COMMENTARY

Cigarette Alternatives: Are they Safe?

Nisha Shantakumari^{1*}, Jayakumary Muttappallymyalil², Lisha Jenny John³, Jayadevan Sreedharan⁴

Abstract

In spite of limited data regarding the safety or effectiveness of electronic cigarette introduced into the market as a healthier alternative to tobacco smoking, its popularity has increased enormously. E-cigarettes have penetrated the market rapidly owing to the elaborate marketing network and attractive marketing strategies. Stated advantages include the claim that they help quit smoking and produce less exposure than conventional smoking. The list of disadvantages is even more elaborate. While the majority of the studies supporting health claims and efficacy for quitting smoking are not scientifically sound, they are also challenged by studies providing contradictory results. Owing to the limited evidence on the potential advantages and disadvantages of e-cigarettes, the debate on their safety continues.

Keywords: E-cigarettes - vapers - smoking cessation - scientific evidence

Asian Pac J Cancer Prev, 16 (8), 3587-3590

Introduction

Tobacco is consumed in different forms across the world as smoke form and smokeless form. The smoke forms of tobacco include; cigarette, cigar, bidi, chutta, dokha, and electronic cigarette (e-cigarette). E-cigarettes came into existence from an invention in the early 2000 by a Chinese Pharmacist, Hon Lik. The United States (US) patent application describes it as a substitute for quitting smoking and as a substitute for cigarettes (Grana, 2014). The electronic cigarette, electronic nicotine delivery system or electronic cigarillos, is a battery-operated vaporizer which produces aerosol similar to smoke(Bertholon JF,2013).It simulates tobacco smoking and other chemicals.

Basic Design of E-Cigarettes

A typical e-cigarette is designed to include a battery, an atomizer or aerosol generator, a flow sensor and cartridge which contain the e-liquid. E-liquids are usually a mixture of propylene glycol, flavoring agents, glycerin and may or may not contain nicotine. The purity and concentration of these substances vary.

The e-liquid is available in the market in bottles or prefilled disposable cartridges or in a kit for the consumers to make the liquid. The concentration of contents in e-liquid will be depicted on the label in mg/ml. When activated the atomizer vaporizes the liquid that produces a visible aerosolized droplets which enters the users mouth and the respiratory tract (Bertholon, 2013).

Types of E-Cigarettes

There is substantial variability in the type of e-cigarettes available. The first generation e-cigarettes are small, with low-capacity batteries, polyfil-filled atomizers and resemble the conventional tobacco cigarettes. The secondgeneration electronic cigarettes or modern electronic cigarettes were invented in 2008 by Dr. Yunqiang Xiu. These e-cigarettes have batteries of higher-capacity, larger atomizers with the ability to refill them with e-liquid. Third-generation devices or 'Mods' consists of lithium batteries of large capacity with electronic circuits that help to change the delivery of voltage or power to the atomizer (Farsalinos and Polosa, 2014).

Factors Contributing Towards Upward Trend in E -Cigarette Smoking

Electronic cigarette usage has been significantly increasing worldwide . However, the prevalence rate varies markedly between countries. A study conducted in 2013 estimated the prevalence rates of e-cigarette use to be as high as 15% in the US, 10% in the United Kingdom, 4% in Canada and 2% in Australia (Adkison, 2013).

The popularity of e-cigarettes has been increasing in spite of limited data regarding their safety or effectiveness. The marketing strategies of e-cigarettes play a major role to in this regard. The marketing network utilizes television, internet sites, social networking sites such as twitter and facebook, and these advertisements project a "cool" image of the users. The access restrictions imposed on tobacco and tobacco related products by the FDA to reinforce

¹Department of Physiology, ²Department of Community Medicine, ³Department of Pharmacology, ⁴Statistical support facility, CABRI, Gulf Medical University, Ajman, UAE *For correspondence: drnishabiju@gmail.com

Nisha Shantakumari et al

its disapproval of tobacco use do not extend towards advertising of e-cigarette which undermines its own efforts at smoking cessation. Increasing number of youth is trying out these products because of the style quotient portrayed, availability of e-cigarettes in attractive colors, varying flavors and some e-cigarettes have fancy decors simulating attractive gadgets. The advertising media also use celebrity endorsements for their product promotion thus appealing to masses (Rooke and Amos, 2013).

