

# Health Hazards and Complications Associated with Electronic Cigarettes: A Review

Aşkın Gülşen<sup>1</sup> , Berat Uslu<sup>2</sup> 

<sup>1</sup>Department of Pneumology, Interdisciplinary Allergy Outpatient Clinic, University of Lübeck, Lübeck, Germany

<sup>2</sup>Department of Chest Diseases, Yedikule Chest Diseases and Thoracic Surgery Education and Research Hospital, İstanbul, Turkey

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## Abstract

Electronic cigarettes (ECs) are devices that vaporize and release a sweetened liquid containing nicotine as a substitute for burning tobacco. EC manufacturers have suggested that “vaping” is a safer alternative to conventional smoking because of the potential reduction of exposure to toxic substances. In 2019, National Youth Tobacco Survey reported that 10.5% and 27.5% of middle and high school students used ECs in the previous 30 days (0.6% and 1.5% in 2011, 3.3% and 11.7% in 2017, and 4.9% and 20.8 in 2018), respectively. Increased EC use among younger individuals is mainly because of the widespread perception that ECs are relatively less harmful than conventional cigarettes as they do not involve smoking tobacco and contain little or no nicotine. This review suggests that ECs may not be completely harmless. There are increasing number of case reports on various complications arising from using ECs, which are especially popular among young individuals and could negatively affect their health. Reported complications include lipoid pneumonia, acute eosinophilic pneumonia, hypersensitivity pneumonia, organizing pneumonia, diffuse alveolar hemorrhage, multiple reactive pulmonary nodules, subacute bronchiolitis, mouth and tongue injuries, dental injuries, complex facial fractures, thermal injuries, nickel contact allergy, C1 and C2 fractures, and fatal intoxication after ingesting liquids. Complications that develop directly from the substances in the devices and those resulting from device explosion and burning are being reported with increasing frequency. There is an urgent need for legislation and restriction regarding the sale of these devices considering their increasing frequency of use by younger individuals.

**KEYWORDS:** Burns, e-cigarette, electronic cigarette, explosions, injuries, pneumonia

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## INTRODUCTION

Electronic cigarettes (ECs) are devices that vaporize and release a sweetened liquid containing nicotine as a substitute for burning tobacco. EC manufacturers have suggested that “vaping” is a safer alternative to conventional smoking considering the potential reduction in exposure to toxic substances. First-generation ECs were similar in shape to cigarettes; however, new-generation ECs are designed as pens, cartridges, boxes, lipsticks, USB sticks, or other everyday consumable products. ECs have various names, including e-cigs, e-cigars, e-shisha, electronic hookahs, personal vaporizers, electronic vapor, vapes, vape pens, and atomizer tank systems.

The concept of ECs dates back to 1963 when Herbert A. Gilbert received the first patent for a smokeless, non-tobacco cigarette [1] that was intended to allow safe smoking of heated, moist, flavored air without burning tobacco. Subsequently in 2003, Hon Lik, a Chinese pharmacist, invented the first EC, which became commercially available in China 1 year later [2]. ECs were first sold in the US in 2007 but were not legally regulated until 2016 [3]. During these years, EC manufacturers produced an increasingly wide range of designs. In the past decade, with the increased use of social media, ECs have become widespread globally and their use has increased exponentially. Consumption of ECs is being steadily encouraged by manufacturers but in the absence of adequate legislature and regulatory control over the devices and composition of e-liquids.

In 2015, the UK Department of Health reported that ECs could be 95% less harmful than cigarettes containing tobacco [4]. Moreover, in 2018, the American Cancer Association issued a position statement encouraging EC use rather than smoking using traditional methods [5]. However, the European Federal Institute for Risk Assessment Institute and German Cancer Research Center have warned all countries regarding underestimating the potential dangers of ECs [6].

