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EDITORIAL

Vaping and Puffing: Know your Risks / Your Life is in Danger

Antonis S. Manolis, MD,¹ Theodora A. Manolis, MD²

¹ *Athens University School of Medicine, Athens, Greece*

² *Red Cross Hospital, Athens, Greece;*

E-mail: asm@otenet.gr

Abstract

The recent spate of lung illnesses and deaths in e-cigarette users has alarmed the regulatory authorities mainly in the US, where the death toll already counts >30 cases, but is also of great concern to global authorities and of course to the vaping community. The issues of e-cigarette toxicity are herein reviewed. *Rhythmoss 2019;14(4):67-70.*

Key Words: e-cigarette; vaping; tetrahydrocannabinol; pneumonitis; acute respiratory distress syndrome; lipoid pneumonia; e-cigarette explosion; cardiovascular disease

Abbreviations: CV = cardiovascular; CDC = Center for Disease Control; EVALI = e-cigarette, or vaping, product use associated lung injury; FDA=Food & Drug Administration; THC=tetrahydrocannabinol

Introduction

Initially conceived as a smoking cessation strategy and interim stage or a means to bridge the period until quitting,

e-cigarette use has skyrocketed, especially among teens, with data for 2019 showing more than a quarter of high school students being recent or current e-cigarette users in the US (<https://medicalxpress.com/news/2019-10-state-e-cigarette-vaping-deaths.html>). However, the recent news of the outbreak of deaths due to a mysterious lung illness has alarmed the American and global community.¹ Prior studies had already pointed to several ill health effects incurred by e-cigarette smoking, stressing the adverse effects of nicotine, ill effects of exposure to harmful chemicals, toxicants and even carcinogens, but also the stronger effects on cytotoxicity, vascular dysfunction, and angiogenesis of e-liquid flavorings compared to nicotine; however, the recent developments were quite unexpected (Table 1).²⁻⁷

Deaths / Lung Disease / Respiratory Failure

The first 33 deaths due to vaping have recently been reported in the US (www.cnn.com/2019/10/17/vaping-illness-deaths-climb-to-33-as-outbreak-spreads-and-doctors-worry-flu-season-could-make-it-worse.html) and this outbreak has alarmed the Medical Authorities and should be a great concern among the vaping community. The Center for Disease Control (CDC) has issued a warning about these calamities attributed to a severe form of lung disease linked to electronic cigarettes and other vaping devices; the warning states that people “should refrain from using e-

cigarette, or vaping products, particularly those containing tetrahydrocannabinol (THC)” while authorities work on discovering the cause of these lung illnesses (www.cdc.gov/media/releases/2019/p1011-guidance-health-lung-injury.html). The number of the e-cigarette, or vaping, product use associated lung injury (EVALI) has recently climbed to ~1480 cases in 49 states; ~70% of the patients are male, ~80% are <35 years, half are <25 years, with 16% aged ≤18 years (www.cdc.gov/mmwr/volumes/68/wr/mm6841e3.htm).¹ The deaths were reported in 21 states, with New York reporting the youngest victim, a 17-year-old boy. Almost all cases of EVALI involved mixture with a cannabis product, as they used vaping liquid that contained vitamin E acetate and THC (the psychoactive chemical derived from marijuana). A broad range of chemicals are being investigated by the FDA laboratory, including nicotine, THC, additives, pesticides, opioids, poisons and toxins. In addition to these deaths, a man in Texas was also killed after an e-cigarette he used exploded in his face and tore his carotid artery causing a massive stroke.

Vaping has been linked to 200 adverse effects on UK e-cigarette users, including pneumonia, cardiac and other disorders (<https://www.thesun.co.uk/news/10066110/vaping-death-toll-rises-diseases-surge/>). Although officially no deaths have been announced in the UK, two deaths from lipoid pneumonia have been reported among vapers.

