



Review

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## Are electronic cigarettes saviors or new culprits?

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### ABSTRACT

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Electronic cigarette (EC) usage in the world is increasing. It might outsell the other tobacco products in the future with this rate of selling increase. Promoters of EC argue that using them will bring additional benefits in the fight against tobacco. By switching from cigarettes to ECs, smokers will not be exposed to a number of dangerous substances thus; morbidity and mortality of smoking would decrease. This may cause major epidemiologic changes. Opponents argue that none of these claims are proven. Nicotine itself is not only addictive but also a harmful substance. Besides it may disseminate tobacco use young people into nicotine addiction with its new harmless image. These devices imitate the hits of nicotine, therefore feed the addiction rather than prevent it. People simply may continue smoking and use EC where cigarettes are socially or legally unacceptable. The solutions of nicotine carry the risk of using unhealthy mixtures and inappropriate nicotine dosing. Users simply may abuse these devices to use other substances such as cocaine. ECs are not recognized as a form of nicotine replacement therapy. In fact most health authorities are negative on ECs. Legal issues like using ECs in public places are not clear. Health professionals are increasingly facing the questions regarding EC usage and fail to provide satisfactory answers.

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### 1. Introduction

After Herbert A Gilbert got a patent for a device for a non-tobacco cigarette at 1963 he intended that he had made a discovery replacing burning tobacco and paper. This invention made little interest because the harmful effects of smoking was not fully understood at those days. Another inventor Hon Lik from China designed a different device basically depending on the principles of piezoelectric ultrasound at 2001. This device got commercial success in both eastern and western markets afterwards. In the past decade there is an increasing trend for electronic cigarettes. In this

review we tried to discuss the current usage, advantages and disadvantages of electronic cigarettes in the view of current literature.

#### What is an electronic cigarette?

Electronic cigarette (EC) is a battery powered electronic device that heats and vaporizes solutions mostly with nicotine. The main parts of the device is presented in Fig. 1. Some have replaceable cartridge, some are disposable. When the liquid evaporate the user inhales this vapor to receive nicotine similar to cigarette' reach to brain ratios. This



**Fig. 1.** Illustration of electronic cigarette

liquid has drugs, chemicals, flavoring and coloring agents which some of them aim to attract young users. Known agents in these liquids up to date are: Nicotine, glycerol, propylene glycol, Ethylene glycol, 1,3 popandiol, thujone, tobacco specific nitrosamines (N-nitrosocotinine, N-nitrosoanabasine, N-nitrosanabatine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone), tobacco-specific impurities (cotinine, anabasine and myosmine), flavouring agents (ethyl vanillin, vanilla extract, malic acid, linalool, menthol beta-daascenone, acetyl pryazine, tabanone, ethylecetate, ethyl maltol, 2,3,5,6-Tetramethylpryazine, 2-Hydroxy-3-Methylcyclopent-2-en-1-one, 2-Acetylpryidine, 4-(2,6,6-Trimethylcyclohex-1-ene-1-yl)-but-3-ene-3-one, L-Menthan-3-one) (Hahn et al., 2014). EC liquids can contain rimonabant and amino-tadalafil. This makes EC a libido enhancing device (Hadwiger et al., 2010).

#### How are they marketed?

Marketing ECs seems to be another success story for tobacco companies as the market grows rapidly. Tobacco companies initiated EC sales in 2006 and reached to estimate billion dollar profits. Global EC market is expected to grow over \$50 billion by 2015 to 2025 (Research and Market, 2015). The companies are achieving these figures despite negative approach of most governments. They are in intense campaign to portray EC as harmless product. Even use term of 'vaping' instead of smoking. It is marketed online or in local suppliers as an aid to smoking cessation or a safe alternative for smoking. Smoking EC cost less than cigarettes. This pricing policy and being able to use

indoors are making EC popular. This popularity created a new generation with nicotine addiction. Authorities are taking a number of steps to limit dissemination of ECs (applying same rules for tobacco i.e., sale ban to people under age 18). Banning the use of flavored nicotine liquid is also considered (FDA, 2015). Some of the powerful cigarette companies are also producing ECs (Reynolds American Plc, Altria, Imperial Brands Plc). Industry can put a lot of resources on marketing and public relations.

#### Rose project

Inhalation is very favorite way of delivering substances aimed for brain. Cigarette is an ingenious way of delivering nicotine as it reaches brain in seconds after a puff. Developing a way to deliver nicotine as efficient as a cigarette is a goal for some scientists. Rose Project is developing a device that does not use heat. When Smokers take a puff pyruvic acid and nicotine mix and form nicotine-pyruvate cloud. Pyruvic acid is a naturally occurring substance in the body so it won't add toxicity to nicotine. Smokers will be free of tars and other harmful substances in the cigarettes (Rose et al., 2010). But using nicotine as a recreational substance contradicts the philosophy of stopping addictions.

