Electronic cigarettes and their effects on human health

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Abstract
In the last decade electronic cigarettes also known as e-cigarettes have gained popularity. These are devices designed to imitate regular cigarettes. They provide nicotine via inhalation without using tobacco. The introduction of alternative nicotine delivery devices to the consumer market has inspired a vivid debate on the harmfulness of these products. It is discussed whether they are regulated, safe and as harmless as it is claimed. The purpose of this article was to describe the chemical composition of the e-cigarettes and its influence on human’s health. The devices contain many various groups of potentially toxic and carcinogenic compounds: carbonyls, volatile organic compounds and nitrosamines. The research has shown that e-cigarettes contain significantly lower concentration of those substances than the traditional cigarettes. On the other hand, it should be remembered that scientists still do not know potential long term pathologies caused by the liquids.

Key words: cigarettes; tobacco; health; nicotine

Introduction
Electronic cigarette (e-cigarette) was created in 2003 by Chinese pharmacist – Hon Lik.¹ In the English-language literature they are known as ENDS (electronic nicotine delivery systems) or PV (Personal vaporizer).² Fundamentally, the device consists of a power supply system and a vaporizing system. Liquid, a solution containing nicotine, is placed in the reservoir called a cartridge, that user can refill independently. Subpressure generated during the inhalation activates the coil heater which heats the nicotine liquid up. This leads to forming an aerosol...
which is inhaled by the user. The location of nicotine absorption to the circulatory system was not clearly determined – it might be the epithelium of the lung or the oral cavity.\textsuperscript{1} The e-cigarette was designed as an alternative source of the nicotine for the traditional tobacco products. It was advertised as a less noxious product than the conventional cigarettes. However, there isn’t enough data to prove that, especially in terms of their safety and effects during long-term usage.\textsuperscript{2} Smoking is commonly associated with the lungs disorders (including cancers). Nevertheless, the most smoking-related deaths are caused by the cardiovascular diseases.\textsuperscript{3} On the authority of the market research group, the amount of e-cigarettes’ users increased from 7 million in 2011 to 35 million in 2016 worldwide. The global market of ENDS was valued at 11.26 billion USD in 2018 and it is expected to increase to 18.16 billion USD in 2024 according to data released by MarketWatch.\textsuperscript{4}
Chemical composition of liquids

E-liquids used in PV’s are a mixture of various ingredients. The main components are propylene glycol (PG) and vegetable glycerin (VG) that are playing the role of a sol vent. When it’s heated, it form an aerosol, which creates the smoke. The aerosol is a suspension in which solid particles are dispersed in a gas phase. Fluids available on the market contains different amounts of nicotine. The studies show that nicotine concentration may range from 14.8 to 87.2 mg/ml. It has been proven that this level may vary from the amount declared on the label even up to 50%. It should be noted that a significant impact on the quantity of the nicotine contained in the aerosol have technical parameters of the device (battery, power, construction, while the efficiency of its absorption is largely dependent on the user experience (inhalation depth, number of puffs and breaks between them). Some fluids may also contain water, ethanol, preservatives and viscosity regulating substances e.g. polyethylene glycol and sodium alginate. Moreover, there are plenty of flavoring and aromatic substances. There are available liquids with the taste of fruits, mint, coffee, tea, tobacco, bubble gum and even chocolate. Currently, the producers offer a wide range of assortment. The list released in 2012 by FDA (Food and Drug Administration) contains 93 deleterious or potentially deleterious substances that are present in tobacco or tobacco smoke. These are carcinogens, which means that they are toxic to the reproductive system and cardiovascular system. The substances adversely affect human development and show addictive properties. The aerosol generated from most liquids contains five of them and in addition to the nicotine they are acetaldehyde, acetone, acroleine and formaldehyde. Into the bargain in the steam generated from the e-cigarettes there were also detected: volatile compounds (VOC-volatile organic compounds, polycyclic organic hydrocarbons (PAH-polycyclic organic hydrocarbons), polycyclic aromatic amines (PAA-polycyclic aromatic amines), phenolic compounds, acetone and metals. It should be noticed that the concentration recorded substances was even several hundred times lower comparing to the tobacco smoke. In contrast to the traditional tobacco smoke, the aerosol from ENDS does not contain heavy metals e.g. cadmium and lead, which are strongly carcinogenic. The power of the e-cigarette battery and the proportions of the main ingredients in the liquid have and additional important impact on the level of the toxic substances in the inhaled aerosol (PG and VG). The increase of the voltage power supply element from 3.2 to 4.8 V may cause even a 200-fold increase in the concentration of the formaldehyde and aldehyde acetic acid, acrolein and acetone in the produced steam. In addition to this, the highest level of carbonyl compounds was observed for the base products based on the PG itself, which suggests that it is more susceptible to the thermal decomposition.