E-cigarettes advocated to emit smokeless vapor are permitted at places where smoking is banned such as public places. The other reason for accelerated sales of e-cigarettes is their increasing availability. E-cigarettes are a cheaper alternative to traditional cigarettes which have taxes imposed on them (Grana and Ling, 2014). Previously they were ordered only from internet sites, while now they are available at places that sell traditional cigarettes: tobacco stores, warehouse/supermarkets, and convenience/gas stations. This is the scenario in countries with weaker tobacco control policies in both tax and smoke-free air. In places with stricter policies, users resort to internet sites for procurement of the product (Rose, 2014).The more available they become, the more "normative" the e-cigarettes appear.

Stated Advantages of E- Cigarettes

E- cigarettes were introduced into the market as a healthier alternative to tobacco smoking and are being widely used for quitting cigarette smoking. Few randomized controlled trials conducted to investigate the efficacy of e-cigarettes in smoking cessation revealed that e-cigarettes with or without nicotine were moderately effective in helping smokers to quit cigarettes and in smokers not intending to quit. E-cigarettes also decreased the number of cigarettes consumed and resulted smoking cessation without significant side-effects (Caponnetto et al., 2013; Bullen et al., 2014). The effect on smoking cessation and relief from withdrawal symptoms were found to be better with nicotine containing e- cigarettes. The nicotine yield from e-cigarettes ranges from zero to 43.2 mg /100 mL puff and is much less in comparison with 152-193 mg nicotine/100 mL puff yielded from a conventional cigarette (Schroeder and Hoffman, 2014).

E-cigarettes are less addictive and have low user liability owing to the lower rates of nicotine absorption. Hence, users report less dependence on e- cigarettes than conventional cigarettes. Smokers find the sensation of using an e-cigarette (mimicking the use of conventional cigarettes) thus satisfying their cravings more completely than other nicotine replacement products such as patches or chewing gums (Etter and Bullen, 2011).

Abstinence for smoking while on e-cigarettes also relives the users from the commonly encountered side effects of smoking such as coughing, dyspnea and unpleasant odors. In comparison with tobacco cigarettes the exposure to smoke vapor produced by e- cigarettes is very small. Risk analysis using e-cigarettes emissions and assessment of indoor air concentrations concluded that there was no significant risk to health from e-liquid vapors while tobacco smoke samples approached risk limits for adult exposure (Etter, 2010). Long-term carbon monoxide (CO) exposure has been linked to cardiovascular disease. CO generated with e- cigarettes is much lower than that produced during cigarette combustion. In part for this reason, substituting for cigarettes has been suggested as a strategy for reducing the harm of tobacco smoking (McAuley et al., 2012). With new generation e- cigarette devices in the market consumers can use them for more time before being discharged. E-cigarettes liquids are available in variety of flavors to cater to the choice of the consumer market. The atomizers have greater capacity and can be refilled with a variety of flavoring liquids instead of having to use prefilled one. (Vansickel et al., 2010).

Stated Disadvantages of E- Cigarettes

The use of e-cigarettes is permitted in places where smoking banned may increase the social exposure to smoking and contribute to the 'renormalization' of smoking behaviors among the youth. Public use of e-cigarettes also provides visual cues to smoke, which undermines quit attempts and promotes relapse (Fairchild et al., 2014). Owing to the increasing popularity of e-cigarettes among the youth it may influence the youth to try other tobacco products, including conventional cigarettes.

The particle size and number in e-cigarettes aerosol are similar to conventional cigarettes and are small enough to enter the systemic circulation. E- Cigarettes use high air flow rate to produce aerosol which increases their penetrability into respiratory passages and circulation. The aerosol contains heavy metals such as lead, nickel, and chromium which are labeled by FDA as potentially harmful elements .E-cigarette aerosols are not merely water vapor as falsely claimed. The lead and chromium concentrations in e-cigarette aerosols are in the range of conventional cigarettes, concentration of nickel is about 2 to 100 times greater than conventional cigarette smoke(Saffari et al., 2014). Animal studies have shown that long-term inhalation of nickel hydroxide nanoparticles have been shown to induce oxidative stress and inflammation in the lungs and cardiac tissues of mice (Kang et al., 2011).

