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Review

Acute Health Consequences from Electronic Cigarettes: A Narrative Review

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Abstract: Electronic cigarettes (e-cigarettes) is relatively recently introduced to the market. Its long-term effects are still unclear and require years of research. On the other hand, knowledge about the short-term effects of e-cigarettes is emerging. The purpose of this review was to examine the current literature on the acute health consequences associated with the e-cigarette. We used pre-specified keywords to conduct searches in academic databases of articles published between 2011 and 2020. This review focused on acute health consequences of e-cigarettes in humans that can be directly attributed to the e-cigarette. Burns and injuries associated with device explosion, e-liquid intoxication, e-cigarette or vaping product use-associated lung injury, and pneumomediastinum were identified as acute health consequences associated with e-cigarettes. Except for pneumomediastinum, these acute health consequences are unique to an e-cigarette that are unlikely to be caused by a conventional cigarette. In the short term, the e-cigarette is likely more harmful than the conventional cigarette. Tightening safety regulations on the manufacturing, distribution, and sale of e-cigarette devices is recommended. Compulsory child-resistant containers for e-liquid containers, banning or restriction the use of colorful labels on e-liquid containers, and compulsory warning labels on e-liquid containers are recommended to prevent child's ingestion of e-liquid.

Keywords: Electronic Cigarette, E-cigarette, Health Consequence, Harm, Narrative Review

1. INTRODUCTION

Electronic cigarette (e-cigarette) is a battery-powered nicotine delivery device that does not generate side-stream smoke. Instead, it produces e-cigarette aerosol, often called vapor. In comparison to tobacco smoke, e-cigarette aerosol contains fewer chemical compounds at lower concentrations [1]. It has been marketed as a less harmful alternative to a conventional cigarette and has been used to facilitate smoke quitting [2].

The e-cigarette was introduced to the market around 2007 [2], which is slightly over a decade ago at the time of writing. As a result, its long-term effects on health have not been well-established. A study from Canada showed an increasing trend in past-month e-cigarette use among students Grade 9-12. Past-month e-cigarette use was associated with cigarette smoking initiation and subsequent daily cigarette use in this group [3]. A systematic review of nine prospective studies found an association between e-cigarette use and subsequent cigarette smoking initiation [4].

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According to the knowledge about the consequences of cigarette smoking, those who begin smoking before the age of 25 and continue to smoke will reach a point of disability due to deteriorated lung function, on average, at the age of 65 [5]. Smokers who began smoking during their adolescence will have an increase in the risk of chronic obstructive pulmonary disease (COPD) in their third decade of life. At the age of 60, the risk of developing COPD diagnosis is 7 % for males and 12 % for females. An increase in the risk of smoking-related heart disease is observed around the age of 40 [6]. A decade or two may be required to establish evidence of e-cigarette related chronic health consequences.

Hence, this study concentrates on the more established parts of the literature—i.e., acute health consequences associated with e-cigarettes. This evidence is emerging. Notably, the Centers for Disease Control and Prevention reported an outbreak of e-cigarette or vaping product use-associated lung injury (EVALI), an acute lung injury associated with e-cigarette use, in the United States in 2019 [7]. Several jurisdictions have recently tightened their regulations on e-cigarettes [8]. The purpose of this review was to examine the existing literature on the acute health consequences associated with the e-cigarette.

2. MATERIAL AND METHODS

2.1 Study design

The study design is a narrative review.

2.2 Data Source

We used pre-specified keywords to conduct searches in the Scopus, Web of Science, and MEDLINE databases. The keywords include "electronic cigarette", "e-cigarette", "electronic nicotine delivery system", "effect", "health effect", "harm", "acute health effect", and "acute harm". This review covered studies published between 2011 and 2020. In this review, e-cigarette does not include heat-not-burn tobacco. This review was conducted from 1st March to 31st July 2021.

2.3 Review Protocol

The studies included in this review must involve acute health consequences of e-cigarettes in humans. To be considered an acute health consequence, the duration between the exposure to e-cigarettes and the onset of such consequence must be 14 days or less, according to the Agency for Toxic Substances and Disease Registry's definition of "acute exposure" [9]. We included only health consequences that can be directly attributed to the e-cigarette. Both authors independently reviewed the titles and abstracts of articles from the database search to determine their eligibility. The original keywords search identified 1,015 studies; 942 studies were excluded by title and abstract screening. The full-text review included studies that were considered relevant by both authors. The consensus was used to resolve any disagreements regarding the inclusion of studies. During the full-text review, relevant studies listed in the bibliographies of included articles were added to the review. There were 158 full-text reviews and 63 studies were considered eligible by both authors.