| Source | Matrix | Unit | Nicotine level | Deviation form the label |
|--------|--------|------|----------------|-------------------------|
| Goniewicz | Cartridge | mg | 0±0.0 to 25±1.1 | −75 to 28% |
|        | Aerosol | mg | 0±0.0 to 19±0.5 | −89 to 25% |
| Cobb | Cartridge | mg/cartridge | 3.23±0.5 to 4.07±0.54 | −80 to −77% |
|        | Aerosol | µg/35 mL puff | 0.3 for puffs 11 to 50 to 1.0 for puffs 1 to 10 | |
| Pellegrino | Cartridge | % W/W | <0.001 to 0.25 | − |
|        | Aerosol | mg/mL | <0.01 to 6.21 | − |

Table 1 Nicotine levels in cartridges and aerosols and their deviation from label.
Impact on the human body
There is currently a lack of scientific data on the health effects of long-term use of electronic cigarettes. Moreover, the number of reports on the short-term effects on the human body is small and is based mainly on surveys.²

Systemic effects
E-smoking may cause headache and dizziness, insomnia, choking, gingivitis, burning in the stomach, release of cytokines and pro-inflammatory mediators.¹² Serious effects also include confusion, convulsions and blindness requiring medical intervention.¹³ There have been also cases of the spontaneous explosion of e-cigarette completed with severe skin burns or fractures of the teeth.¹⁴

Cancers
Research conducted by scientists from the Veterans Affairs San Diego Healthcare System shows that e-cigarettes accelerate cell death and may be the cause of cancer and the lung diseases. Researchers have shown that e-cigarettes damage cells in a way that leads to the cancer. In the study, nicotine-containing agents caused greater damage, but interestingly, damage occurred even when liquids without this substance were used. This may indicate that not only nicotine, but also other aerosol agents damage cells.¹

Respiratory system
From a pulmonological point of view, it is important that the particles present in the aerosol generated from the e-cigarette are of a size that allows them to be aspirated into the lungs. The components of e-liquid cause inflammation in the lungs and are a source of oxidative stress.¹⁵ The use of e-cigarettes can lead to allergic airway inflammation and irritation of the upper respiratory tract. A common side effect is dry cough.¹
In one of the studies it has been shown that replacement of the traditional cigarettes to e-cigarettes in asthmatics may lead to improvement in symptoms and lung function.¹⁵

Cardiovascular system
Available research results indicate that the main cause of the negative impact of aerosol from the electronic cigarettes on the cardiovascular system is nicotine. When using e-cigarettes, the amount of compounds aspirated to the lungs is limited compared to the amount delivered to the body while smoking classic cigarettes. Consequently, this should lead to a reduction in the risk of cardiovascular disease, but without eliminating it.³ Various potentially harmful inhaled substances increase the risk of arrhythmias and hypertension. Adverse effects increase the resistance to respiratory flow.¹⁶
Nicotine enhances the release of catecholamines, which causes endothelial dysfunction and insulin resistance. Mild intoxication is manifested by tachycardia, tremor, chest pain and hypertension. More serious symptoms include bradycardia, hypotension, respiratory paralysis, atrial fibrillation and shortness of breath.¹
Pregnancy
Intrauterine nicotine exposure in animal models is associated with adverse effects on the lungs, cardiovascular system and brain of offspring. No amount of the nicotine is safe during pregnancy.\textsuperscript{17}

