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# Pain Associated with the Use of Electronic Cigarettes

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## Abstract

Hitherto, lots of efforts have been made to illustrate the consequence of consuming conventional cigarette. The relationship between its utilization and the occurrence, deterioration, and variation of pain has been demonstrated for decades. As a result, electronic cigarette was investigated for its harmless and ideal replacement for conventional cigarette. Proposed and endorsed for almost 15 years, e-cigarette has established its success and induced many consumers. Later on, with greater attention to the increasing population indulging in or switching to electronic cigarette, complaints and side effects occurred and accumulated. Betwixt, headache, chest pain, thermal injury, withdrawal symptoms, and chronic pain had been described either via case reports or by experimental or clinical researches. Through comprehensively reviewing current publications, this chapter illustrates respective pain. With the introduction of this chapter, it will be helpful for the general public to understand the potential health implications of using e-cigarettes and evoke the readers' interest to learn more about this topic.

**Keywords:** electronic cigarette, conventional cigarette, pain, nicotine, thermal injury, withdrawal symptoms

## 1. Introduction

The harmful health and environmental implications of conventional cigarettes have been firmly established after decades of studies. Researchers and scientists have been engaged in unearthing and asserting their adverse effects. With the corporation of academic associations and governments, guidelines and law enforcements for cigarette control and management have achieved great success. However, because of the addiction to cigarette (mainly caused by nicotine, a pivotal component of conventional cigarette), it is challenging to propose a smooth transition period for smokers who want to quit. The emergence of electronic cigarettes (EC) greatly solved this issue for a short time and it became a dramatically successful approach for a period of time. More and more researchers assumed EC's harmlessness compared to conventional cigarette, since it is designed as an ideal replacement of conventional cigarette. But in the meanwhile, potential harmful consequences were found among adolescent and pregnant women who attempted to utilize or had been exposed to e-cigarette [1, 2]. The prevalent utilization of electronic cigarette has become a controversial topic and people hold contrasting opinions. On the one hand, American Cancer Society and Benowitz et al. hold its positive attitude toward EC because of its comparative less side-effect and well-behaved tolerance [3, 4]. On

the other hand, accumulated evidence further expose the increasingly serious side effect of EC products [5, 6]. As a war of words, EC may be better to consumers' health than conventional cigarette, but it still plays a bad role in deteriorating the cardiovascular system and causing chest pain, especially for those who are undergoing existing cardiovascular disease. Scientists need a fresh mind to think about how EC correlates with pain feeling for its consumers [7].

Electronic cigarettes (ECs) or e-cigarettes are battery-operated products designed to deliver nicotine (can be without) combined with other chemicals such as flavors. An internal heat source turns nicotine and other chemicals into vapor when inhaled by the user. The main components of an EC include a cartridge, a heating atomizer, and a battery. With current evidence, the ingredients in the cartridge, the heating process, and spontaneous explosion of battery have the potential to do harm and cause pain to human beings [8–10]. Compared with pain caused by conventional cigarette, thermally induced pain is an emerging concern and effective preventative methods have not been developed yet [9–11]. Owing to its unpredictability, caution should be taken when carrying or vaping EC.

Finally, EC has grasped considerable public attention since 2014 based on the publication data of PubMed released. With relatively few years of investigation, neither the benefits nor the adverse effects of electronic cigarettes could be fully unearthed. Currently, the association between EC and various pains mainly depends on case reports and clinical questionnaire studies [12–14]. In this chapter, a systematic review will be conducted regarding both the common pains that EC consumers complained about using abundant data and the rare discomforts based on occasional cases. Moreover, a comprehensive comparison between conventional cigarette users and EC users can effectively demonstrate the potential effects of EC consumption, no matter first, second, or third hand.

## **2. Methods**

Publications searching was conducted using PubMed and EMBASE with keywords: “electronic cigarette” or “e-cigarette” or “electronic nicotine delivery systems” or “vaping” or “tobacco products” or “cigarette smoking” and “pain” or “ache” or “musculoskeletal pain” or “chronic pain” or “headache” or “injury” without requirement of released time for the articles. All articles were written in English. All abstracts had been reviewed; if they met the topic of relationship between EC and pain, full-length articles were checked.