3. RESULTS AND DISCUSSION

Four acute health consequences directly linked to e-cigarettes were identified. These include burns and injuries from device explosions, e-liquid intoxication, e-cigarette or vaping product use-associated lung injury (EVALI), and pneumomediastinum. Each component of an e-cigarette is associated with a specific consequence. The battery is a primary source of explosions. E-liquid contains a high concentration of nicotine, of which a few drops of ingestion can be fatal. Constituents of e-cigarette vapor contribute to EVALI development. Certain vaping-related behaviors cause an increase in intrathoracic pressure, which results in pneumomediastinum.

3.1 Burns and Injuries from Device Explosion

An e-cigarette device may spontaneously explode. The explosion potentially causes serious injury or death. We reviewed 39 incidents of burns and injuries caused by e-cigarette explosions from published case reports and case series (Table 1). The majority of cases were male (37 of these 39 cases). Their ages ranged from 15 to 59 years old. Most (84.6 %) were aged ≤ 40 years old.

The majority of explosions occurred when the e-cigarette was carried in the pocket of the pants

(21 of 39). This resulted in injuries to the lower extremities (particularly the thigh), genital area, and hand. In ten incidents, the explosions occurred while the victims were vaping. This resulted in the oral cavity (mucosa and teeth) and facial (maxillofacial fracture) injuries, as well as injuries to the eyes, vertebra, and brain. In three instances, the explosion occurred during or adjacent to the process of changing or charging the battery. Other incidents occurred when e-cigarettes were held in one's hand or placed in a bag/chest pocket. There was one fatality as a result of an e-cigarette explosion. A man's body was discovered in his house with 80 % of his total body surface area burned (TBSA). The x-ray of the head taken postmortem revealed that the e-cigarette device was lodged in the cranium and brain [10].

The majority of cases suffered from partial or full-thickness burns of affected body parts. The burning area varied from 1 to 80 % of TBSA. The thigh and other lower extremity areas were the most frequently affected body parts. Other affected body parts included the hand, buttock, genitalia, oral cavity, face, neck, eyes, and abdomen. Two cases of corneal burns occurred, impairing the affected individuals' vision [11]. Most cases were hospitalized for at least seven days.

Apart from these case reports, an attempt was made to estimate the number of emergency department visits caused by e-cigarette explosions in the United States using national data. Between 2015 and 2017, an estimated number of visits was 2035 in total [12]. The estimate for 2019 was 676 [13]. The authors noted that these figures were underestimated. Although considered rare in absolute terms, burns and injuries from e-cigarettes are significant enough that a group of plastic surgeons proposed a specific guideline for the management of e-cigarette burn injuries [14]. According to the guideline, inhalation injury and chemical burns must be considered in addition to burns and injuries from flame.

The battery in the e-cigarette device is thought to be the cause of the explosion. Lithium-ion batteries are used in the majority of e-cigarettes. The lithium-ion battery is vulnerable to a phenomenon known as "thermal runaway," which is a type of battery failure that results in overheating. This phenomenon can lead to an explosion of the battery [15, 16]. Mechanical, electrical, and thermal issues can lead to thermal runaway [16]. In the case of the e-cigarette explosion, it is unclear what triggers the phenomenon. As a result, the device's explosion is largely unpredictable. Cobalt, manganese, and other chemical substances are also found in some lithium-ion batteries. This may result in heavy metal toxicity and chemical burns, causing additional health problems for those who are affected [17]. This warrants more stringent e-cigarette device and battery regulations. The regulations may be complicated for jurisdictions that prohibit the use and sale of e-cigarettes, whereas a portion of the population still uses e-cigarettes, such as in Thailand [18]