Youth and children
Electronic cigarettes pose a potential threat to children. They are very popular among young people due to the content of flavorings and the use of new technologies. However, the presence of a high content of nicotine in the e-cigarette cartridge makes them dangerous to life and health.\textsuperscript{15} In addition, the results of some studies indicate that the use of e-cigarettes significantly increases the risk of developing smoking addiction in young people.\textsuperscript{15} Young users of e-cigarettes report depression, panic disorder and reduced life joy more often than non-smokers. However, less often than conventional smokers suffer from generalized anxiety, panic attacks or social phobia.\textsuperscript{1}

Secondhand smoke
Czogala et al. generated an aerosol from e-cigarettes of three brands and measured the concentrations of the substances contained in it. It turned out that e-cigarettes are a source of passive exposure to nicotine of non-smokers, but they are not a significant source of toxic substances from tobacco burning. The average concentration of nicotine as a result of smoking e-cigarettes was nearly 10 times lower than when smoking an equivalent amount of traditional cigarettes.\textsuperscript{18}
Another study compared the concentrations of substances to which people in the vicinity of conventional smokers and e-cigarettes are exposed. In the case of traditional cigarettes, the presence of 20 compounds exhaled by smokers was found, in the case of e-cigarettes only 6 which were in many times lower concentrations.\textsuperscript{1}

Nicotine replacement therapy
Many experts recommend using e-cigarettes as an aid in quitting smoking addiction. However, cross-sectional and observational studies provide divergent results.\textsuperscript{15} According to some scientists, the key to stop smoking using e-cigarettes, in addition to providing nicotine, is the way it is used. E-cigarettes are used in a similar way to classic cigarettes. This device is held in the palm of your hand and you can puff. These features are important for many people trying to quit smoking.\textsuperscript{2} However, one study found that the chance to quit smoking was 28% lower for those who used e-cigarettes compared to those who didn’t use them.\textsuperscript{1}
Bullen et al. conducted a study on adult patients who smoked 10 or more cigarettes a day. The desire to smoke after night abstinence was compared in three groups. The first of them could use a nicotine inhaler, another e-cigarette with nicotine and the third e-cigarette without nicotine. In the study presented, both the inhaler and the nicotine e-cigarette reduced the desire to reach for a cigarette compared to placebo.\textsuperscript{1}
Another study compared the effectiveness of e-cigarettes and nicotine patches. E-cigarettes, both with and without nicotine, were moderately effective in helping to stop smoking and to similarly abstinence with nicotine patches. However, there is uncertainty about the
effectiveness of using e-cigarettes as a means of nicotine replacement therapy and further research is needed in this case.\textsuperscript{1}

**Summary**

Increasing popularity of PV’s is mostly connected with a widespread belief that they are harmless.\textsuperscript{19} The recent researches shows that substituting traditional cigarette with ENDS should result in reducing a potential pathogenic effects of conventional smoking; however, it will not eliminate the risk completely.\textsuperscript{3} The aerosol from e-cigarettes consists of many potentially deleterious substances that may increase risk of suffering CVD or lung cancer.\textsuperscript{1} It should be stated that the consumer is not aware of what ingredients are actually present in the e-fluid. Considering the actual reports regarding to the analysis of the chemical compositions of liquids, there is lack of a comprehensive research on both substances present in aerosols and directly in the liquid, that is used to refill cartridge.\textsuperscript{13} It is important to remember that the long-term effects of using e-cigarettes have not yet been demonstrated. Small amounts of the formaldehyde and acetaldehyde as well as other aromatic compounds that are present in the aerosol may be causing pathologies that are still unknown to people.\textsuperscript{19}

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