The propylene glycol in e-cigarettes is an irritant to the respiratory tract and causes broncho constriction. There is increased dynamic airway resistance which could be of grave concern to people with chronic obstructive lung diseases (Vardavas et al., 2012). Heating up of nicotine tank systems release formaldehyde and acetaldehyde which are potent carcinogens (Kosmider et al., 2014). E-cigarette vapors have been reported to increase virulence of drug-resistant bacteria (Crotty Alexander et al., 2014).

The flavoring agents used in e-cigarettes have been shown to be cytotoxic to human embryonic stem cells. This could be cause of concern to pregnant women who use e-cigarettes or are exposed second hand to their aerosol (Bahl et al., 2012). The water vapor produced by the e-cigarette emission is reported to be a source of indoor air pollution (Schober et al., 2014).

Human factors also have a considerable impact on the

risk associated with e-cigarettes. Poor product design or improper user behavior can exacerbate the risk of exposure to e-liquids from leaks or spills (Yang, 2014). E-liquids have also been reported to be intentionally misused to aid in suicide attempts. Explosions of e-cigarette devices have resulted in sensory impairments, oral disfigurement and property damage to users. Less serious side effects include irritation of respiratory tract and oral cavity (Chen, 2013).

The e-cigarettes available or marketed usually lack product brochures and are inappropriately labeled including misleading, ambiguous and incomplete labeling. This could pose a health hazard owing to the complexity of e-cigarette products and their potential risks (McQueen et al., 2011). There is a lack of information on the proper disposal of e-cigarette products and accessories, including cartridges. The nicotine from discarded cartridges can contaminate soil and water sources and could adversely impact the environment (Chang, 2014).

Critique on Safety

The growing popularity of e- cigarettes is owing to a cleverly advertised belief that it helps in effective reduction or complete cessation of traditional cigarette smoking. While there has been evidence in contrary with population studies suggesting that e- cigarette users are less likely to quit smoking (Adkison et al., 2013; Vickerman et al., 2013). The popularity of e-cigarettes has led to increasing prevalence among the youth and subsequently shifting to the adolescents. Furthermore the proportion of ever users and dual users of conventional tobacco and e-cigarettes are also on a rise. Thus the e-cigarettes are further increasing the existing tobacco related public health burden rather than reducing it (Lee, 2014).

Majority of the research data suggest that e-cigarettes may deliver nicotine at levels sufficient to substitute for cigarettes and hence are an effective substitute for smoking. A closer look at the studies favoring the use of e-cigarettes reveals a lot of loop holes in their research methodology including lack of control groups for comparison and high dropout rates.1Researchers safely conclude that more studies are needed to establish the safety and effectiveness of e-cigarettes. It has been a frequent occurring that multinational tobacco companies are funding prospective studies with results in favor of e-cigarettes. This raises a conflict of interest argument, and could well be a tactic of commissioning research to suit personal interests. Also the fact that needs to be emphasized is that e-cigarettes are not been approved as smoking cessation aids by the FDA or even subject to any regulation until recently. It is only in April 2014 that FDA has announced its intention to regulate e- cigarettes as tobacco product (Song and Glantz, 2015).

The content of nicotine, the primary addictive substance of tobacco products, is much lower in e-cigarettes than conventional cigarettes. The concentration of nicotine yields differ in different e-cigarette brands and there is no uniformity in the delivery of nicotine either across products or from puff-to-puff of the same brand (Goniewicz et al., 2013). Apart from the concentration of nicotine, its absorption rates and exposure influences

DOI:http://dx.doi.org/10.7314/APJCP.2015.16.8.3587 Cigarette Alternatives: Are they Safe?

the dependence and abuse liability of nicotine products. An important factor which affects nicotine exposure is the product use behavior. E-cigarettes deliver nicotine through the pulmonary and buccal routes in inexperienced e-cigarette users. Absorption rates are higher through pulmonary than buccal routes. It is found that experienced users however use the device more intensively, with longer puffs and lower inhalation time, than inexperienced users and hence can achieve nicotine exposures equivalent to traditional cigarettes by adapting their use behaviors and hence maintain their nicotine dependence (McQueen et al., 2011).

