



## Electronic cigarette (e-cigarette)

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### ABSTRACT

Electronic cigarette (e-cigarette) is a device developed with an intent to enable smokers to quit smoking and avoid the unhealthful effects of cigarettes. The popularity of e-cigarette has increased rapidly in recent years. The increase in its use during the adolescence period is attention-grabbing. Despite the fact that e-cigarette has become popular in a dramatic way, there are certain differences of opinion regarding its long-term effects on health, in particular. While some people assert that it is less harmful than conventional cigarettes, some others assert the contrary. Although e-cigarette contains less toxic substances compared to conventional cigarette, it contains certain carcinogens existing in conventional cigarette such as formaldehyde and acetaldehyde. It also contains heavy metals (nickel, chrome) that conventional cigarette does not contain; and therefore, raises concerns about health. E-cigarette leads to upper and lower respiratory tract irritation as well as an increased airway resistance and an increased bacterial colonization in the respiratory tract. It may also cause tachycardia and increase diastolic blood pressure. Although e-cigarette has been found to have certain benefits in terms of smoking cessation, most of the studies have shown unfavorable results. In this collected work, the effects of e-cigarette on health and its role in smoking cessation are discussed in detail.

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## 1. Introduction

Electronic cigarette (e-cigarette) used today has not a long history. It was first developed in 2003 by Hon Lik, a Chinese pharmacist, with intent to enable his father, who was a lung cancer patient and a heavy smoker, to quit smoking. E-cigarettes are products that typically vaporize a liquid substance containing nicotine, flavoring agents, propylene glycol and/or glycerol.<sup>1</sup> The popularity of e-cigarette has increased rapidly in recent years. Its prevalence among smokers in the United States was 2% in 2010, and reached 30% in 2012.<sup>2</sup> Its prevalence in the adolescent period was ranging from 1 to 3% between 2010 and 2011. And this rate reached 10–20% between 2013 and 2014.<sup>3</sup> Increases at similar levels were found in European and Asian countries, as well.<sup>4,5</sup>

E-cigarette use among middle and high school students in America tripled in the last 2 years, according to the report from the Centers for Disease Control and Prevention. In 2014, more than 2

million middle and high school students used e-cigarettes. The greatest increase in e-cigarette use among American students was recorded between 2013 and 2014. The rate of use rose from 4.5% to 13.4%, with an increase in the number of high school students using e-cigarettes, which was 660,000 in 2013 and reached 2 million in 2014.<sup>6</sup> In a study carried out by Wills et al on 2338 students, the rate of initiation of e-cigarette use in the adolescence period was found to be high.<sup>7</sup>

E-cigarette patented by Hon Lik in 2003 officially entered the American market in 2007. In those years, its sales began in many countries.<sup>8,9</sup> In consequence of some evidence, the US Preventive Services Task Force recommended adults to use e-cigarette for smoking cessation in 2015, but there are conflicting results in this regard.<sup>10</sup> Despite the fact that e-cigarette has become popular in a dramatic way, there are certain differences of opinion regarding its long-term effects on health, in particular. Some people assert that it is less harmful than conventional cigarettes, but some others assert the contrary.

In this collected work, we aimed at revealing whether e-cigarette is really one of the methods for smoking cessation, and whether it can be used with intent to be less affected by the harmful effects of smoking.

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### 1.1. General information about E-cigarette device

In general, there are two types of e-cigarettes. The most widely known and used model includes battery-powered and often cigarette-shaped devices evaporating a liquid that contains propylene glycol and/or glycerol in a rechargeable cartridge. Propylene glycol contained in the fluid in the cartridge provides the formation of an odor similar to cigarette smoke. The battery-powered microprocessor also turns on the red-orange light (LED; Light Emitting Diode) on the tip of the rode; and in this way, provides the appearance of a burning fire on the tip of a cigarette.<sup>1</sup>

The process of tobacco combustion does not occur in this type of e-cigarettes. According to e-cigarette manufacturers, the vapor inhaled by users does not contain CO (carbon monoxide), tar (cigarette tar) or other toxic materials contained in cigarettes. The comparison of toxic substances in e-cigarettes with toxic substances in normal cigarettes is given in Table 1. Their cartridges contain various amounts of nicotine (from 0 to 26 mg). In e-cigarette, the amount of nicotine intake is determined by the user, and some users can prefer completely nicotine-free cigarettes. The products produced by different manufacturers generally differ from each other in terms of their sweeteners (tobacco, menthol, chocolate, fruit, and coffee), appearances, and whether the color of their tips changes during inhalation. But the uniform features that all products have include a cartridge that contains a solution, a tube used by the user when inhaling the vapor, and a battery-powered part called the atomizer that absorbs and heat the solution. In some products, the cartridge and atomizer are combined to create a single part called the cartomizer. In an e-cigarette device, the solution is evaporated by heating or vibrating it.<sup>11,12</sup>