#### Nicotine inhalers

Nicotine inhalers (NIs) are established form of nicotine replacement therapy (NRT). However they are not ECs and they have different action mechanisms. The nicotine inhaler consists of a plastic mouthpiece and plastic tube with a cartridge containing nicotine. People can practice the hand-to-mouth ritual of smoking,

When take a puff the inhalator releases nicotine into mouth then absorbed through the lining of the mouth, throat and upper esophagus just like nicotine gum. There is no risk of passive nicotine exposure. Each puff contains about 10 times less nicotine than a puff of a cigarette hence no risk of addiction to nicotine. Peak nicotine dose occur after 10-15 minutes.

### **The rationale behind the use of EC**

E-cigarettes are cheaper, cleaner, more flavorful, and less harmful than tobacco. They seem to be viable alternative to smoking cigarettes. Almost one-fifth of smokers who try ECs once go on to become regular users (Etter and Bullen, 2014). Cigarette smokers may switch to ECs in order the decrease the risks of smoking. If ECs are used instead of tobacco, users will not be exposed to many harmful chemicals and tar normally present in cigarettes. Around 4000 different chemicals with 40 known cancerogens make tobacco a very dangerous substance. If only nicotine is responsible for addiction supplying only nicotine with similar delivery system seems to make sense. The ideal goal is stopping cigarette all together. But unfortunately fighting nicotine addiction is difficult task with high relapse rate. ECs may help prevention of relapse in people with severe cravings. It may help to those who want to stop smoking. Smokers are addicted to the behaviors associated with smoking besides nicotine. ECs may fulfill these hands to mouth rituals and fight psychological components of smoking.

The most common reason for using ECs is to reduce consumption of cigarettes. ECs may be useful in cutting the number of cigarettes when compared to nicotine patch and placebo. EC may also protect those exposed to frequent secondhand smoke. If ECs were to replace conventional cigarettes, it could have a substantial impact on public health. Smoking related morbidity and mortality would decrease.

People with depression and schizophrenia use nicotine to self medicate themselves. In fact many psychiatric wards have a smoking room. While there may be some short term benefits of using cigarettes for psychiatric patients the health risks are too great. ECs may provide alternative solution for these people. No serious adverse event (SAEs) in the short term related to EC use is reported. All these benefits seem to make EC a good alternative to smoking. However the grades of quality of these studies are classed as low and very low (Boyce et al., 2016).

### **Arguments against EC**

EC promoters wants to create an image that EC is less dangerous than smoking in the same way they did in 1950s when they introduced filtered cigarettes and claimed that filtered cigarettes do not cause cancer. Two main arguments against ECs are: Lack of evidence

of efficacy and safety and the unknown long term effects. ECs are not an accepted form of NRT. Quality and ingredients of ECs needs monitoring. The vapor in these devices is not proved to be safe. ECs expose both users and bystanders to particulate matter (Schober et al., 2014). Lung and immune system damage is being documented on mice (Sussan et al., 2015). They may trigger curiosity and encourage young people for usage. It still is not clear whether EC may help smokers to quit, or make people user of EC and tobacco cigarettes (CDC, 2015). No country is endorsed ECs and they are bringing same legislation as tobacco.

### **Nicotine**

Nicotine is a strong addictive substance. Cigarettes are the most efficient nicotine-delivery device. Inhaling smoke loaded with nicotine disseminates through the lungs and rapid nicotine boost into the bloodstream occurs. The acute effects of nicotine diminish in a few minutes and the smoker should continue dosing for pleasure and prevention of withdrawal symptoms. No NRT can imitate this action. Only ECs are capable of delivering nicotine in the vapor. Therefore ECs are proposing recreational use of nicotine. If medical establishment accepts EC as a form of NRT, it will have endorsed and legitimized an addictive substance. This may disseminate nicotine addiction.

