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Electronic Cigarettes: Do They Have a Role in Smoking Cessation?

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Abstract

Electronic cigarettes have gained popularity among patients as a smoking cessation aid despite not being approved or supported for this purpose by the United States Food and Drug Administration due to concerns with poor manufacturing practices and the presence of known carcinogens in the limited products that they tested. A few studies have evaluated the effects of electronic cigarettes on plasma nicotine levels and heart rate but found negligible effects. Safety data are mainly limited to surveys in which patients report only minor side effects, such as mouth and throat irritation, headache, vertigo, and nausea. The efficacy of electronic cigarettes has been evaluated in studies in which patients report great success with being able to cut back or stop tobacco cigarette consumption. However, many of these studies introduce bias due to recruiting on e-cigarette Web sites and having tobacco cigarette use self-reported by the participant rather than objectively tested. A few studies have formally evaluated nicotine craving when using electronic cigarettes with mixed results. Although patients support the use of electronic cigarettes in smoking cessation, more formal studies on safety and efficacy should be completed in order to determine whether these products have a role in smoking cessation.

Keywords

electronic cigarette, smoking cessation, tobacco cessation, e-cigarette, tobacco

Background

Tobacco use is a worldwide health issue resulting in an increased risk of several disease states including cardiovascular disease, respiratory diseases, stroke, and cancer.[1] The health benefits of smoking cessation are immense. However, failure rates are high despite the availability of multiple smoking cessation aids such as nicotine patches, lozenges, gum, inhalers, a nasal spray, bupropion, and varenicline. A new technology, referred to as an electronic cigarette (e-cigarette), has gained popularity among patients to aid in tobacco cessation despite not being tested for this purpose or supported by the United States Food and Drug Administration (FDA).[2] This review will analyze the limited data surrounding the safety and efficacy of these products when used as smoking cessation aids.

What are E-Cigarettes?

E-cigarettes were developed by a Chinese pharmacist, Hon Lik, and patented in 2003.[3] They are battery-powered devices, often similar in appearance to cigarettes that vaporize a solution containing nicotine and propylene glycol in a refillable cartridge. According to the e-cigarette manufacturers, the vapor that is inhaled does not contain tar or many of the other toxic chemicals found in cigarettes.[3,4] The e-cigarettes are produced by a variety of manufacturers that offer some differences between the products, such as lit or unlit tips upon inhalation, flavorings (such as tobacco, menthol, chocolate, fruit, and coffee), and different appearances of devices. The products range in price from $29.95 to $149.95 for the device and $9.95 to $19.95 for the cartridges. The longevity of the cartridges varies by type, but one cartridge is typically similar to one pack of cigarettes.[5-9]

FDA Concerns Regarding E-Cigarettes and Conflicting Data

The FDA has concerns regarding the content of e-cigarettes. An FDA analysis of cartridges from two leading brands detected very small amounts of carcinogenic tobacco-specific nitrosamines, and one of 18 cartridges tested contained diethylene glycol which is toxic to humans. The FDA is also concerned about the variability in nicotine delivery per puff

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Table 1. Undesirable Side Effects of E-Cigarettes[13,15,16,19]

Design	Survey[15a]	Survey[16b]	Randomized Cross-over	Observational[19c]
n	81	3037	40	40
Duration	N/A	N/A	9 hours Per product	24 weeks
Throat				
Dry mouth and/or throat	26.2%	26.2%	N/A	8.8%
Burning/sore throat	N/A	22.1%	N/A	11.8%
Mouth and throat irritation	N/A	N/A	38%	N/A
Mouth irritation	N/A	N/A	N/A	20.6%
Throat irritation	N/A	N/A	N/A	32.4%
Dry cough	N/A	N/A	N/A	32.4%
Central nervous system				
Vertigo, headache, nausea	11.5%	N/A	N/A	N/A
Vertigo/dizziness	N/A	N/A	21%	14.7%
Headache	N/A	N/A	18%	11.8%
Nausea	N/A	N/A	29%	14.7%

Abbreviation: N/A, not applicable or not reported.
[a]Values reflect percentage of comments of undesirable effects, not the percentage of patients due to the open-ended question format of the survey. The remaining values in the table reflect percentage of patients.
[b]Values reported are for the 16 mg nicotine e-cigarette.
[c]Values reported are at week 4.

between manufacturers despite similar labeling. Additionally, one cartridge listed as containing no nicotine had low amounts of nicotine present.[2] The FDA sent warning letters to five manufacturers in 2010 regarding unsubstantiated claims for aiding in smoking cessation and poor manufacturing practices.[10]

In opposition to the FDA concerns, one article[3] stated that the tobacco-specific nitrosamines in e-cigarettes are much lower than those in regular cigarettes and are similar to the total amount found in the NicoDerm® CQ® patch. The article also stated that of the 16 studies, only the FDA study identified diethylene glycol in one cartridge, although this finding should be taken seriously. Studies[11,12] that have evaluated the effects of e-cigarettes on various measurable end points such as plasma nicotine levels, expired carbon monoxide (CO) concentrations, and heart rate have not identified significant harm, but these studies are short in duration. Additionally, the peak average serum nicotine levels over one hour in 16 mg e-cigarettes were found to be lower than the nicotine inhaler, an FDA approved smoking cessation product.[13]

Survey Results on Safety and Efficacy

Most e-cigarette data on safety and efficacy are derived from the surveys of current or past e-cigarette users.[14-18] The surveys have reported successful reduction in smoking and benign side effects, such as dry mouth, throat irritation, dry cough, vertigo, headache, and nausea (Tables 1). Most survey participants were male and from the Unites States, Europe, and Canada. Respondents were typically recruited by posting links on e-cigarette or smoking cessation Web sites and/or sending e-mails with survey links to consumers of e-cigarettes. One survey[18] recruited subjects by handing out questionnaires at an e-cigarette enthusiast meeting. Many of these surveys[14,15,17,18] provided only descriptive analyses to understand the usage patterns and opinions of e-cigarettes along with baseline demographics such as previous quit attempts. One survey[16] found a statistically higher amount of throat burning in current smokers versus former smokers and in e-cigarettes with nicotine versus e-cigarettes without nicotine. No differences were found for the side effect of dry mouth/throat.