## **3. Headache**

Headache is a symptom that could happen in any part of the brain with different mechanisms and in various ways. Based on an international online questionnaire study with large numbers of participants aiming to investigate the side effects and potential benefits of EC, headache was reported by 11.4% of who currently or previously consumed EC products [5]. It is worth mentioning that, for those participants who used EC, the concentration of nicotine was varied. Electronic cigarettes provide a gradual nicotine reduction strategy for those smokers who want to quit conventional smoking. According to this survey, there was no clear relationship between the frequency and severity of adverse effects and nicotine absorbed [5]. In an open-labeled, randomized, parallel group, clinical trial study was conducted at a certain nicotine concentration to probe the comparison between conventional smokers who switched to EC and those who continued with conventional cigarette

for over 12 weeks. Researchers found no significant health improvement among those who switched, but rather adverse effects such as headaches and some other agonies, especially during the first week, and these symptoms could partially be ascribed to nicotine withdrawal [15]. Later on, the same participants participated in a trial that wanted to evaluate the long-term effects of EC consumption; after 24 months of investigation, the study showed that headache was the most complained symptom and there were no worse clinical presentation compared with the baseline condition [12]. Similarly, systems that retrospectively reviewed and summarized the recent clinical complications of using EC found that headache was actually the most frequently reported adverse effect [16].

Headache, either associated with nicotine withdrawal symptoms or unknown mechanisms, could impressively prevent smokers to quit conventional smoking and switch to low-harmful EC products. In the studies shown above, there were no details on how the headaches happened nor its frequency and severity. Furthermore, some of the clinical studies were mainly based on online questionnaires; thus, there could have been selection bias and the criteria might have been interpreted more subjectively than objectively. More studies are needed in both experimental and clinical fields.

#### **4. Chest pain**

Among those e-cigarette-using individuals who complained about chest pain, the most reported syndromes were related with either lung malfunction, structure disfigures [17, 18], or potential cardiovascular diseases [19].

Consistent evidence has shown that conventional cigarette users are readily trapped in lung problems. However, only a limited number of studies have focused on EC users who caught chest pain. Dr. Sommerfeld et al.'s study [17] presented a previously healthy young woman who developed pleuritic chest pain after EC use. Soon the chest pain deteriorated into acute respiratory distress syndrome after acute respiratory failure. With completed routine and pathological examination, this patient was diagnosed with hypersensitivity pneumonitis after using EC products with unknown mechanism. This particular case reminds clinicians and consumers of EC's rare but dreadful consequences. Another patient was a previous conventional cigarette consumer who switched to EC to quit smoking. A month later, this patient was referred to the pulmonary department and complained about a month-long pain that was sharp, intermittent, and on both sides of the chest. Upon inpatient studies, dyspnea was confirmed and the doctors ascribed her symptoms to the recent EC use. Later, she was diagnosed with organizing pneumonia via pathological examination and was improved with steroids along with abstinence from e-cigarette use [18]. This case demonstrated that EC contributes to the deterioration of patients' health and possibly causes chest pain through various mechanisms. According to an international survey, about 3% of EC users have struggled with chest pain [5]. Even without thoroughly investigating the disadvantages of EC, attention should be paid when EC is used without other choices.

Nicotine, the major component of conventional cigarette, was ascertained to induce addiction, which impedes smokers to quit conventional cigarette by causing difficult withdrawal symptoms [1, 8]. This leads to the rise of electronic cigarettes, designed to help quit smoking with less withdrawal agony. Its designer claimed that it is the ideal replacement for conventional cigarette but with much less nicotine inside. But when surveys were conducted to clarify the components of EC, the concentration of nicotine varied among different brands and products [4]. A randomized, partially single-blinded, 6-period crossover clinical study of adult smokers

was conducted to compare how nicotine alteration impacts smoking urge between EC users and conventional cigarette users. Though obvious blood plasma nicotine levels were detected, subjects who were exposed to EC products behaved better than conventional cigarette users [20]. On the other hand, holding alternative opinion toward the advantage of using EC, Lee et al. [21] demonstrated that smoking electronic cigarettes could damage DNA and reduce repair activity in mouse lung, heart, and bladder via various chemical measurements and predicted its harm in human lung and bladder cells [21].

With regard to cardiovascular symptoms induced by EC, the mainstream opinion is mostly positive because it is relatively harmless compared with conventional cigarette [3, 4, 7]. However, consumers should be cautious that smoking EC is not totally free of danger as cases have shown EC users develop cardiovascular diseases, especially among young people and women who are pregnant [4, 7]. Based on experimental studies, EC components have the potential to activate platelet activation, adhesion, inflammation, and aggregation, which are critical steps for the occurrence and development of cardiovascular diseases [22]. The unfavorable influence of EC has also been demonstrated on young smokers who were previously free of cardiovascular diseases. The researchers suggested that using EC can increase aortic stiffness and blood pressure in addition to the unfavorable effect on the cardiovascular system [19].