3.2 E-liquid Intoxication

E-liquid is a liquid used with e-cigarettes that usually contains nicotine, propylene glycol, glycerin, and flavor [19]. The majority of e-liquids contain nicotine to simulate the sensation of smoking. Nicotine can be absorbed via alveoli, intestinal mucosa, oral mucosa, and nasal mucosa. Symptoms of acute nicotine toxicity include nausea, vomiting, diarrhea, sweating, tremor, confusion, irregular pulse, convulsion, respiratory failure, circulatory failure, and death [20]. Currently, there is no agreement on the lethal dose of nicotine. Previously, the oral LD50 of 0.8 mg/kg (equivalent to 60 mg of ingested nicotine) was thought to be lethal [21]. Recent studies have suggested significantly higher lethal doses, such as an oral LD50 of 6.5–13.0 mg/kg (corresponding to 500–1,000 mg of ingested nicotine) [21] and a plasma concentration of 0.8–1.6 mg/L (corresponding to 264–534 mg of ingested nicotine) [22]. Nicotine concentrations in e-liquid range from 10 to >200 mg/mL [23, 24]. As a result, ingesting just 1–5 mL of e-liquid with a high nicotine concentration could be fatal. Accordingly, e-liquid is a potentially hazardous product.

Nineteen cases of e-liquid intoxication were reviewed (Table 2). The age of these cases ranged from 15 months to 53 years. Ten were female. All incidents involving children aged 6 years or less were accidental, whereas most incidents in adolescents and adults involved suicidal attempts. Six cases had documented mental problems (depression, anxiety, and psychosis). Ingestion was the most frequently reported route of exposure, followed by intravenous injection in four cases.

In six instances, e-liquid was consumed alongside alcohol. Seven of these 19 cases resulted in death. Gastrointestinal symptoms like nausea, vomiting, and diarrhea were common in these cases. Ten cases involving severe conditions including respiratory failure, cardiac arrest, or death were found in ten cases. Two had seizures or seizure-like symptoms. Twelve cases provided enough data to estimate total nicotine intake, which ranged from 30 to 3,600 mg. Among the fatal cases in adults, nicotine intake ranged from 1,440 to 3,600 mg, which was higher than all of the estimated oral LD50 of nicotine. A 15-month-old patient died after consuming 500 mg of nicotine. One patient had a plasma propylene glycol concentration of 300 ug/L at 14 hours after ingestion of e-liquid. The initial propylene glycol level could be higher than 1000 mg/L, which could be toxic. E-liquid contains a variety of toxic substances in addition to nicotine. More toxicology research on the e-liquid solvent is required [25].

Using the United States national data, there were an estimated 1,555 emergency department visits of children who ingested e-liquid or used an e-cigarette in 2018–2019. Nearly 70 % of the cases involved children under two years old. Ingestion of food- or fruit-flavored e-liquid has been reported in some cases [13]. E-liquid poses a unique risk to children and adults. Regulations on nicotine concentration, flavor, solvents, and packaging are urgently needed.

3.3 E-Cigarette or Vaping Product Use-Associated Lung Injury (EVALI)

EVALI is a term that refers to an acute lung injury that occurs as a result of e-cigarette use. Its symptoms resemble those of pneumonia. The diagnosis of EVALI is established by ruling out other causes of pulmonary infection and lung injury plus the history of e-cigarette use within 90 days before the onset and presence of pulmonary infiltrate. Clinical manifestations of EVALI involve respiratory system (i.e., shortness of breath, cough, chest pain, tachypnea, and oxygen desaturation) and gastrointestinal system (i.e., nausea, vomiting, and abdominal pain). Additionally, fever, fatigue, and muscle pain are common manifestations [26].

Tetrahydrocannabinol (THC) and vitamin E acetate in e-liquid are associated with EVALI. Studies reported more than 80 % of patients with EVALI used THC with their e-cigarettes within 90 days of the onset [26, 27]. Vitamin E acetate was detected in bronchoalveolar-lavage fluid of more than 90 % of patients with EVALI [28]. A possible pathogenesis of EVALI is that volatile organic compounds, products of heating e-liquid, generate THC or vitamin E acetate carbonyl complexes, which are toxic to lung cells [29]. Exposure to e-cigarette vapor also leads to lung epithelial barrier dysfunction and damaged monocytes [30].

Since 2012, acute lung injury following e-cigarette vaping has been reported in the literature under a variety of different diagnoses [31, 32]. The diagnosis includes lipoid pneumonia, organizing pneumonia, and eosinophilic pneumonitis [31-33]. However, it received increased attention in 2019 following an outbreak of more than 200 cases of severe pulmonary disease linked to e-cigarette use in 25 states of the United States [7]. Thus, during this outbreak, the term “EVALI” was coined to refer to this condition [34]. Between August 2019 and January 2020, a total of 2,602 patients with EVALI were reported in the United States [27].