Table 1. Adverse health effects of e-cigarettes

- *Death from lung injury (EVALI) and respiratory failure (suspected toxicity from chemicals / ?THC)*
- *Pneumonitis / Lipoid pneumonia / ARDS*
- *Health impact of unsafe chemicals and toxicants*
- *Health impact of heavy metals*
- *Carcinogenic potential*
- *Nicotine poisoning*
- *CV events (e.g. increased blood pressure and heart rate, triggering of MI)*
- *Worse pulmonary-related health outcomes (respiratory tract irritation, bronchitis, cough, emphysema)*
- *Proinflammatory effect / Immunosuppression*
- *CNS effects (behavioral changes, memory impairment, addiction)*
- *Ocular, throat, mouth, skin irritation*
- *Exhaled air-pollutants, e.g. PM2.5 (source of first- and second-hand PM2 exposure) / PM2.5-induced CV and pulmonary toxicity*
- *E-cigarette explosion injuries*

ARDS = acute respiratory distress syndrome; CNS = central nervous system; CV = cardiovascular; EVALI = e-cigarette, or vaping, product use associated lung injury; MI = myocardial infarction; PM = particulate matter; THC = tetrahydrocannabinol

Pneumonitis / Lipoid Pneumonia / ARDS

A case of hypersensitivity pneumonitis was reported last year in an 18-year-old after vaping that progressed to acute respiratory distress syndrome requiring intubation and finally responding to treatment with steroids.⁸

A preliminary report was just published in the New England Journal of Medicine of 53 patients (median age 19 years) indulged in vaping who were afflicted by the lung disease (EVALI).⁹ All patients had bilateral lung infiltrates on chest imaging. One third required intubation and mechanical ventilation and 1 patient died. Although patients reported using a variety of products and devices, 84% admitted to using THC. The authors concluded that “this cluster of illnesses represents an emerging clinical syndrome or syndromes” that should be further investigated.

A growing number of vaping-related “lipoid pneumonia” cases are being reported in young persons (18-35 years) with bilateral lung infiltrates on chest x-ray.¹⁰ A recent pathology report refuted the possibility that vaping-associated lung injury may represent exogenous lipoid pneumonia. These investigators reported their findings of lung biopsies from 17 patients (13 men; median age 35 years) who presented with acute or subacute lung disease with bilateral lung infiltrates, all of whom had a history of vaping (71% with marijuana or cannabis oils).¹¹ They suggested that their pathology findings point to a form of airway-centered chemical pneumonitis from one or more inhaled toxic substances rather than exogenous lipoid pneumonia as such, but the agents responsible remain unknown. Despite treatment with glucocorticoids and maximum supportive care, two patients with diffuse alveolar damage died.

After the spate of illnesses linked to vaping (EVALI), states in the US have started to push through legislation banning use of e-cigarettes for anyone under 21. Michigan was the first state to ban the sale of flavored nicotine vaping products in stores and online. The state governor stated that the ban will also prohibit “misleading marketing of vaping products, including the use of terms like ‘clean,’ ‘safe,’ and ‘healthy,’ that perpetuate beliefs that these products are harmless”. Governors are calling for prohibitions on flavors like bubble gum, cotton candy and banana split, which many consider are meant to entice young people into trying vaping. In some states, lawmakers are contemplating raising taxes on vaping products in order to discourage their use. The US government announced September 11, 2019 that it is also contemplating a nation-wide ban on flavored e-cigarette products.¹² Massachusetts was the first state to issue an outright ban on all e-cigarette devices in September 2019.

Cardiovascular Effects / Myocardial Infarction

Nicotine exerts pharmacologic effects that could contribute to acute cardiovascular (CV) events and accelerated atherogenesis.¹³ Although the risks of nicotine without tobacco combustion products (cigarette smoke) seem to be low compared to cigarette smoking, they are still of concern especially in people with CV disease. In addition to nicotine, e-cigarettes emit other potentially harmful constituents like carbonyls that include aldehydes, such as formaldehyde, acetaldehyde, and acrolein, which result from thermal degradation of propylene glycol and glycerol (most commonly used solvents in e-liquids).⁷ Aldehydes are cytotoxic, and may produce adverse CV effects including a sympathomimetic effect raising blood pressure and heart rate, as well as a prothrombotic effect. Acrolein has also been noted to increase blood pressure, while it has prothrombotic, negative inotropic and arrhythmogenic effects, and it may induce vascular injury.

It was recently reported that daily e-cigarette use (n=776), adjusted for smoking conventional cigarettes as well as other risk factors, was associated with increased risk of myocardial infarction (MI) in a sample of National Health Interview Survey (NHIS) individuals (N=69452).¹⁴ A study in 42 participants indicated that habitual e-cigarette use was associated with a shift in cardiac autonomic balance toward sympathetic predominance and increased oxidative stress, both associated with increased CV risk.¹⁵

Recent experimental data have indicated that acute exposure to vaping with use of flavored e-liquids exacerbates endothelial dysfunction, which often precedes CV diseases.⁶ Furthermore, e-cigarette exposure causes a pro-inflammatory response from human neutrophils.⁵ Thus, several components of e-cigarettes with different mechanisms may contribute to the emergence of CV adverse effects.

