The Electronic Cigarette: The Good, the Bad, and the Ugly

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Electronic cigarettes (EC) are battery-powered nicotine delivery systems that have increased in popularity since they entered the US market. EC has been reported to contain less carcinogens than traditional cigarettes, cause less acute lung effects in healthy individuals, and may help with smoking cessation. It has also been viewed as a potential safer alternative for asthmatic smokers, but its effects on lung functions are unclear. However, EC do carry some harmful aspects as they contain formaldehyde and formaldehyde-forming hemiacetals as well as potentially toxic particulate matter that deposits on surfaces. EC are an increasingly popular device that could serve as a gateway into traditional cigarette smoking or illicit drugs. The popularity of EC has brought with it money from large tobacco corporations and mass marketing. Lack of regulation has generated product inconsistency and potential health hazards. This review highlights what is known and what still needs to be answered about EC. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:498-505)

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Electronic cigarettes (EC) are battery-powered devices that deliver aerosolized nicotine and other additives to users.[1] EC were first commercialized in China in 2003 and entered the US market in 2007.[2,3] Most devices resemble cigarettes, whereas others resemble pens, hookah tips, or screw drivers (Figure 1).[3,4] The liquid contained in the EC, referred to as e-liquid, generally consists of nicotine, water, propylene glycol (PG), glycerin, flavorings, and/or other additives.[5] The e-liquid may be packaged in replaceable cartridges, refill liquids, or contained in disposable EC themselves. The EC device, usually powered by a small rechargeable lithium-ion battery, is activated by inhalation at the tip or, on some models, by pressing a button. The microprocessor controls the power light-emitting diode (LED) tip and the heating element once the EC is activated. The LED tip glows when the vaporizer is in use and the heating element produces the vapor mist that carries the nicotine vapor (Figure 2).[3]

EC are currently not federally regulated in the United States, and there are only limited safety data regarding their acute and long-term use.[5] Despite this, the sale and use of EC is rising.[5] This article is a structured review of the available literature regarding the health effects of EC and a summary of the potential harms and benefits of their use in comparison with combustible cigarettes.

THE GOOD

Combustible cigarette smoke contains at least 70 carcinogens including formaldehyde, free radicals, toxic gases, heavy metals, and tobacco-specific nitrosamines.[6] These toxins have been measured at 9-fold to 450-fold greater than those found in EC aerosol.[5] Another form of toxin exposure, termed thirdhand smoke, results from the particulate matter (PM) depositing on surfaces and can linger for months.[7] Pellegrino et al found that the PM emissions from EC aerosol were 15 times lower than emissions found in combustible cigarette smoke, though the levels still exceeded the World Health Organization (WHO) air quality guidelines.[8] These findings should be interpreted with caution as the actual levels of toxicants in this study may be higher than what was measured due to variations in puff topography among naïve and experienced users and variability between various EC devices and liquids.[5]

Combustible cigarettes are estimated to cause more than 480,000 deaths annually. Smokers who quit before the age of 40 reduce the risk of dying from tobacco-related diseases by up to 90%.[9,10] The large health burden related to combustible cigarette use has led to efforts to identify healthier alternatives and means to quit smoking, including the use of EC.

Bullen et al conducted one of the largest studies investigating the efficacy of EC versus nicotine patches in achieving smoking cessation.[11] This study enrolled 657 smokers interested in quitting. Subjects were randomized in a 4:4:1 ratio to either 16 mg nicotine EC, 21 mg nicotine patch, or placebo EC, respectively. They were followed for a 6-month period, with assessments at 1 and 3 months. At 6 months, tobacco cessation was evident in 7.3% with nicotine EC, 5.3% with nicotine patches, and 4.1% with placebo EC.[11] Although this study was one of the largest trials, tobacco cessation was significantly lower than that expected for the power calculation. As a result, nicotine EC use did not demonstrate any advantage in tobacco cessation when compared with nicotine patches or placebo EC. A recent Cochrane review analyzed studies evaluating the use of EC in tobacco cessation and concluded that the role of EC is limited by the small number

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Abbreviations used
CO- Carbon monoxide
EC- Electronic cigarette
FDA- Food and Drug Administration
LED- Light-emitting diode
PG- Propylene glycol
PM- Particulate matter
WHO- World Health Organization

of trials, low event rates, and the wide confidence intervals around the estimates mean.[12]

EC are marketed as a safer alternative to combustible cigarettes. To help assess the acute effect of EC usage, Flouris et al evaluated 30 healthy volunteers separated into 2 groups: 15 smokers and 15 never-smokers.[2] The smokers were exposed to room air (as a control), active tobacco smoking (2 cigarettes of their favorite brand), and an active EC smoking session for 30 minutes. The nonsmokers were exposed to room air (as a control), a passive tobacco cigarette session (smoke chamber for 1 hour), and a passive EC session (1 hour in a vapor chamber). Spirometry was measured before, immediately after, and 1 hour after each exposure. The authors concluded that no change was detected in FEV_1 or FEV_1/FVC with active or passive EC exposure in either group, whereas combustible cigarette use reduced FEV_1/FVC by 7.2%.[2]