3.4 Spontaneous Pneumomediastinum

Pneumomediastinum, a condition characterized by the presence of free air in mediastinum, has been linked to e-cigarette use. There have been three cases of spontaneous pneumomediastinum developed after e-cigarette use reported in the literature (Table 3). All of these cases were male in their adolescent or early adult years. The symptoms include chest pain, dyspnea, dysphagia, neck stiffness, and voice change. The duration between vaping and symptom onset varied from immediately following vaping to one day. All three cases were hospitalized for two days and did not require surgical intervention. Two cases were followed up one week and two months after discharge. In both cases, no long-term effect was detected.

Pneumomediastinum occurs as a result of an increase in intrathoracic pressure, which results in air leakage from the alveoli [70]. Vaping-related behaviors such as deep inhalation [71], increased frequency of use [72], and a strong cough [73] may trigger this phenomenon.

Table 1. Case reports of burns and injuries from e-cigarette device explosion

Age (yr), sex	Location of e-cig. during explosion	Affected body part	Degree of injury	Reference
35, M	Changing battery	Hand	Deep partial-thickness and full-thickness burns	[35]
22, M	Charging battery	Hand and foot	1%TBSA, superficial partial-thickness	[36]
38, M	Found dead with an e-cigarette in the cranium	Head and body	Death caused by a projectile wound to the head from the explosion of a modified electronic cigarette device; 80 % of TBSA burns	[37]
20, M	Hold in hand	Face	1.5-cm depressed soft-tissue defect over the right nasal bone and 5-15 % of facial fractures	[38]
30, M	Hold in hand	Hand and fingers	2nd degree burns of the tip of the index finger, with mild first-degree burns to the middle and proximal phalanges and minor burns to the long and ring fingers	[39]
53, M	Hold in hand after changing the battery	Head, face, abdomen, and hand	First degree burns to abdomen, fracturing right thumb, maxillofacial trauma, and tooth fracture and avulsion	[40]
17, M	Stored in breast pocket	Right chest wall and palm	4 % TBSA, partial thickness burns	[17]
20, M	Stored in pant pocket	Left lower extremity	16 % TBSA, partial thickness burns	[17]
27, M	Stored in pant pocket	Right thigh and leg	10 % TBSA, partial and full thickness burns	[17]
29, M	Stored in pant pocket	Left lower extremity	5 % TBSA, partial and full thickness burns	[17]

Age (yr), sex	Location of e-cig. during explosion	Affected body part	Degree of injury	Reference
36, M	Stored in pant pocket	Left and right thigh	7 % TBSA, partial and full thickness burns	[17]
40, M	Stored in pant pocket	Left thigh	Severe burns at left posterior thigh	[41]
47, M	Stored in pant pocket	Left thigh, left hand, scrotum, and penis	9 % TBSA, partial thickness burns	[17]
19, M	Stored in pocket	Thigh and calf	7 %TBSA, partial and full thickness	[42]
Mid 20, M	Stored in pocket	Thigh and leg	6 % TBSA partial thickness burns	[43]
22, M	Stored in pocket	Thigh, scrotum, and hand	1%TBSA mixed depth burns to right thigh and scrotum; superficial partial thickness burns to left hand	[36]
23, M	Stored in pocket	Left thigh and left hand	5 % TBSA, partial thickness burns	[17]
29, M	Stored in pocket	Left and right thigh, scrotum, and penis	8 % TBSA, partial thickness burns	[17]
Early 30, M	Stored in pocket	Thigh, leg, and hands	10% TBSA, partial thickness burns; 2 -3 % TBSA, full thickness burns to left lower extremity	[43]
30, M	Stored in pocket	Thigh, and hand	3 %TBSA, partial thickness burns	[44]
30, M	Stored in pocket	Thigh and leg	8 %TBSA, partial thickness burns	[45]
31, M	Stored in pocket	Thigh, leg, and buttock	10 %TBSA, partial and full thickness burns	[46]
34, M	Stored in pocket	Leg	15 %TBSA, deep partial thickness and full thickness	[42]