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**Address for Correspondence:** Aşkın Gülşen, Department of Pneumology, University of Lübeck, Interdisciplinary Allergy Outpatient Clinic, Lübeck, Germany

E-mail: askingulsen@hotmail.com

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Between 2011 and 2017, EC use increased significantly, especially among secondary and high school students in the US [7]. In the 2019 National Youth Tobacco Survey, 10.5% of middle school students and 27.5% of high school students reported using ECs in the previous 30 days, with respective rates of 0.6% and 1.5% in 2011, 3.3% and 11.7% in 2017, and 4.9% and 20.8% in 2018 [7]. The main reason for this steady increase in use of ECs in younger individuals is the widespread perception that ECs are less harmful than conventional cigarettes as they do not involve smoking tobacco and contain little or no nicotine.

Given the controversy surrounding the use of ECs, this literature review was undertaken to investigate the risks and complications associated with ECs.

### Clinical and Research Consequences

Four international databases (Web of Science, PubMed, Google Scholar, and Scopus) have been scanned to find suitable articles / case reports / case series for our review. Only English articles were taken. The search term will be used as follows: "e-cigarette", OR "electronic cigarette", AND "injuries", OR "explosion", OR "burn", OR "complication", OR "health hazard".

### Structure and Properties

EC devices have an outer casing made of stainless steel and contain three inner components, i.e., a power supply (battery), an electric heating element (nebulizer and atomizer), and an aromatic liquid (cartridge) for evaporation [8]. The largest component of the EC is the rechargeable power supply. Recently, lithium batteries and light-emitting diode lamps have been developed so that the devices can be lit during use. When an EC user breathes through the nozzle, a pressure-sensitive circuit activates the atomizer, which then heats the liquid in the cartridge and produces a smoke-like vapor. The vapor is then drawn through the mouthpiece and exhaled by the user. Unlike tobacco smoking, combustion does not occur [9].

The cartridge typically houses a liquid consisting of propylene glycol and/or vegetable glycerin, water, and a sweetener. The resulting aerosol consists of fine and ultrafine liquid particles that may include formaldehyde, acetaldehyde, acrolein, reactive oxygen compounds, and metals such as nickel, chromium, or lead, depending on the sweeteners and flavors added to the liquid [10]. These pollutants are usually present

in the EC aerosol in much smaller amounts than those in tobacco smoke but can be present at similar or higher concentrations under certain operating conditions [10]. Formaldehyde is present in ECs in concentrations similar to lead and chromium concentrations in tobacco cigarettes, whereas nickel was found to be present at higher concentrations [11]. The properties and harmful effects of substances in ECs are presented in Table 1.

Globally, more than 8,000 substances are presently used as flavors and aromas in ECs, with the most popular flavors being tobacco, mint, chocolate, and various fruits. ECs with strawberry, caramel, and gelatinous candy flavors are also marketed to cater for as many tastes as possible. However, very few of these flavoring substances have been tested for safety in humans.

A typical tobacco cigarette contains approximately 10–15 mg of nicotine, approximately 10% (1-2 mg) of which reaches the systemic circulation [12]. The liquids used in ECs generally contain 14.8-87.2 mg/mL of nicotine; however, they may also contain less nicotine concentrations (0-36 mg/mL) or be nicotine free [9, 13]. However, the amount of nicotine in the e-liquid that reaches the circulation varies depending on a number of factors, including duration and frequency of inhalation and vapor density. In some samples, the nicotine content of the cartridge fluid does not match the amount stated on the label [13]. In simulated EC use, the amount of nicotine per puff varied between 0 and 35 µg, depending on the product [13, 14]. This finding indicates that approximately 30 puffs of an EC deliver 1 mg of nicotine, which is equivalent to the amount delivered by one conventional cigarette. A puff from an EC with the highest nicotine content delivers 20% of the nicotine from a puff from a regular cigarette [13]. However, the level of exposure to nicotine in EC users varies considerably.