While the whole focus of nicotine replacement therapies is to lower levels of nicotine, what also needs to be taken in to account are the other constituents like anabasine, nor nicotine, and acetaldehyde found in several types of e-cigarettes that are also known to contribute to their use and dependence. The dependence is then also likely to expose the user to the risks raised by several such liquid impurities detectable above the level set for nicotine products (Vansickel et al., 2013; Etter et al., 2013; Dawkins and Corcoran, 2014). The quantities of flavorings in the e-cigarette liquids need validation, as the quantity determines the degree of cytotoxicity of these flavorings. There is a lack of information regarding the chemicals used in manufacturing e-cigarettes or those synthesized during vapor generation. Cigarettes emit fine and ultrafine inhalable liquid particles, carcinogens and nicotine into the indoor air, thus raising the level of these particulates. The dose-response relationship predisposes the user and people subjected to second hand exposure to greater health risks. Nicotine has a role in neuro-degeneration and can cause developmental abnormalities in children and fetuses. The potential harmful effects of e-cigarette need to be investigated further especially in vulnerable populations including children and pregnant women (Bam et al., 2014).

E-cigarettes are presently being used in a wide range of environments when compared to conventional cigarettes. Appropriate product use and risk consequences of recharging of reusable devices could be affected by the environment. Product quality, potency and function can be affected by the environment in which it is stored. There is a need for research to adequately characterize the environments for e-cigarettes use and storage (FDA, 2000).

E -Cigarette usage has become popular over the last four or five years only, hence biological effects of ecigarette aerosol exposure has been investigated directly only in few studies and for short duration of exposure. While robust literature exists on links between smoking conventional cigarette and cancer, epidemiological studies need to be conducted to investigate the long term health effects of e-cigarettes. Hence it is too early to conclude that e-cigarettes are safe.

Recommended Regulation

The existing restrictions as conventional cigarettes should be imposed on e-cigarettes as well. This would help ensure that e-cigarettes do not undermine progress in reducing tobacco use. Not only should there be a ban

Nisha Shantakumari et al

on the sale and use of e-cigarettes wherever tobacco sales are banned but also there is a need to monitor advertising, product placement, celebrity endorsement, and other marketing approaches. These measures would prevent promotion likely to work against public health, particularly children and other non-smokers. Classifying them as medicinal products available only on prescription would compel them to follow a costly and lengthy authorization and limit free sales over the internet. FCTC Article 5.3 can serve as a guideline for developing and implementing regulations for E-cigarettes.

However the most effective recommendation would be to counsel smokers or adhere to the nicotine replacement therapies which are approved by FDA until we have more evidence on the safety and efficacy of e-cigarettes for smoking cessation.

References

- Adkison SE., O'Connor RJ, Bansal-Travers M, et al (2013). Electronic nicotine delivery systems international tobacco control four-country survey. Am J Prev Med, 44, 207-15.
- Bahl V, Lin S, Xu N, et al (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reprod Toxicol*, **34**, 529-37.
- Bam TS, Bellew W, Berezhnova I, et al (2014). Position statement on electronic cigarettes or electronic nicotine delivery systems. Int J Tuberc Lung Dis, 18, 5-7
- Bertholon JF, Becquemin MH, Roy M, et al (2013). Comparison of the aerosol produced by electronic cigarettes with conventional cigarettes and the shisha. *Rev Mal Respir*, 30, 752-57.
- Bullen C, Howe C, Laugesen M, et al (2014). Electronic cigarettes for smoking cessation: a randomized controlled trial. *Lancet*, **382**, 1629-37.
- Caponnetto P,Campagna D,Cibella F, et al (2013). Efficiency and safety of an electronic cigarette (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PLoS One*, **8**, 66317.
- Chang H (2014). Research gaps related to the environmental impacts of electronic cigarettes. *Tob Control*, 23, 54-8
- Chen IL (2013). FDA summary of adverse events on electronic cigarettes. *Nicotine Tob Res*, 15, 615-16.
- Crotty Alexander LE, Enany S, Hwang H, et al (2014). Electronic cigarette vapor (ECV) exposure decreases Staphylococcus aureus susceptibility to macrophage and neutrophil killing. Presented at: 2014 American Thoracic Society meeting; May 16-21; San Diego, California. Abstract 57341.
- Dawkins L, Corcoran O (2014). Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. *Psychopharmacology (Berl)*, **231**, 401-7.
- Etter JF (2010). Electronic cigarettes: a survey of users. *BMC Public Health*, **10**, 231.
- Etter JF, Bullen C (2011). Electronic cigarette: users profile, utilization, satisfaction and perceived efficacy. *Addiction*, **106**, 2017-28.
- Etter JF, Zather E, Svensson S (2013). Analysis of refill liquids for electronic cigarettes. *Addiction*, **108**, 1671-9
- Fairchild AL, Bayer R,Colgrove J (2014). The renormalization of smoking? e-cigarettes and the tobacco "Endgame". N Engl J Med, 370, 293-5
- Farsalinos KE and Polosa R (2014). Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. *Ther Adv Drug Saf*, **5**, 67-86.
- FDA (2000). Guidance for industry and FDA premarket