Chest pain seems to be caused less frequently and less seriously with EC consumption than with conventional cigarette usage. However, due to shortage of investigation, no conclusive statement about its harm could be drawn. To summarize, EC users still encounter various kinds of chest pain; among them, chest pain induced by cardiovascular system is relatively specific and likely caused by the effects of nicotine [7, 20], while, for other chest pains that are mainly ascribed to respiratory system malfunction, acute pain was prone to happen and is probably correlated with hyper-immune response [5, 17, 18].

## **5. Other specific pains**

There are still other specific pains reported as a consequence of EC consumption. Such aches mainly occurred in the abdomen [23] and the oral cavity [24].

Dr. Madsen et al. reported a 45-year-old female who presented with abdominal pain and fever, conceivably caused by inflammatory reaction after abrupt EC use. Imaging evidence suggested lung cancer metastasis, while pathological examination was negative for malignant findings and suggested a foreign body reaction. Upon cessation of e-cigarette use, this patient made a recovery. This was a unique case leading inflammatory reaction of EC to mimic metastatic cancer [23].

A cross-sectional study aimed to investigate the relationship between EC use and oral health among adolescents showed that EC use possibly increased the risk of tongue and inside-cheek pain among student users in Korea [24]. Specific to this study, gingival pain was not found significantly more frequent when compared with the non-EC group [24]. However, an international questionnaire survey suggested that 13.1% of EC users developed gingivitis in about a 10-month follow-up [5]. Some have tried to explain the difference in findings by considering ethnic differences or ways of vaping.

Reported occasionally and lacking profound investigation, these aches were possibly correlated with EC use. Likewise, EC caused chest pain through induced inflammatory reaction [17] and induced abdominal pain via a similar mechanism [23]. For oral pain, inconsistent results were obtained from surveys. Gingival pain did occur more frequently among EC users even though there were no complete

statistical agreements. More studies and surveys should be conducted to address this issue.

## **6. Thermal injury**

Thermal injury hardly happens during conventional cigarette use. However, due to the instability of device and improper carrying methods, both physical and chemical exposure could happen to EC users. There seems to be no effective way to prevent thermal injury other than quitting. Most recent thermal injury cases reported were associated with the explosion of battery or high-temperature vaping [9–11, 25, 26]. Since a considerable number of cases and researches concluded that EC use is responsible for thermal pain, greater public attention is needed.

Paley et al. [25] reported two cases in which the explosion of EC products caused corneoscleral laceration and ocular burns and such effects were like nightmares for the patients and their family. Through retrospectively reviewing the institutional burn database of EC injury, Serror et al. [9] illustrated the potential mechanism underlying thermal EC injury. They reached four possible mechanisms: (1) thermal burns by flames due to a phenomenon called “thermal runaway,” (2) blast lesions secondary to the explosion, (3) chemical alkali burns caused by the spread of the electrolyte solution, and (4) thermal burns without flames due to overheating. Their results provide a way to redesign and improve the safety of EC devices. Meanwhile, another retrospective survey was conducted to investigate the severity of pain those patients suffered; they concluded that the majority of EC explosions caused second- and third-degree burns within the same wound bed. Among those who got injured, the spontaneous explosion of the battery was the most common reason. Explosion of these products also occasionally made an unbearable impact on spine and caused C1 and C2 fractures in a young EC user. Data collected from the US Consumer Product Safety Commission’s National Electronic Injury Surveillance System revealed more explosion and burn injuries recently [11].

Thermal injury is increasingly threatening to those EC users who are not cautious; incidents that occurred can actually cause a serious condition and victims should be referred to emergency treatment. The critical point is thermal injury seems unpredictable without suitable regulation of these devices since it can happen spontaneously.

## **7. Withdrawal symptoms and chronic pain**

Withdrawal symptoms should mainly be attributed to nicotine, a miraculous compound that causes addictive feeling and prevents current smokers from quitting. Withdrawal symptoms are a series of discomforts arisen owing to the short of nicotine. To investigate the pain behavior in smokers and non-smokers, experiments unearthed that smoking withdrawal was associated with blunted stress response and increased pain sensitivity [27]. This finding suggests that during the time when smokers are trying to quit cigarette consumption, they will suffer more pain sensitivity and consequently be unable to keep up with the process. The same story is revealed by an online survey that aimed to test the association between pain and the potential to quit smoking. They found that smokers who suffered chronic pain had less willingness, lower confidence, and greater difficulty to quit cigarette [28]. Moreover, based on a rat model, nicotine deprivation (which produces a similar mechanism as nicotine withdrawal) increased the pain threshold and decreased the pain tolerance [29]. Along the same lines, researches revealed that

pain severity was significantly and positively associated with e-cigarette dependence [6, 13]. These experiments had demonstrated the relationship between pain-taking and the possibility of getting rid of nicotine-based cigarette.