Age (yr), sex	Location of e-cig. during explosion	Affected body part	Degree of injury	Reference
			burns	
35, M	Stored in pocket	Thigh	2 % TBSA, partial and full thickness burns	[42]
36, M	Stored in pocket	Thigh and hand	3 %TBSA, deep partial thickness and full thickness burns to right thigh and superficial partial thickness burns to right hand	[46]
39, M	Stored in pocket	Thigh and hand	4 %TBSA, partial thickness burns to right thigh and minor superficial burns to right hand	[44]
Early 40, M	Stored in pocket	Thigh, genitalia, and hands	3 -4 % TBSA, partial and full thickness burns to right thigh, scrotum, and penis; <1% TBSA partial thickness burns to bilateral hands	[43]
49, M	Stored in pocket	Thigh	7 %TBSA, superficial partial thickness burns	[36]
15, F	Stored in the bag	Hand and fingers	Partial and full thickness burns	[47]
16, M	Vaping	Eye, face, and neck	Facial and bilateral corneal burns, severe bilateral eye pain and vision impairment, facial and neck pain	[11]
18, M	Vaping	Oral cavity and abdomen	Oral and abdominal burns, oral lacerations, tooth fracture, and avulsion	[48]
18, M	Vaping	Oral cavity, face, hand, and tooth	Oral burns, laceration, and dental trauma	[49]
20, M	Vaping	Oral mucosa and teeth	Tooth pain and fracture and wound on oral mucosa	[50]
26, M	Vaping	Upper abdomen, shoulder, and chest	Burns and superficial skin pain to the shoulder, chest, and abdomen	[51]
28, M	Vaping	Oral cavity	Intraoral burns, tooth fracture, and avulsion	[52]

Age (yr), sex	Location of e-cig. during explosion	Affected body part	Degree of injury	Reference
30, F	Vaping	Face, oral cavity, hand, and neck	Fractured vertebrae, dental trauma, facial fractured, and hand with superficial lacerations	[53]
45, M	Vaping	Eye, face, and hand	Partial-thickness corneal laceration and bilateral corneal burns, first-degree facial and hand burns, vision impairment	[11]
59, M	Vaping	Head, face, and hand	Maxillofacial fractures, blurred vision, pneumocephalus, and dismissed hearing	[54]
27, M	Vaping after changing the battery	Neck, face, and teeth	Fractured vertebrae, partial-thickness burns to his lips and tongue, and fractures of bilateral upper incisors	[55]

Note: yr = year; e-cig. = e-cigarette; M = male; F= female; TBSA = total body surface area

Table 2. Case reports on e-liquid intoxication

Age, sex	Exposure	Co-intox.	Clinical findings	Serum nic. and cot. level	Outcome	Reference
15 mo, F	Accidental ingestion, 5 mL e-liquid (nic. conc. 10 mg/mL) Total nic. exposed: 500 mg	None	Vomiting, unconsciousness, anoxic brain injury	Nic.: Not reported Cot.: 1,716 ng/mL after 12 hr	Death	[24]
2 yr, F	Accidental ingestion, e-liquid (nic. conc. 24 mg/mL) Total nic. exposed: cannot estimate	None	Vomiting and irritability	Nic.: Not reported Cot.: Not reported	Survived	[56]
30 mo, F	Accidental ingestion Total nic. exposed: cannot estimate	None	Vomiting	Nic.: Not reported Cot.: Not reported	Survived	[57]
6 yr, F	Accidental ingestion, 10 mL e-liquid (nic. conc. 70.3 mg/mL)	None	Vomiting, diaphoresis, and copious secretions	Nic.: 348 ng/mL after 1 hr	Survived	[58]