### Health Hazards

Evidence regarding the effects of ECs on human health is limited because of the wide range of products available and the small number of investigations performed. A review by Meo et al. [15] mentioned that ECs can cause nausea, vomiting, headache, dizziness, suffocation, burns, upper respiratory tract irritation, dry cough, dry eye, production of cytokines, release of pro-inflammatory mediators, allergic inflammation of the airway, decreased synthesis of nitric oxide in the lungs, changes in gene expression in the bronchus, and increase the risk of lung cancer. The main carcinogenic substances found in EC vapor are formaldehyde, chromium, nickel, acetaldehyde, and tobacco-specific nitrosamines [11]. Furthermore, propylene glycol and glycerin, which are the main components of e-liquid in the cartridge, can irritate the eyes and respiratory tract, and their prolonged or repeated inhalation in a manufacturing environment may affect the central nervous system, behavior, and the spleen [11, 16]. The American Chemistry Council has warned against use of these substances to create fog in theaters because of their potentially harmful effects and as their repeated use may have negative effects on the central nervous system [16]. Moreover, recent research has shown that EC vapor is cytotoxic and oxidative and negatively impacts the functioning of alveolar macrophages [17]. Considering this, the inves-

### MAIN POINTS

- Electronic cigarettes are at least as harmful to health as conventional cigarettes, and are particularly dangerous because of the risk of explosion, fractures and thermal injuries as well as diseases of the lungs.
- The erroneous belief that ECs are less harmful to health than tobacco-containing cigarettes must be addressed with urgency.
- There is an urgent need for legislation and restriction regarding the sale of these devices in view of their increasing frequency of use among the younger individuals.

**Table 1.** Substances in electronic cigarette aerosol and their effects<sup>a</sup>

Ingredients	Function of the liquid	Health hazards
Propylene glycol	Main component of the liquid to produce aerosols	<ul style="list-style-type: none"> <li>• Respiratory tract irritation</li> <li>• Effect of long-term inhalation is unknown</li> </ul>
Glycerin	Main component of the liquid to produce aerosols	<ul style="list-style-type: none"> <li>• Effect of long-term inhalation is unknown</li> </ul>
Tobacco	Component of the fluid	<ul style="list-style-type: none"> <li>• Dependency potential</li> <li>• Cardiovascular diseases, Type-2 diabetes, tumor growth</li> <li>• It might affect fetal lung development</li> <li>• Toxic effects</li> </ul>
Diacetyl	Aroma of many sweet liquids	<ul style="list-style-type: none"> <li>• Suspected to cause bronchiolitis obliterans</li> </ul>
Benzaldehyde	Aroma (artificial bitter almond oil)	<ul style="list-style-type: none"> <li>• Respiratory tract irritation</li> </ul>
Cinnamom aldehyde	Aroma (Cinnamon)	<ul style="list-style-type: none"> <li>• Cytotoxic effect on cell cultures</li> </ul>
Acrolein	Occurs when heating the liquid	<ul style="list-style-type: none"> <li>• Poisonous</li> <li>• Irritant</li> </ul>
Acetaldehyde	Occurs when heating the liquid	<ul style="list-style-type: none"> <li>• Possibly carcinogenic (category 2B)</li> </ul>
Formaldehyde	Occurs when heating the liquid	<ul style="list-style-type: none"> <li>• Carcinogenic (category 1)</li> </ul>
Lead	Probably comes out of the wick/solder joints	<ul style="list-style-type: none"> <li>• Poisonous</li> <li>• Possibly carcinogenic (category 2B)</li> </ul>
Chromium	Probably comes out of the wick/solder joints	<ul style="list-style-type: none"> <li>• Carcinogenic (Category 1 for chromium-IV compounds)</li> </ul>
Nickel	Probably comes out of the wick/solder joints	<ul style="list-style-type: none"> <li>• Carcinogenic when inhaled (category 1)</li> </ul>
Tobacco-specific nitrosamines	Rare pollution in some individual liquids	<ul style="list-style-type: none"> <li>• Carcinogenic</li> </ul>
Fine and fine particles (PM2.5, PM10)	Occurs during evaporation of liquid	<ul style="list-style-type: none"> <li>• Particulates are associated with respiratory problems, chronic respiratory and cardiovascular disease exacerbations, reduced lung function, and premature death.</li> <li>• Health effects of the particles in the electronic cigarette aerosol are unknown.</li> </ul>

<sup>a</sup>Quoted from Schaller K, et al. [10], and permission was taken from © Georg Thieme Verlag KG.

tigators have questioned the widespread opinion that ECs are harmless.