Consistent and severe pain feeling caused by withdrawal syndrome was the most critical problem that hampered users to quit tobacco products. Even though EC products claimed to have less nicotine, they still arouse ache among EC consumers, especially for those who used conventional and electronic cigarette at the same time. Most pains were unspecific for those individuals who complained about withdrawal symptoms, which had no simple approaches to cure. As a consequence, chronic pains in withdrawal symptoms correlate with EC usage; it cannot be neglected and should be taken into serious consideration.

## **8. Compounds and potential pains**

Aerosol and e-liquid are the major components of EC products that are mixed with various ingredients [3]. The process of vaping can produce some heavy metal contamination to smokers and second-hand or third-hand delivered harm. Though few researches have been done to interpret the side effects of EC, experimental studies illustrate the effects of some chemicals. Through reflection X-ray fluorescence spectroscopy, aldehydes, cadmium, lead, nickel, copper, arsenic, and chromium were detected in different types of EC products and they are likely to be harmful to human health [30].

Studies using ALDH2\*1/\*2 heterozygous mice, designed to be impaired in the metabolic aldehydes, found they were significantly more sensitive to painful stimuli than other wild-type mice and this alteration can be inhibited by an ALDH2-selective activator [31]. This experiment proposed the possibility of aldehydes altering the threshold of pain. Furthermore, EC users are possibly exposed to toluene and formalin owing to vaping. Cervantes-Duran et al. [32] suggested that acute toluene exposure fomented formalin-induced acute and long-lasting nociceptive hypersensitivity in rats [32]. Meanwhile, propylene glycol could attenuate the adverse effects of high-dose nicotine and allow EC users to develop high tolerance toward EC products [33]. By analyzing urinary cadmium levels, La-Up et al. [34] found there was a positive relationship between urinary cadmium level and chronic musculoskeletal pain. The survey showed that for the cadmium-contaminated areas in northwest Thailand, people had high risk of being trapped in chronic musculoskeletal pain. This finding in turn suggests that exposure to cadmium, which is contained in EC vaping, may cause chronic musculoskeletal pain [34].

All in all, the compounds in EC products vary. Some of them are found in conventional cigarettes while others are newly discovered. A large amount of these compounds have the potential to alter pain threshold or induce pain feeling. Until recently, the cause mechanism was not fully illustrated and individuals are still exposed to false advertisements and potential second- or third-hand vaping. Such conditions are partially caused by the lack of clear quality control and quality assurance, since different EC products could have different ingredients.

## **9. Conclusion**

Electronic cigarettes, once considered an ideal replacement of conventional cigarette for current smokers, have caused considerable problems and grasped public and researchers' attention recently. First of all, EC products are not harmless [3, 5] and EC consumers have not fully understood the potential harms of EC usage yet

[1, 4]. In addition, even with a limited number of studies, lots of researches were conducted to compare conventional cigarette and EC; their findings agreed that EC does have its disadvantages and the relationship between EC use and pain is still on its way to become fully clarified.

The apparent safety of EC appeals to current conventional cigarette users, who consider using it to help them avoid the dreadful consequences of cigarette consumption [6]. Meanwhile, EC also allows youngsters to satisfy their curiosity without violating the law and without causing obvious health concerns compared to conventional cigarette (at least before major health and environmental concerns are brought to public attention). Thanks to the enthusiasm on investigating EC and recent findings, stricter prohibition of EC usage in public areas and better prevention of EC exposure to youngsters and women have been enacted [14].

Above all, consuming EC products does have its harm toward human health, though it is relatively safe compared with conventional cigarette usage [3, 4]. EC consumption has possibly led to headache [5, 12, 15], chest pain [5, 17], thermal injury [10, 11], and other pain-related agonies. Fortunately, scientists have begun to test EC components more thoroughly and are trying to conclude the adverse effects of EC consumption.

While the discussion of EC's advantage and disadvantage is still fierce and there is still uncertainty about mechanism and the prevalence of pain, researches and clinical cases will reach a comprehensive evaluation of EC with growing evidence.

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