Injuries and Deaths from e-Cigarette Explosions

Although e-cigarette explosions were thought to be isolated events, the injuries reported in the New Journal of Medicine in 2016 among 15 patients add to growing evidence that e-cigarettes are a public safety concern. These 15 patients were treated for severe injuries from e-cigarette explosions due to the lithium-ion battery component; these injuries included flame burns (80%), chemical burns (33%) and blast injuries (27%).¹⁶ The injuries were located in the face (20%), hands (33%), and thigh or groin (53%), and produced substantial cosmetic, functional and disfiguring consequences. Since 2016, the published reports of e-cigarette explosion total 35 to date, including case reports and case series. One full report in

2017 concerned 30 injured patients with a mean age of 30 years, of whom 26 required hospital admission and 9 required surgery.¹⁷ The mean size of burn was 4% total body surface area. The thighs, hands, and genitalia were the most common sites of injury. In summary, according to the latest e-cigarette injury surveillance from the US, from 2015 to 2017, there were an estimated 2035 e-cigarette explosion and burn injuries presenting to US hospital emergency departments.¹⁸ Finally, according to media reports, there have been at least two deaths attributable to e-cigarette explosions (<https://edition.cnn.com/2019/02/05/health/exploding-vape-pen-death-trnd/index.html>).

Regulatory Authorities

More than 100 countries in the world regulate e-cigarettes, at the level of sale, marketing, packaging, manufacturing, taxation, reporting, and clean air laws. The tendency is to *treat tobacco smoking and vaping equivalently in workplace policies*.¹⁹ However, some countries have already banned e-cigarettes and several are considering to do it after the latest developments. Massachusetts became the first American state to issue an outright ban on all e-cigarette devices in September 2019.

As mentioned, the CDC has issued a warning against use of vaping (www.cdc.gov/media/releases/2019/p1011-guidance-health-lung-injury.html). More specifically, the CDC recommends that e-cigarette or vaping products that contain THC should not be used, as THC-containing products seem to play a role in this outbreak. In addition, the CDC warns that no youth, young adult, or pregnant women should be using any e-cigarette, or vaping, product, regardless of the substance. A similar warning was issued by the FDA recommending to stop using THC-containing vaping products and any vaping products obtained off the street (www.fda.gov/consumers/consumer-updates/vaping-illness-update-fda-warns-public-stop-using-tetrahydrocannabinol-thc-containing-vaping).

However, it's only recently that most authorities are coming to grips with the reality that use of e-cigarettes has not helped with or contributed much to the reduction of tobacco smoking, the reduction of harm has been minimal, if at all, as many individuals end up using both e-cigarettes and conventional ones, worse pulmonary-related health outcomes have been reported, there is massive adoption and use of e-cigarettes among the youth, while the evidence for the risks of e-cigarette use is mounting, especially with the recent outbreak of lung injuries and deaths.^{16, 20, 21} This grisly reality paves the way for changes in e-cigarette policies worldwide.²⁰

Conclusion

Although the number of injuries from e-cigarette explosion is not negligible, more dreadful is the fact that use of e-cigarettes or vaping turns out to confer an unexpectedly high risk of death due to a curious lung injury (EVALI). The specific chemical exposure(s) causing the outbreak is currently unknown. While the investigation is ongoing, the US CDC and FDA recommend that persons consider refraining from using e-cigarette, or vaping products, particularly those containing THC.¹ As a recent BMJ paper indicates, the effectiveness of e-cigarettes as a smoking cessation intervention, their impact at a population level, and whether they are less harmful than conventional tobacco products are highly controversial.²² Studies to date have shown that e-cigarettes confer adverse biologic effects on organ and cellular health in humans, in animals, and in vitro, including co-mutagenic and cancer-initiating effects of e-cigarette vapor and several adverse CV and respiratory effects of e-cigarette constituents.^{7, 23} Whether the ill effects of e-cigarette use on the respiratory and CV systems are less than those of tobacco products has not been settled. Rather, the acute lung illness (EVALI) that has recently emerged speaks otherwise, indicating that we are dealing with a formidable and lethal smoking alternative. However, the fight against this health enemy will not be easy as vaping is currently a multibillion-dollar industry that appeals to current and former smokers, with a growing wave among the youth.

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