and design control reviewers: medical device usesafety: incorporating human factors engineering into risk management. Washington, DC: U.S. Food and Drug Administration.

- Goniewicz ML, Kuma T, Gawron M, et al (2013). Nicotine levels in electronic cigarettes. *Nicotine Tob Res*, **15**, 158-66.
- Grana R, Benowitz N, Glantz SA(2014). E-cigarettes: a scientific review. *Circulation*, **129**, 1972-86.
- Grana RA, Ling PM (2014). Smoking revolution? A content analysis of electronic cigarette retail websites. *Am J Prev Med*, **46**, 395-403.
- Kang GS, Gillespie PA, Gunnison A, et al (2011). Long-term inhalation exposure to nickel nanoparticles exacerbated atherosclerosis in a susceptible mouse model. *Environ Health Perspect*, **119**, 176-81.
- Kosmider L, Sobczak A, Fik M, et al (2014). Carbonyl compounds in electronic cigarette vapors-effects of nicotine solvent and battery output voltage *Nicotine Tob Res*, 16, 1319-26
- Lee S, Grana RA, Glantz SA (2014). Electronic-cigarette use among Korean adolescents: a cross-sectional study of market penetration, dual use, and relationship to quit attempts and former smoking. *Adolesc Health*, **54**, 684-90.
- McAuley TR, Hopke PK, Zhao J, Babaian S (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhal Toxicol*, **24**, 850-7.
- McQueen A, Tower S, Summer W (2011). Interviews with "vapers": implications for future research with electronic cigarettes. *Nicotine Tob Res*, **13**, 860-7.
- Rooke C, Amos A (2013). News media representations of electronic cigarettes: an analysis of newspaper coverage in the UK and Scotland. *Tob Control*, 23, 507-12.
- Rose SW, Barker DC, D'Angelo H, et al (2014). The availability of electronic cigarettes in US retail outlets, 2012: results of two national studies. *Tob Control*, **23**, 10-16
- Saffari A, Daher N, Ruprecht A, et al (2014). Particulate metals and organic compounds from electronic and tobaccocontaining cigarettes: comparison of emission rates and secondhand exposure, *Environ Sci Processes Impacts*, **16**, 2259-67
- Schober W, Szendrei K, Matzen W, et al (2014). Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. *Int J Hyg Environ Health*, **217**, 628-37.
- Schroeder MJ, Hoffman AC (2014). Electronic cigarettes and nicotine clinical pharmacology. *Tob Control*, 23, 30-35.
- Song AV, Glantz SA (2015). Assessing tobacco regulation: moving beyond economists. *Tob Control*, 1-2.
- Vansickel AR, Cobb CO, Weaver MF, Eissenberg TEA (2010). clinical laboratori model for evaluating the acute effects of electronic "cigarettes":nicotine delivery profile and cardiovascular and subjective effects. Cancer Epidemiol Biomarkers Prev, **19**, 1945-53.
- Vansickel AR, Eissenberg T (2013). Electronic cigarettes: Effective nicotine delivery after acute administration. *Nicotine Tob Res*, 15, 267-70.
- Vardavas CI, Anagnostopoulos N, Kougias M, et al (2012). Short-term pulmonary effects of using an electronic cigarette: impact on respiratory flow resistance, impedance, and exhaled nitric oxide. *Chest*, **141**, 1400-6
- Vickerman KA, Carpenter KM, Altman T et al (2013). Use of electronic cigarettes among state tobacco cessation quitline callers. *Nicotine Tob Res*, 15, 1787-91.
- Yang L, Rudy SF, Cheng JM et al (2014). Electronic cigarettes: incorporating human factors engineering into risk assessments. *Tob Control*, 23, 47-53