In other type of e-cigarettes, tobacco is used but is combusted at a lower temperature. The combustion temperature of tobacco in a conventional cigarette is approximately 750 °C, while it is 350 °C in this type of e-cigarettes called “heat-not-burn Tobacco Products”. According to animal experiments conducted by the cigarettes industry, combustion of tobacco at a low a temperature leads to up to 90% less release of harmful chemicals and carcinogens.<sup>13</sup>

### 1.2. E-cigarette's effect on health

Physiological effects developed as a result of e-cigarette use are given in Table 2.

Although the long-term effect of e-cigarette in terms of cancer is unknown, the carcinogens that e-cigarette users are exposed to known. The U.S. Food and Drug Administration (FDA) have

analyzed two popular brands in this regard. As a result, various levels of nicotine and carcinogens were found. Formaldehyde and acetaldehyde can be given as examples of carcinogens found in electronic cigarettes. Based on these findings, the FDA has issued a warning about the potential hazards of e-cigarettes.<sup>16</sup> In the study carried out by Kim et al, nitrosonornicotine (NNN), 4-(nitroso methyl-amino)-1-(3-pyridyl)-butanone (NNK) and nitrosoanatabins (NAT) among the nitrosamines specific to tobacco, known to be carcinogenic, were found in the content of e-cigarette.<sup>17</sup> In the comparison of 12 brands of e-cigarettes with cigarette smoke, e-cigarette aerosols were found to have lower levels of toxic substances. Carcinogen levels of e-cigarettes were found to be 9–450 times lower than that of tobacco products.<sup>14</sup> However, in a study carried out on a new product defined as a high-voltage battery powered “tank-style” system, e-cigarette users were ascertained to be exposed to more formaldehyde.<sup>18</sup> In preclinical studies, e-cigarette vapor was found to be associated with also an increased inflammation, oxidative stress and endothelial barrier dysfunction, besides the development of oral cancer and lung cancer.<sup>19</sup> In another study, increased necrosis and apoptosis rates, especially decreased vitality of cells, as well as development of DNA breaks were found in cells exposed to e-cigarettes.<sup>20</sup>

Since e-cigarette does not burn and emit smoke like a normal cigarette, it can be thought not to cause passive smoking effect, but the studies suggest the contrary. Schober et al carried out a study to investigate indoor pollution associated with e-cigarette use; and consequently, they found 7 polyaromatic hydrocarbons, a high level of nicotine, propane-1-2-diol, glycerin, and aluminum classified as carcinogenic agents by the International Agency for Research on Cancer. Similarly, another study showed that formaldehyde, acetaldehyde, isoprene, acetic acid, 2-butanedione, acetone, propanol, propylene glycol, diacetyl (emitted from aromatizing additives), aromatic oils, and nicotine diffused around from the vapor given to the environment during the use of e-cigarettes.<sup>21,22</sup>

In the literature, there are a limited number of case reports about e-cigarette's effect on the lung. Propylene glycol in the content of e-cigarette may cause upper and lower respiratory tract irritation.<sup>15</sup> In the literature, there are case reports about eosinophilic pneumonia and subacute bronchiolitis development associated with e-cigarette use.<sup>23,24</sup> In a study carried out by Gennimata et al, acute effects of e-cigarettes were tried to determined. The study enrolled 32 volunteers. 8 were never smokers and 24 were regular smokers. 11 the volunteers had normal pulmonary functions, whereas 13 had asthma or chronic obstructive pulmonary disease (COPD). Changes were observed in the results of spirometry tests performed before and after inhalation of e-cigarette vapor for a period of 10 min. The 10-min inhalation of e-cigarette vapor was found to cause an instant increase in the airway resistance in both never smokers and regular smokers. In COPD and asthmatic patients, no significant increase was observed in the airway resistance, as a result of 10-min e-cigarette use. In conclusion, researchers stated that they found a significant increase in the airway resistances of the participants of the study, associated with e-cigarette use.<sup>25</sup> And in a study carried out by Sussan et al, e-cigarette use was shown to weaken the defense mechanism of mice that the lung creates against bacteria.<sup>26</sup> In another study, it was observed to cause inflammation in the airway and consequently trigger hyperactivation of the airway caused by allergens.<sup>27</sup> As a result of some studies, it was ascertained that e-cigarette could increase the rate of viral and bacterial infection development as well as virulence of the pathogens such as methicillin-resistant *Staphylococcus aureus*, due to its effects on the respiratory tract.<sup>26,28,29</sup> In their study, Hwang et al found that exposure to e-cigarette vapor increased the up-regulation of the virulence gene in the respiratory tract, led the bacteria to adhere to more epithelial