Regarding efficacy (Table 2), most respondents were able to successfully cut back on tobacco use and believe that e-cigarettes helped in smoking cessation. These respondents included subjects with multiple past quit attempts using currently available smoking cessation products. A concern has been raised that e-cigarettes sustain tobacco cigarette use, but this concern has not been supported in survey data in which most respondents reported using e-cigarettes to replace tobacco rather than in addition to tobacco, and in turn, felt better about their overall health.

Overall, the responses regarding adverse effects to e-cigarette surveys were not concerning, and patients had success in quitting, however, the currently available surveys have several limitations. A major concern is that the surveys introduce selection bias since they were typically offered to visitors of e-cigarette manufacturer Web sites and/or users of e-cigarette blogs. One study[17] reported only a 4.5% survey response rate. Another study[16] evaluated the difference between e-cigarette users who self-enrolled in a survey on an e-cigarette forum compared to those who enrolled on a more neutral Web site. The respondents who enrolled on e-cigarette forums reported statistically better outcomes in helping to reduce or quit tobacco and less throat burning. Recall bias is introduced in some studies since the respondents may have stopped using e-cigarettes prior to the survey. Another concern with the efficacy data is that

Table 2. The Efficacy of E-Cigarette Use on Smoking Cessation[14-16,17-19]

Design	Survey[14a]	Survey[15]	Survey[16]	Observational[19]	Survey[17]	Survey[18]
n	270	81	3037	40	216	104
Tobacco cigarette abstinence after using e-cigarettes						
	82%	N/A	N/A	22.5%	31.0%	N/A
Reduced cigarettes/day after using e-cigarettes						
	N/A	N/A	92.2%	32.5%	66.8%	N/A
Believe e-cigarettes helped in quitting smoking tobacco						
	N/A	95%	N/A	N/A	N/A	99%

Abbreviation: N/A, not applicable or not reported; [a]Percentages reflect percentage of patients.

smoking abstinence was not verified objectively. The mixed message between the FDA's safety warnings and the experiences of e-cigarette users emphasizes the importance of well-designed trials before these products can be recommended to the public.

Trial Results on Safety and Efficacy

Very few trials have been conducted to evaluate the safety and efficacy of e-cigarettes. One trial[13] used a randomized, single blind, cross-over design (n = 40) in which patients who smoked $\geq$10 cigarettes daily for at least one year and were not trying to quit used a 16 mg nicotine e-cigarette, 0 mg nicotine e-cigarette, nicotine inhaler, or their own cigarettes over a nine-hour period. This study found that the side effects of mouth and throat irritation were statistically significantly lower when using e-cigarettes compared with the nicotine inhaler. The 16 mg e-cigarette and nicotine inhaler had a similar reduction in the desire to smoke compared to the 0 mg nicotine e-cigarette using an intent-to-treat analysis and area under the curve over 60 minutes. Limitations to this study include the small sample size and short duration. Similarly, another study[12] measured the effect on nicotine cravings in e-cigarette users. This study found that of the two e-cigarette brands, one brand was unable to decrease cravings while the other brand was able to significantly reduce cravings for at least 1 prespecified time interval.

The longest study assessing adverse events was an observational six-month study[19] in which eligible participants smoked $\geq$15 cigarettes/day for at least ten years with no intent to quit smoking. The participants/day were invited to use an e-cigarette and tobacco cigarettes at their own discretion and maintain a diary of e-cigarette and tobacco use and adverse events. The participants met at baseline, four weeks, eight weeks, 12 weeks, and 24 weeks to record expired level, get more e-cigarette supplies, and turn in their diaries. Only descriptive data without statistical analysis were included for adverse events. Mouth and throat irritation were most commonly reported, but these were experienced more frequently at the beginning of the study than at the end. No serious adverse events were reported. At week 24, 32.5% of participants reduced tobacco use by at least half and 22.5% were abstinent as verified by an exhaled CO. The results are promising especially in a population that is not planning to quit smoking. Limitations include the small sample size (n=40) and the fact that cigarette use was self-reported. Also, 32.5% of participants were lost to follow-up. Whether or not these participants had problems with e-cigarette use is unknown.

Additional Public Health Concerns

In addition to the safety concerns and unproven efficacy as smoking cessation aids, public health concerns exist with e-cigarettes. The current public health goal is tobacco cessation, but current smokers may become addicted to e-cigarettes rather than quitting smoking. Also, the public perception that these products are ''safe'' may not be true since little is known about the long-term effects of these products. The flavor and appearance of e-cigarettes might appeal to nonsmokers or young adults who would otherwise not use nicotine products. Another concern is that e-cigarettes will be used in public places enabling current tobacco users to maintain use.[3,18]

Conclusion

E-cigarettes are increasing in popularity and are marketed as safer cigarettes for both the user and the public because they deliver nicotine without the harmful additional components of tobacco cigarettes. Evaluation of the literature for e-cigarettes has shown promise in helping patients quit tobacco, but well-designed safety and efficacy studies are lacking including evaluation of these products in comparison to currently available smoking cessation medication aids. The long-term effects of e-cigarettes are unknown and very few patients have been objectively studied. Well-designed studies will help to clarify whether e-cigarettes have a possible role in smoking cessation, but until this occurs, they cannot be recommended.

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