Nicotine has toxic effects. Exposure to nicotine during pregnancy harms the developing fetus, and causes lasting consequences for the developing brain and lung function in newborns. Nicotine exposure also affects maternal and fetal health during pregnancy, and can result in low birth weights, preterm delivery and stillbirth. Nicotine has a negative impact on adolescent brain development. Human brain development continues far longer than was previously realized, and nicotine use during adolescence and young adulthood has been associated with lasting cognitive and behavioral impairments, including effects on working memory and attention (Surgeon General Report, 2014). Nicotine may be carcinogen and appears to promote the spread of existing tumors (Sanner and Grimsrud, 2015). Nicotine is toxic when ingested. The lethal dose is 6-13 mg/kg. Side effects of the nicotine with different forms are: Dyspepsia, nausea, diarrhea, dry mouth, hiccup, flatulence, increased salivation, stomatitis, oral blistering, tooth disorder, glossitis, unpleasant taste, decrease in lower esophageal sphincter pressure, heartburn, chest discomfort, bronchitis, bronchospasm in patients with asthma, sore throat, increase in heart rate and blood pressure, new ventricular and supraventricular tachycardia, ST- or T-wave changes, rare MI, local skin irritation with patches, lightheadedness, headache, sleep disturbances, abnormal dreams, irritability, dizziness, and tremor. Stroke due to severe cerebral artery vasospasm has

been reported in a patient with a recent history of subarachnoid hemorrhage shortly after applying a 10 mg nicotine. Longterm side effect are included as arthralgia, myalgia, jaw pain, increased platelet aggregation and thrombus formation, hyperinsulinemia and insuline resistance (Drugs.com, 2016).

### **Nicotine solutions and safety of the device**

Nicotine solutions are not regulated yet, their labels may be inaccurate, their contents and inhalation devices are prone to contamination. They are available usually in 100 mg bottles with various concentrations. The lethal dose when ingested is 6-13 mg/kg. One sip of 5 ml can render a child 500 mg of nicotine. Nicotine acts like succinylcholine causing seizures and paralysis in 15-30 minutes. Rapid response with treatment of benzodiazepins and induced coma is required. Succinylcholine should not be used for intubation.

Propylene glycol, glycerol or ethylene glycol in these solutions may form toxic or cancer-causing compounds when vaporized. ECs produces formaldehyde in similar level or higher than cigarettes. Anabisine, myosmine and beta nikotryinne also detected in ECs. Anabisine is present in tobacco to protect the plant from harmful pests. Some food additives are generally considered safe when eaten; this does not mean that these chemicals are safe when inhaled, as a vapor (Hutzler et al., 2014). Further problem might occur when people starts experimenting with different recreational chemicals in these solutions. Possibilities are endless.

Diacetyl, a buttery flavored chemical often added to food products such as popcorn, caramel, and dairy products, has also been found in some ECs with flavors. Diacetyl can cause a serious and irreversible lung disease commonly known as "popcorn lung." Many of these chemicals are produced for oral consumption. We don't know effects of these chemicals when they are inhaled (Farsalinos et al., 2014).

### **Dopamine and addiction mechanisms**

Dopamine is critically important in reward and motivation. It is released as a reward in taking drugs, smoking, having sex, and eating food. In addicted persons the phasic dopamine release is heightened, compelling person the pursuit of abused substances. When a smoker stops smoking low dopamine levels occur as a result of withdrawal. This is the main reason

for relapse due to unpleasant feelings of withdrawal (Wonnacott et al., 2005). Withdrawal symptoms are; Anhedonia, anxiety-related behavior, conditioned fear, irritability, anger, difficulty concentrating, sleep disturbance, increased appetite, weight gain and threat-induced anxiety (Hogle et al., 2010). As long as this abnormal dopamine conducting system in the brain continues the addiction and relapse risk will continue. Therefore the aim should be vane of nicotine addiction altogether. ECs seem to feed these addiction pathways to remain.

### **Young people and EC**

Limbic system is matured before prefrontal cortex control systems. This renders developing youth brains more susceptible for addictions. Therefore it is dangerous to encourage young people to use an EC (Villanti et al., 2015). In fact Use of ECs is increasing rapidly (CDC, 2016). Even it has been reported that ECs are associated with more cigarette smoking (Rigotti, 2015). Youths are using EC when they cannot use cigarettes in social settings. They don't see it as an aid to stop smoking. People who do not smoke may be attracted to EC for its less harmful, socially more acceptable image. For a youth it may be a way to seek attention and simple out of curiosity. The appeal of flavored e-cigarettes to children and adolescents are alarming. Nicotine is highly addictive substance and once they are hooked they may easily switch to regular cigarette. When EC is accepted as a viable and healthier option for smoker's nicotine addiction may disseminate easier. It may have an image of socially acceptable, harmless activity. These images may act like magnets for youths.

There may be some benefits of ECs namely quitting or decreasing the number of cigarettes. Moreover no significant adverse effect is reported with EC use. However these claims are not proven and quality of evidences are poor. Arguments against ECs seem to have better rationale. ECs are running the dangers of luring young people into nicotine addiction. People simply may use EC and cigarettes at the same time. EC may feed addiction rather than stop it by providing dopamine peaks. Official view of most health authorities on EC negative. Until now there is not sufficient evidence to recommend EC as a first-line option in smoking cessation services.

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