**Table 1**  
Toxic substances in e-cigarettes, and their comparison with substances in conventional cigarettes<sup>14</sup>

Toxic substance	Average value for 15 inhalations from 12 different brands of e-cigarettes	Average value for mainstream smoke from a conventional cigarette
Formaldehyde, µg	0.2–5.61	1.6–52
Acetaldehyde, µg	0.11–1.36	52–140
Acrolein, µg	0.07–4.19	2.4–62
o-Methyl-benzaldehyde, µg	0.13–0.71	–
Toluene, µg	0.0–0.63	8.3–70
Nitrosonornicotine, µg	0.0–0.00043	0.005–0.19
4-(nitroso methyl-amino)-1-(3-pyridyl)-butanone, µg	0.0–0.0283	0.012–0.11
Cadmium, ng	0.0–0.022	–
Nickel, ng	0.011–0.029	–
Lead, ng	0.003–0.057	–

**Table 2**  
Physiological effects developed as a result of e-cigarette use<sup>15</sup>

Parameters	Effect
Serum carbon monoxide level	As a result of the conflicting results, the effect could not be exactly identified.
Diastolic blood pressure	It causes a significant increase.
Systolic blood pressure	Any significant increase is not observed.
Ventricular systolic and diastolic function	It has no effect
Heartbeat	A significant increase is observed as a result of use for 5–10 min.
Hemogram	There is no change in leukocytes, lymphocytes, and granulocytes.
Exhaled nitric oxide (FeNO)	A significant decrease is observed after a short-term use.
Respiratory impedances (a marker of peripheral airway flow resistance)	It causes a significant increase (18%).
Airway resistance	It causes a significant increase.

cells, resulting in an increased invasion, and enhanced the *Staphylococcus aureus* colonization by increasing the resistance to human antimicrobial peptide LL-37. It is believed that e-cigarette vapor led to an increase in IL-1 and pentraxin-3 level and a decrease in IL-3 level, and bactericidal functions of alveolar macrophages and neutrophils; and consequently increased the bacterial colonization and virulence.<sup>30</sup>

The effects of e-cigarette use on the cardiovascular system were studied, as well. E-cigarette can increase the heart rate, blood pressure, and the risk of getting heart diseases that pave the way for cardiac arrhythmias.<sup>31</sup> But in some studies, no change was found in cardiac functions during echocardiographic assessments of the heart after e-cigarette use.<sup>32</sup> Glycerol contained in e-cigarette can turn into an irritant substance when heated, and this is believed to cause an increased risk of cardiovascular disease.<sup>33</sup>

It was predicted that some heavy metals at toxic levels detected in e-cigarettes may have a potential to lead to problems bigger than the problem of conventional cigarette consumption. Although e-cigarettes seem to be less harmful than ordinary cigarettes, they cause concern due to their metal contents such as nickel and chromium, which are poisonous for humans. Nickel and chromium, the heavy metals detected in e-cigarette most intensively, are thought to be caused by the cartridge.<sup>34</sup>

In consequence of the increase in e-cigarette use, the number of phone calls to poison control centers for adverse effects experienced after exposure to e-cigarette increased. The number of yearly e-cigarette exposures reported to Texas poison centers was 2 in 2009, and this figure reached 43 in 2012. The most commonly detected findings and symptoms in these phone calls were nausea, vomiting, mouth and airway irritation, chest pain, and heart palpitations.<sup>15</sup> According to 2014 report published by the U.S. Centers for Disease Control and Prevention, the number of phone calls to the poison information centers about e-cigarette use has dramatically increased in the last five years. Accordingly, the number of calls increased from just one call per month in 2010 to 215 calls per month in 2014. The fact that more than half of the affected individuals were aged less than 25 years old, gave rise to anxiety among the experts.<sup>35</sup>