The most commonly observed adverse effects of ECs are those concerning the impact of the inhaled liquids on the respiratory tract. Inhaled chemicals, particularly glycol and glycerol vapors and particulates, irritate the pharynx and upper and lower respiratory tracts and often cause dry cough [18]. In one study, 27 healthy subjects without asthma experienced a 2% reduction in forced expiratory volume in 1 s (FEV<sub>1</sub>)/forced vital capacity (FVC), an increase in FVC of 40 mL, and a decrease in FEV<sub>1</sub> by 30 mL as a result of acute exposure to propylene glycol for 1 min [19]. In another study on 101 individuals working in environments producing theater fog, a 5% reduction in FEV<sub>1</sub> and FVC was reported in those working within 10 feet of fog-producing machines [20]. These results demonstrate the effects of these substances on respiratory function. However, although it is clear that EC vapor causes acute bronchoconstriction, further research is needed. Moreover, EC vapor reduces the synthesis of nitric oxide in the lungs and increases airway resistance [21]. Despite being toxic and carcinogenic, EC vapor also affects

cellular genetics in a tobacco-like manner [14]. In a study conducted in mice, EC stimulated the production of cytokines, including interleukin (IL)-4, IL-5, IL-13, and immunoglobulin E, and increased airway hyperreactivity by increasing allergic inflammation [22]. These results suggest that EC vapor may be an important contributor to increased symptoms in patients with asthma.

Exogenous nicotine can cause nausea, vomiting, and dizziness depending on the dose inhaled or ingested. Furthermore, nicotine can exacerbate ulcerative colitis [23], and EC use may be associated with palpitations, chest pain, paroxysmal atrial fibrillation, and acute myocardial infarction [15, 23].

Nicotine has important effects on the nervous system, which can develop after using ECs that contain nicotine. For example, nicotine inhibits prenatal development of the autonomic nuclei in the brain stem, causes changes in the neocortex, hippocampus, and cerebellum in the early postnatal period, and delays maturation by affecting the limbic system during adolescence [24]. However, there has been a report of reversible cerebral vasoconstriction syndrome and headache in an EC user [23].

**Table 2.** Complications associated with electronic cigarettes

Author	Year	Complication
CBS NEWS [29]	2012	Mouth and tongue injuries
McCauley L. [30]	2012	Lipoid pneumonia
Hureaux J. [31]	2014	Subacute bronchiolitis
Thota D. [32]	2014	Acute eosinophilic pneumonia
Moore K. [33]	2015	Pneumonia and bilateral pleural effusion
Jablow LM. [34]	2015	Leg burn and injury
Maridet C. [35]	2015	Nickel contact allergy
Chen BC. [36]	2015	Death following intentional e-liquid intake
Ring Madsen L. [37]	2016	Multiple pulmonary nodules mimicking metastatic cancer
Shastry S. [38]	2016	Shotgun-like superficial injury and contusion
Rogér JM. [39]	2016	Oral trauma and dental avulsion
Paley GL. [26]	2016	Corneoscleral rupture and ocular burn
Archambeau BA. [40]	2016	Complex facial fractures and pneumocephalus
Vaught B. [41]	2016	Facial trauma and fractures
Brooks JK. [42]	2017	Extensive intraoral injuries
van der Meer DH. [43]	2017	Fatal intoxication after ingestion of liquids
Norii T. [44]	2017	C1 and C2 fracture
Foran I. [45]	2017	High-pressure injection injury of the finger
Sommerfeld CG. [46]	2018	Hypersensitivity pneumonia and ARDS
Agustin M. [47]	2018	Diffuse alveolar hemorrhage
Viswam D. [48]	2018	Respiratory failure and lipoid pneumonia
Hickey S. [3]	2018	Thermal Injuries
Khan MS. [49]	2018	Organizing pneumonia

