range of device designs, different nicotine solution formulations and varying usage patterns among individuals present considerable challenges in precisely evaluating the true toxicological impact of e-cigarettes on the respiratory and cardiovascular systems. The variability in device temperature settings, coil metal element materials and liquid compositions can lead to differences in the production of harmful byproducts, such as formaldehyde and acetaldehyde, which may contribute to respiratory irritation and long-term lung pathology.

Additionally, the lack of standardised testing protocols and the evolving nature of e-cigarette technology make it difficult to establish clear comparisons between the severity of toxicological effects from e-cigarettes and those from traditional combustible cigarettes. Further research is needed to better understand the potential risks associated with prolonged e-cigarette use, particularly in vulnerable populations such as individuals with pre-existing cardio-respiratory conditions or immunosuppression.

Another area where knowledge is lacking concerns the effects of e-cigarettes on teenagers. At this time of writing, no existing studies have directly examined cardiovascular health in adolescents under 18 years of age who may be more sensitive to acute toxicities. This is particularly concerning given that adolescents represent a key demographic likely to use e-cigarettes extensively, often experimenting with vaping at an early age and engaging in frequent or heavy use. Due to their ongoing physiological development, including the maturation of the cardiovascular and respiratory systems, adolescents may be at greater risk for adverse health effects from e-cigarette exposure. Without direct studies evaluating the cardiovascular impact in this age group, there remains a critical gap in understanding the potential long-term health consequences.

Furthermore, a screening tool could be devised to assess individuals at risk of developing bronchiolitis obliterans or any other form of e-cigarette, or vaping, product use associated lung injury (EVALI) before advising individuals to use e-cigarettes as an adjunct for a smoking cessation regimen. Interestingly, the Illinois Department of Public Health (IDPH) created and administered a structured questionnaire to EVALI patients as part of the EVALI outbreak investigation within the USA in 2019 [18]. The proposed screening tool should include elements from the IDPH questionnaire to assess for the presence of risk factors for bronchiolitis obliterans such as counterfeit THC-containing products, recent use of combustible marijuana or the use of nicotine-containing e-cigarettes more than five times per day [4]. A standardised screening tool based on risk factors with significant weighting could be used to generate a risk score. A risk score can then facilitate risk stratification to guide clinicians on how to advise individuals who seek to cease tobacco smoking.

Landman et al. also described difficulty in establishing the causal agent that resulted in the patient developing bronchiolitis obliterans, as the patient vaped multiple substances of which more than one may have been the cause of the pulmonary insult [1]. In the UK, it is common practice for patients to keep a blue card or yellow book in close possession which represents the current use of steroid or anticoagulant medication, respectively [20-21]. The reason for this practice is to allow clinicians to understand the exact medication a patient currently uses to inform their diagnostic reasoning or contraindications to treatment. Given the diagnostic

challenge encountered by Landman et al., we recommend that a similar physical alert system should be considered for individuals who use e-cigarettes with information on the specific substances within the e-liquid to allow for swift diagnosis and appropriate management by clinicians.

It is hoped that the recommendations in this article may facilitate improved regulation of e-cigarettes and associated aerosolization devices. The exponential growth of the e-cigarette market and lack of definitive regulation on e-cigarettes may lead to the repetition of similar public health consequences we have witnessed in the tobacco industry since approximately 70 years ago until the present day. Additionally, the growing prevalence of bronchiolitis obliterans in economically developed countries warrants further research and collaboration between health policymakers to ensure the safe use of e-cigarettes and avoid unnecessary healthcare costs.

Declarations

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