Age, sex	Exposure	Co-intox.	Clinical findings	Serum nic. and cot. level	Outcome	Reference
	Total nic. exposed: 703 mg			Cot.: 742 ng/mL		
17 yr, F	Ingestion, 10 mL e-liquid (nic. conc. 210 mg/mL) Total nic. exposed: 2,100 mg	None	Tonic-clonic movement, and cardiac arrest	Nic.: Not reported Cot.: Not reported	Survived	[23]
19 yr, F (depression)	IV injection, undiluted e-liquid Total nic. exposed: cannot estimate	None	Cardiac arrest	Nic.: 0.002 µg/mL Cot.: Not reported	Death	[59]
21 yr, F	Ingestion, 30 mL e-liquid (nic. conc. 12 mg/mL) Total nic. exposed: 360 mg	None	Nausea, vomiting, pale skin, anxiety, hypotension, and miosis	Nic.: 95 µg/L Cot.: 2,800–4,400 µg/L	Survived	[60]
22 yr, F (mental health problem)	IV injection, 2 mL e-liquid (nic. conc. 18 mg/mL) with methadone Ingestion, 60 mL of the mixed solution Total nic. exposed: 30 mg (injection only)	None	Tachycardia, flushing, salivation, and nausea	Nic.: Not reported Cot.: Not reported	Survived	[59, 61]
23 yr, M	Ingestion with suicidal attempt Total nic. exposed: cannot estimate	None	Unconsciousness, bradycardia, and respiratory muscle paralysis	Nic.: 1,900 µg/L Cot.: 2,100 µg/L	Death	[62]
24 yr, F (depression)	Ingestion, 15 mL e-liquid (nic. conc. 100 mg/mL) Total nic. exposed: 1,500 mg	Alcohol	Cardiac arrest and brain damage	Nic.: >1,000 ng/mL Cot.: >1,000 ng/mL	Death	[63]
27 yr, M	Ingestion with suicidal attempt, e-liquid Total nic. exposed: 420 mg	Alcohol	Vomiting and sinus tachycardia	Nic.: 50 µg/L at 2 hr Cot.: 250 µg/L at 2 hr	Survived	[64]

Age, sex	Exposure	Co-intox.	Clinical findings	Serum nic. and cot. level	Outcome	Reference
27 yr, M	Ingestion with suicidal attempt, e-liquid (nic. conc. 16mg/mL and 18 mg/mL) equivalent to 23 mg/kg of nic. exposure Total nic. exposed: 1,380 mg	Alcohol	Seizure-like movement and cardiac arrest	Nic.: Not reported Cot.: Not reported	Survived	[23]
32 yr, F (depression and anxiety)	Ingestion, 10 mg e-liquid with attempted to suicide Total nic. exposed: cannot estimate	Alcohol	Dizziness, nausea, abdominal pain, and severe left ventricular systolic dysfunction	Nic.: Not reported Cot.: 7,069 ng/mL	Death	[65]
32 yr, M	Ingestion, 20 mL e-liquid (nic. conc. 72 mg/mL) Total nic. exposed: 1,440 mg	Alcohol	Brain hypoxia and cardiac arrest	Nic.: 1,600 ng/mL after 24 hr Cot.: Not reported	Death	[66]
32 yr, M (mental health problem)	IV injection with suicidal attempt, 4 mL e-liquid (nic. conc. 32 mg/mL) Total nic. exposed: 128 mg	Alcohol	Unconsciousness, respiratory failure, and bradypnea	Nic.: 500–800 µg/L after 2 hr Cot.: 1,300–2,400 µg/L after 2 hr	Survived	[60]
34 yr, M (psychosis)	Ingestion, 50 mL e-liquid (nic. conc. 72 mg/mL) Total nic. exposed: 3,600 mg	None	Death	Nic.: 5.5 mg/L in femoral, 136 mg/L in heart blood Cot.: 0.9 mg/L in femoral, 7.6 mg/L heart blood	Death	[67]
44 yr, M	Ingestion, 30 mL e-liquid Total nic. exposed: cannot estimate	None	Headache, nausea, abdominal pain, ventricular extra systoles, and tachypnea	Nic.: 21 µg/L after 13.5 hr Cot.: 102 µg/L	Survived	[25]

Age, sex	Exposure	Co-intox.	Clinical findings	Serum nic. and cot. level	Outcome	Reference
51 yr, M	IV injection with suicidal attempt, 10 mL e-liquid Total nic. exposed: 1,000 mg	None	Tachycardia, coma, bradypnea, mydriasis, myoclonus, flaccid paresia, and NSTEMI	Nic.: 12 µg/L Cot.: 3,210 µg/L	Survived	[68]
53 yr, M	Ingestion with suicidal attempt, 3 mL e-liquid Total nic. exposed: cannot estimate	None	Unconsciousness, diarrhea, vomiting, and cardiac arrest	Nic.: Not reported Cot.: 1,296 ng/mL	Survived	[69]

Note: co-intox. = co-intoxication; nic. = nicotine; cot. = cotinine; mo = month; yr = year; M = male; F= female; conc. = concentration; hr = hour; IV = intravenous; NSTEMI = non-ST segment elevation myocardial infarction