ARDS: Acute respiratory distress syndrome

The effects of ECs on the urinary tract can be expected to be similar to those of conventional cigarettes; however, the relevant literature is limited. Furthermore, the effects of ECs on the reproductive system have not been fully investigated. Conventional cigarettes decrease semen volume and negatively affect sperm concentration and motility [15]. A report suggested that sweeteners used in ECs negatively impact sperm quality and damage the cells in the testicles that produce sperm [25]. The same report concluded that the substance used to produce cinnamon aroma slowed sperm motility and that a chewing gum flavor damaged the testicular cells that produce sperm.

Other adverse effects of nicotine include headache, insomnia, difficulty in falling asleep, dizziness, gingivitis, and black tongue, along with suicidal tendency as indicated in one report [15]. Furthermore, EC vapor causes ocular irritation and redness, along with dry eye [15]; therefore, continuous exposure to these substances is hazardous and may permanently damage the eyes [26].

**Effect on Smoking Cessation**

It is suggested that cigarette smokers can quit smoking or reduce the harm caused by continued smoking by using ECs. However, many studies report conflicting results regarding the of transitioning from tobacco to ECs [27]. Few randomized double-blind studies have investigated the efficacy of

ECs for smoking cessation. The overall evidence may be classified as either low or very low, making it impossible to draw reliable conclusions based on the available research. According to another report, ECs should not be recommended as effective smoking cessation aids until evidence of efficacy is presented [28].

**Complications of ECs**

ECs are becoming more popular than traditional cigarettes. Therefore, the number of reports on their side effects and complications are increasing. Case presentations are shown in Table 2 and are briefly summarized below.

**Report 1**

The first notification of mouth and tongue injuries caused by the explosion of an EC device was reported in 2012. The case involved a 57-year-old man and was covered by CBS News [29].

**Report 2**

A 42-year-old woman was admitted to hospital with a 7-month history of dyspnea, sputum production, and subjective fever. In the preceding months, she underwent multiple courses of antibiotic treatment. Her complaints coincided with the start of EC use. Computed tomography (CT) scans revealed a “crazy-paving” pattern in the upper and lower lobes bilaterally, with signs of interlobular septal thickening. Bronchoscopy

and bronchioalveolar lavage (BAL) revealed 48% neutrophils, 43% monocytes, 8% lymphocytes, and 1% eosinophils. Bacterial and viral cultures were negative. Lipid-laden macrophages secondary to chronic inflammation were detected on further examination of BAL. The diagnosis of lipoid pneumonia was established. Most EC brands contain glycerin, which when inhaled might cause lipoid pneumonia [30].

#### Report 3

In 2014, a 43-year-old patient with lung adenocarcinoma (stage pT3N0M1b) who had been smoking 20 cigarettes a day decided to switch to ECs on a friend's advice in an effort to quit smoking [31]. The patient vaped approximately 25 times daily using a liquid containing 19 mg/mL of nicotine, taking 5-6 puffs each time. According to the packaging, the liquid in the EC product contained glycerol (<90%), purified water (<10%), food flavoring, tobacco flavoring, and nicotine. After 48 h of vaping, the patient started coughing whitish secretions and developed progressive shortness of breath over a period of 1 week. His FEV<sub>1</sub> decreased from 3.06 L (73.7%) to 1.87 L (45.2%), and he was diagnosed with sub-acute bronchial toxicity caused by EC use [31].

#### Report 4

A 20-year-old man with no history of being unwell was hospitalized after 3 days of persistent cough, shortness of breath, and facial flushing. His symptoms had started an hour after using an EC. The patient was diagnosed with mild leukocytosis, and a chest radiograph showed subtle diffuse patchy reticulonodular opacities. Lung CT revealed diffuse ground-glass opacities that were more common in the upper and middle lobes than in the lower lobes. Large number of macrophages, eosinophils, and scattered benign respiratory epithelial cells was detected in the BAL fluid. The cell count showed 3% neutrophils, 2% basophils, 17% macrophages, and 74% eosinophils. No evidence of bacterial, viral, fungal, or parasitic infection or of a neoplasm was found on bronchoscopy, culture, or serum laboratory tests. The patient was found to have acute eosinophilic pneumonia and was successfully treated with a corticosteroid [32].