### 1.3. E-cigarette's role in smoking cessation

One of the important strategies used in e-cigarette sales is to show e-cigarette as useful for smoking cessation; however, there are conflicting data obtained from studies carried out on this subject. Although e-cigarette manufacturers suggest that it is efficacious in smoking cessation, FDA has not given approval in this regard.<sup>15</sup> In a randomized controlled trial carried out by Bullen et al that enrolled a total of 657 people, 289 people were included in the e-cigarette group, 295 in the nicotine patch group, and 73 in the placebo e-cigarette group. At the end of the follow up period of 6 months, 7.3% of the people given e-cigarette and 5.8% of the people

given nicotine patch were found to be successful in quitting smoking. As a result of this study, e-cigarette was said to be an effective way for smoking cessation.<sup>36</sup> In another study on 1374 people, carried out by Biener et al, it was ascertained that using e-cigarette on a daily basis for a period of 1 month was effective for smoking cessation.<sup>37</sup> In the smoking cessation program applied by Hajec et al to 100 smokers, e-cigarette was found to be effective in 69% of the participants.<sup>38</sup> In a randomized study on 40 smokers with high addiction levels, who had not tried to quit smoking, normal cigarette provided the greatest reduction in the withdrawal symptoms; however, also nicotine containing e-cigarette reduced the desire of smoking and withdrawal symptoms like nicotine inhalers; and it was observed to be tolerated better than nicotine inhalers and cause relatively less mouth and throat irritation. Although nicotine containing e-cigarette reduces withdrawal symptoms more compared to nicotine-free e-cigarette, the reduction was not considered to be statistically significant.<sup>39</sup> In a study that involved a 6-month prospective follow up period, 40 regular smokers who did not intended to quit smoking used e-cigarettes of the same brand. The participants of the study used 2–3 cartridges a day during the study period, and significant reductions were observed in their smoking. In terms of the number of daily cigarette consumption, 50% and 80% continued reductions were observed in 32.5% and 12.5% of the participants, respectively. The results obtained with this study were interpreted in such a way as to suggest that e-cigarette is a promising method for quitting tobacco cigarettes.<sup>40</sup>

Contrary to the studies showing that e-cigarette use is useful for smoking cessation, there are also studies showing that it does not play an active role in smoking cessation, and moreover, causes more smoking addiction. Leventhal and his friends that included 2530 students in 10 schools in a working e-cigarettes, has been found to facilitate the initiation of smoking.<sup>41</sup> Contrary to the studies showing that e-cigarette use is useful for smoking cessation, there are also studies showing that it does not play an active role in smoking cessation, and moreover, leads to more smoking addiction. According to the study conducted on 3847 students (median age was 16 years) in the United States, 5.4% of the students were found to use e-cigarettes to vaporize cannabis. It is very alarming that electronic cigarettes are used as a new and unobtrusive way of using cannabis.<sup>42</sup>

At the end of the study carried out by Adkison et al, which included the U.S., Canada, the UK, and Australia, no difference was found between the smokers who stated that they used e-cigarettes with intent to quit smoking and the smokers who did not use e-cigarettes.<sup>43</sup> In the study carried out by Vickerman et al, the rate of smoking cessation was found to be statistically lower in e-cigarette users compared to those who did not use e-cigarettes ( $p < 0.001$ ).<sup>44</sup> A study on 106 patients diagnosed with head and neck cancer showed that e-cigarettes did not provide any benefit when used for smoking cessation.<sup>45</sup> In another randomized

controlled study, carried out by Caponnetto et al, no difference was found in terms of smoking cessation rates, between the e-cigarette users and those who did not use e-cigarettes.<sup>46</sup> In a meta-analysis on e-cigarette use for smoking cessation, published in 2016, quitting cigarettes was observed to be 28% lower in those who used e-cigarettes compared to those who did not use e-cigarette (odds ratio [OR] 0.72, 95% CI 0.57–0.91). As a result of the meta-analysis, it was ascertained that there was a poor relation between e-cigarette use and smoking cessation.<sup>47</sup>

## 2. Conclusion

In consequence of the reduction in smoking, manufacturers have turned their steps towards e-cigarettes. Manufacturers state that e-cigarettes are less harmful than normal cigarettes, and that they can be preferred as a method for quitting smoking. Although some studies showed that it was useful in smoking cessation, in many other studies it was observed not to play an effective role in this regard. On the other hand, the effect that e-cigarette creates on health when used for smoking cessation should not be ignored. In Turkey, electronic cigarette use was regulated under law in 2013, in line with the studies conducted on health. In this scope, advertisement and indoor use of these products as well as their sales to anyone under the age of 18 have been prohibited.<sup>48</sup> Similarly, in developed countries like the United States and Canada, certain comprehensive prohibitions are applied against e-cigarette.<sup>49</sup> The report about the adverse effects of e-cigarettes on health, published by the World Health Organization, emphasized that strict controls should be ensured and strict measures should be taken for the sales and use of e-cigarettes.<sup>50</sup>

In conclusion, e-smoking is a personal choice; however, it should be kept in mind that it has some adverse effects on health like normal cigarettes; and that its success rates are low when used with intent to quit smoking. Another important point is that e-cigarette paves the way for smoking addiction in children and young people. Preventive works, intended for this worrying fact, should be done.

## Conflict of interest

The authors have declared that no competing interests exist.

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