Research regarding the acute health effects of EC is limited due to user variability, EC use experience, and differences between devices. Vansickel et al sought to describe a consistent clinical laboratory method that could be used to characterize EC users' nicotine and carbon monoxide (CO) exposure and to evaluate a variety of acute effects resulting from active "vaping." They enrolled 32 adult EC naïve combustible cigarette smokers to each of the following 4 conditions: 150 minutes of own brand cigarette, 150 minutes of "NPRO" EC (18 mg cartridge), 150 minutes of "Hydro" EC (16 mg cartridge), and 150 minutes of sham (unlit cigarette). Plasma nicotine, expired air CO, and heart rate were measured and questionnaires were used to assess a reduction in desire to smoke.[13] Results demonstrated an increase in plasma nicotine levels, expired air CO, and heart rate only after own brand cigarette use. Interestingly, despite failure to deliver nicotine, acute use of EC demonstrated a reduced craving for cigarettes and a feeling of satisfaction.[13]

Vansickel et al further evaluated the effects of EC use in 8 adult experienced EC users during a single 5-hour session that consisted of 4 phases: baseline, 10 puffs from the device, 1-hour *ad lib* puffing period, and a 2-hour rest period (no puffing). Participants had a history of at least 3 months of EC use with 2-3 mL of nicotine solution or 2 cartridges per day, used nicotine solution of at least 10 mg/mL nicotine, and smoked less than 5 cigarettes per day. For the study intervention, participants used their own EC devices and the flavor and/or strength they preferred. As in the prior study, plasma nicotine, expired air CO, and heart rate were measured and questionnaires were used to assess a reduction in desire to smoke.[14] The study revealed that when compared with baseline measurements, plasma nicotine and heart rate increased significantly within 5 minutes of the first puff and remained elevated throughout the *ad lib* puffing period. Additionally, subjects reported pleasurable effects of EC use when compared with baseline, such as "feel awake," "calm you down," and "concentrate."[15] In comparison to the previous study in naïve EC users, these findings likely reflect the impact of longer puff duration on nicotine delivery in experienced EC users.

Patients with asthma experience many health benefits from smoking cessation including less symptoms and improvements in lung function.[16–18] Polosa et al assessed the effects of smoking abstinence and reduction in asthmatic smokers who switched to EC.[14] The 18 patients with asthma who participated in the study were tobacco smokers of approximately 1 pack per day and reported regular use of EC during the study at 2 consecutive visits. All participants had either mild to moderate disease based on the Global Initiative for Asthma criteria. The baseline treatment for a majority of the participants consisted of daily use of inhaled corticosteroids and/or long-acting β_2-agonist and, as needed, short-acting β_2-agonists.[14] Participant data were obtained at each clinic visit: prebaseline visit (confirm disease stability, 6-12 months before baseline visit), baseline visit (before switching to EC), follow-up visit 1 (6 months after baseline visit), and follow-up visit 2 (12 months after baseline visit). During each visit, participants were evaluated through clinical examination, review of smoking history, questionnaires, spirometry, and, if indicated, methacholine challenge.[14]

Results of the study demonstrated that at 6 months both single users (use of EC alone) and dual users (use of EC and 5 or less conventional cigarettes/day) exhibited significant improvements in forced expiratory flow 25%-75% and Asthma Control Questionnaire scores when compared with baseline measurements. At 12 months, a substantial improvement was observed in all asthma outcome parameters measured (except FVC in single users), including methacholine challenge. Additionally, a total of 10 patients with asthma switched solely to EC use during this study, whereas the other 8 were dual users and reduced their cigarette consumption to less than 5 cigarettes per day. Although there was a reduction in asthma exacerbations at 6 months, this was not statistically significant. This trial was the first study to demonstrate improvement in airway hyperresponsiveness, pulmonary function, and asthma control in asthmatic smokers who switched to EC use either completely or by reducing daily combustible tobacco consumption. Many questions remain regarding the possible harms and benefits of long-term EC versus combustible cigarette use. EC appear to be here to stay and do have some "good" aspects. Table I summarizes the beneficial effects of EC versus combustible cigarette use noted in the literature to date. Although EC may appear to be the safer alternative to combustible cigarettes, the regulation and standardization of EC is needed to allow further evaluation of safety and the impact on health with long-term use.

THE BAD

The greatest fear for the majority of health care professionals is that EC might pose unforeseen health problems either in the short term or long term. These harms stem from the toxic or carcinogenic constituents of the vapor, deleterious effects on lung function, or some unexpected consequence. The potential harms go beyond an individual vaping, as others may experience secondhand or thirdhand exposures through direct physical contact with product components or inhalation of the vapor or possible exposure even after vapor has cleared from the room.[19,20] The refill liquids of EC generally contain a mixture of nicotine, glycerin, and PG with water and flavor. However, once