#### Report 5

A 43-year-old man who regularly vaped throughout the day for three consecutive days was admitted to hospital with acute dyspnea, pleuritic chest pain, and tachycardia. Physical examination revealed bibasilar crackles. The influenza panel was negative for influenza A and B. A chest radiograph revealed hypoinflated lungs with bibasilar parenchymal consolidation and associated pleural effusions bilaterally [33].

#### Report 6

A 30-year-old man sustained partial thickness burns to his right foot and knee after an EC battery exploded in his trouser pocket [34].

#### Report 7

A 52-year-old woman presented to hospital with an 8-month history of pruritic erythematous dermatitis on her right hand, which coincided with starting EC use. A dimethylglyoxime nickel spot test was positive. The patient reported holding the device with her right hand. The device was found to be worn and released nickel as a result of sweating of hands. So far, this is a unique report of contact allergy attributed to ECs [35].

#### Report 8

A 24-year-old woman was hospitalized after intentionally swallowing 3,000 mg of liquid nicotine intended for use in ECs. She was unconscious on admission and subsequently died despite cardiopulmonary resuscitation and aggressive support. Toxicology tests performed after resuscitation reported high plasma nicotine (>1,000 ng/mL) and cotinine levels. Magnetic resonance imaging revealed multiple acute infarctions consistent with severe anoxic brain injury [36].

#### Report 9

A 45-year-old woman with no significant medical history was admitted to the hospital for suspected dissemination of malignant disease. She had a 4-week history of abdominal pain and intermittent low-grade fever. A full-body CT scan revealed multiple nodules in the lungs and multiple metastatic lesions in the liver. She had a 20 pack-year history of smoking and had been using ECs (10 mg, 38 mg/mL) for the past 20 months. A liver biopsy showed nonspecific reactive changes. Positron emission tomography confirmed a positive tumor response. A small tumor was then resected thoracoscopically. Biopsy revealed inflamed lung tissue with no evidence of malignancy. Re-examination of the lung biopsy specimen revealed an area containing multinucleated giant cells, suggesting a foreign body reaction consistent with glycerin-based fats found in the droplets from EC vapor. The findings in this patient were thought to have developed as secondary reactions to glycerin exposure [37].

#### Report 10

A 26-year-old man who was a paid tester for an EC company sustained injuries after the battery in an experimental device he was testing exploded, causing the device to disintegrate and scatter like shrapnel. He was admitted to the emergency department by ambulance with burns to the upper abdomen, left shoulder, and chest [38].

#### Report 11

An 18-year-old man was hospitalized with oral and abdominal burns, oral lacerations, tooth fractures, and dental avulsion after an EC exploded in his mouth [39].

#### Report 12

In 2016, two cases of bilateral corneal burns, corneoscleral laceration, and prolapsed iris tissue were reported after explosion of an EC device. The patients were aged 45 and 16 years [26].

#### Report 13

A 59-year-old man with leukemia, hyperlipidemia, chronic back pain, and right hearing loss presented to the hospital after the explosion of an EC while he was vaping. The patient had bought the device via the Internet and had been using it for 2 days. He complained of epistaxis, blurred vision in his right eye, and hearing loss on the left side. A CT scan showed petrous, ethmoid, cribriform plaque, nasal choana, nasal septal, and right medial orbital wall fractures accompanied by pneumocephalus [40].

#### Report 14

A 20-year-old man was admitted to hospital with projectile point fractures of the anterior/posterior frontal sinus and right naso-orbital-ethmoid complex as a result of malfunction

tion and explosion of an EC. The battery was dislodged, and a flare of up to few meters was observed at the time of the explosion [41].