Table 3 Case reports of pneumomediastinum following e-cigarette use

Age (yr), Sex	Symptoms	Time from last vaping to onset	Treatment	Reference
17, M	Dyspnea and dysphagia	Immediately	Hospitalized for 2 days and discharged without specific treatment	[71]
20, M	Sudden chest pain after strong cough	2 hours	Hospitalized for 2 days and discharged without specific treatment	[73]
25, M	Substernal chest pain, neck stiffness, and voice change (to nasal voice)	1 day	Hospitalized for 2 days and discharged without specific treatment	[72]

Note. yr = year; M = male; F= female

4. DISCUSSION

Invented in 2003 and introduced to the market in 2007, the long-term health effects of an e-cigarette are not well-established [2]. Nonetheless, evidence regarding the acute consequences of e-cigarettes has emerged. This review identified four acute health consequences attributed to the e-cigarette. As with conventional cigarettes, a major cause of burn injuries, the e-cigarette can result in burns and injuries. Unlike conventional cigarettes, e-cigarette devices can explode on their own, whereas conventional cigarettes can explode when they come into contact with other explosive substances, such as ammonium nitrate [74]. Conventional cigarette contributes to the explosion frequently in higher-risk circumstances [74, 75], whereas the majority of e-cigarette device explosions occurred during normal daily activities (Table 1). Due to the unpredictable nature of e-cigarette device explosions, the implementation of prevention measures is challenging.

Nicotine intoxication from the conventional cigarette is extremely rare. Only two case reports of such incidents were found in the literature. In these cases, tobacco was extracted from nine and twenty conventional cigarettes and consumed in apparent suicidal attempts [76, 77]. One of these two cases was dead. In comparison, at least 19 cases of nicotine intoxication from e-liquid have been reported, resulting in seven deaths. Additionally, 1,555 cases of nicotine intoxication were estimated in the United States between 2018 and 2019 [13]. Ingestion of e-liquid can be both intentional and accidental. Accidental ingestion was common among children. As a result, e-cigarette contributes significantly more to nicotine intoxication than the conventional cigarette.

Short-term exposure to conventional cigarette smoking has a proinflammatory effect on lung tissues [78]. This enhances the risk of lung injury due to other causes, as demonstrated in animal models [78-80]. Conventional cigarette smoking in the short term is not associated with clinically significant lung injury [78, 79]. In comparison, short-term exposure to e-cigarette vapor can result in acute severe lung injury, referred to as EVALI. Since 2012, EVALI has been reported under different diagnoses [31, 32]. It is relatively common, as there has been a nationwide outbreak of EVALI in the United States since 2019 [7, 27]. In terms of acute lung injury, the e-cigarette is substantially more harmful than the conventional cigarette.

Three cases of spontaneous pneumomediastinum associated with e-cigarette use have been reported. This condition has been linked to illicit drug use, most notably marijuana and cracks cocaine [81-84]. A narrative review found that 29.6 % of pneumomediastinum cases had a smoking history [85]. Hence, an e-cigarette may be added to the list of risk factors for pneumomediastinum.

Device explosion, nicotine intoxication, and EVALI are all distinct acute health consequences associated with the e-cigarette. These conditions are unlikely to be caused by a conventional cigarette. Accordingly, the claim that e-cigarette is a safer alternative to conventional cigarette is losing ground. This review shows that e-cigarette is more harmful than a conventional cigarette in the short term. Further studies examining the risk-benefit of e-cigarette use in comparison to conventional cigarettes should be conducted using a short analysis time frame. According to this review, we recommend tightening safety regulations on the manufacturing, distribution, and sale of e-cigarette devices. To prevent child's ingestion of e-liquid, we recommend compulsory child-resistant containers for e-liquid containers, banning or restriction the use of colorful labels on e-liquid containers, and compulsory warning label on e-liquid containers.

5. CONCLUSION

This review identified four distinct acute harms associated with e-cigarettes: burns and injuries associated with device explosion, e-liquid intoxication, e-cigarette or vaping product use-associated lung injury (EVALI), and pneumomediastinum. Except for pneumomediastinum, three of these are unique health consequences of e-cigarettes. In the short term, the e-cigarette is likely more harmful than the conventional cigarette.

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7. CONFLICT OF INTEREST

The authors declare no competing interest.

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