#### Report 15

An 18-year-old man presented to a clinic with extensive injuries to teeth and intraoral soft tissues. He stated that a sudden explosion had occurred immediately after he had filled an EC with e-liquid after having left the lithium ion battery to charge overnight. The device had exploded while he was placing the device in his mouth [42].

#### Report 16

A 42-year-old man was admitted to a hospital with cardiac arrest and poor neurological function. The information available suggested that he had swallowed a large amount of e-liquid containing nicotine. On admission, he had a plasma nicotine level of 3.0 mg/L (reference range for smokers, 0.01-0.05 mg/L). The patient died of post-anoxic encephalopathy despite all efforts and treatments. Nicotine e-liquids are known to contain very dense substances, and it should be known that deliberate ingestion of these fluids can lead to nicotine poisoning, cardiac arrhythmias, and other life-threatening conditions [43].

#### Report 17

A 27-year-old man was admitted to the emergency room after an EC had exploded in his mouth during use. He had recently replaced the EC battery with a new lithium ion battery. He complained of foreign body sensation, throat pain, and difficulty swallowing. A CT scan of the neck revealed fractures of the superior cortex of the anterior arch at C1 along with the presence of foreign bodies [44].

#### Report 18

This study from 2017 reported an EC explosion that resulted in high-pressure injection injury of the finger [45].

#### Report 19

A previously healthy 18-year-old woman presented to hospital with dyspnea, cough, and pleural pain after using an EC. She had started using the EC approximately 3 weeks earlier and then stopped using it 1-2 days before the onset of her symptoms. On admission, she had a respiratory rate of 32 breaths per minute and pulse rate of 130 per minute. Her oxygen saturation was at 84% at room air. CT angiography did not reveal an embolism. However, dependent opacities at both lung bases, interlobular septal thickening, and bilateral small to moderate pleural effusions were reported. She was intubated in the intensive care unit considering her deteriorating clinical status. The erythrocyte count was 900 and the leukocyte count was 340 (26% neutrophils, 13% lymphocytes, 14% monocytes, 25% mononuclear cells, and 22% eosinophils) in the BAL fluid. No growths were identified on bacterial or fungal culture. The diagnosis was hypersensitivity pneumonitis and acute respiratory distress syndrome secondary to EC exposure. The patient responded well to prednisolone [46].

#### Report 20

A 33-year-old man with a history of diabetes and epilepsy was admitted to the emergency department with worsening

dyspnea and hemoptysis. Nearly 2 weeks earlier, he had been diagnosed with community-acquired pneumonia and was treated with antibiotics but without complete resolution. The patient had been using ECs for the previous 2 months and had tried new flavors. A CT scan of the chest revealed areas of patchy consolidation and diffuse ground-glass opacities bilaterally. A BAL cell count revealed 30,000 erythrocytes and 800 leukocytes (42% neutrophils, 36% lymphocytes, 21% macrophages, and 1% eosinophils). Serological markers of inflammation were negative. A right wedge resection lung biopsy was performed; the diagnosis was bland pulmonary hemorrhage with no evidence of capillaritis or diffuse alveolar damage [47].

#### Report 21

A young female vaper was admitted to hospital with cough, fever, night sweats, and breathlessness. Her biochemical and inflammatory marker levels were normal. High-resolution CT revealed diffuse ground-glass infiltrates with reticulation. As bronchoscopic findings were inconclusive, she underwent a video-assisted thoracoscopic surgical biopsy and was diagnosed with lipoid pneumonia. The lipid source was suspected to be the plant-based glycerol in the EC she used [48]. Most brands of EC contain glycerin whose inhalation is associated with lipoid pneumonia [30] and acute eosinophilic pneumonia [32].

#### Report 22

This report, published in 2018, included 14 patients with thermal and blast injuries as a result of exploding ECs. The mean patient age was 28.6±8.6 years. Fifty-seven percent of the patients had third-degree burns, 29% had deep second-degree burns, and 14% had superficial second-degree burns [3].

#### Report 23

A 40-year-old woman was hospitalized with a 1-month history of increased shortness of breath and sharp chest pain bilaterally. She had been a cigarette smoker but had switched to ECs since the past 1 month in an effort to quit smoking. CT revealed multifocal, diffuse, confluent ground-glass opacities in the lung lobes bilaterally. Bronchoscopy results were normal. The results of bacterial and fungal cultures and viral serology were negative. Open lung biopsy was performed, and the histopathological diagnosis was organizing pneumonia [49].

## DISCUSSION

This review of literature reveals that ECs are harmful to health or at least as harmful as tobacco. In 2006, the World Health Organization declared that all forms of smoking are harmful to health and reported that the tobacco industry is "hiding" behind words such as "light" and "ultra-light" [50]. Terminology such as "menthol," "non-nicotine," "electronic," "vaping," "harmless," and "less harmful" can be added today. The erroneous belief that ECs are less harmful to health than tobacco-containing cigarettes must be addressed with urgency. Given the current scenario, it is clear that the fight against the tobacco industry needs to be stepped up.

The diversity of the cases reported in this review suggests that we are currently facing a problem of an unknown magnitude.

If we consider the problem only from the point of view of the lungs, then lipoid pneumonia [30, 48], subacute bronchiolitis [31], acute eosinophilic pneumonia [32], multiple reactive pulmonary nodules [37], hypersensitivity pneumonia [46], diffuse alveolar hemorrhage [47], and organizing pneumonia [49] are among the reported complications. All these complications are attributable to the substances contained in ECs that cause inflammatory and irritative reactions of the lungs. It is possible that lipoid pneumonia is caused by the inhalation of glycerin. However, the effects of other substances on the lungs are not fully understood. Our lack of knowledge about the substances or fragrances contained in EC liquids, the ability of EC devices to vaporize these liquids, and the frequency at which users inhale from these devices pose a challenge when attempting to determine the effects of ECs. Our personal experience is that there are many people who switch from cigarettes to ECs but end up using both. The diversity of EC devices and liquids is rapidly increasing as a result of loopholes in legislation. Therefore, it is not possible to individually examine the components of the e-liquids. The risk of injury associated with device explosion is another important issue. Hand/finger [35, 45], dental [39], corneal [26], mouth/tongue [29], leg [34], facial [40, 41] injuries/fractures, and a C1/C2 fracture have been reported [44]. Explosion of the device during use frequently occurs because of the battery.

The main issue with ECs is whether they have a benefit in terms of smoking cessation. The answer to this question is quite confusing. However, some of the publications in the literature should be evaluated carefully for bias [27]. Another important issue is that there have been some studies comparing tobacco-containing cigarettes and ECs with specific blood and lung function parameters. A review by Callahan-Lyon [18] found a degree of bias in studies concluding that ECs are less harmful to health. The studies cited in this review did not include non-smoking controls, contained study populations of inadequate size, and did not investigate the consequences of short-term vs long-term exposure; thus, these studies were considered to be of poor quality [18].

However, there is an urgent need for well-designed, robust, evidence-based studies investigating the long-term effects of ECs, the individuals in whom they might be useful, and when and where they could be used. The variety of EC devices and e-liquids is rapidly increasing, making these devices attractive for many people but creating methodological difficulties for researchers. There is an urgent need for legislation and restriction regarding the sale of these devices in view of their increasing frequency of use among the younger individuals.

In conclusion, ECs are at least as harmful to health as conventional cigarettes and are particularly dangerous because of the risk of explosion. Complications that develop directly as a result of the substances contained in the devices and the adverse events resulting from device explosion and burning are being reported with increasing frequency. In addition, using ECs can cause serious lung conditions, such as lipoid pneumonia, acute eosinophilic pneumonia, hypersensitivity pneumonitis, organized pneumonia, bronchiolitis, diffuse alveolar hemorrhage, reactive pulmonary nodules, and respiratory failure.

**Peer-review:** Externally peer-reviewed.

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