CE 1.5 ANCC Contact Hours

Pharmacology Consult
Column Editor: Patricia Anne O'Malley, PhD, RN, CNS

Safety and Efficacy of Electronic Cigarettes

Update for the Clinical Nurse Specialist

Patricia Anne O'Malley, PhD, RN, CNS

Electronic cigarettes, or E-cigarettes, are battery-powered devices designed to inhale nicotine vapor without fire, smoke, or ash.[1] Components usually include nicotine liquid, which is vaporized by the heating element. Rather than tobacco combustion, nicotine and other components such as flavors are aerosolized and then inhaled.[2] The consumer is provided a smoking experience without carbon monoxide and the chemicals and toxins found in traditional cigarettes. Liquid nicotine may contain water, propylene glycol, glycerol, and/or vegetable glycerin.[1]

Invented by the Chinese pharmacist Hon Lik in 2003, e-cigarettes received an international patent in 2007. Rapid acceptance by all ages, especially millennials, is a growing public health concern. Acceptance of e-cigarettes is based on the belief that e-cigarettes are safer than tobacco cigarettes.[3] Industry expansion and demand are hard to believe. In a recent report, analysis revealed that there were 7764 unique vaping flavors available online, with 242 new favors added per month for 466 brands.[4] Marketing, explicit and implied, suggests the e-cigarettes can help smokers quit or reduce smoking and are less toxic and "safe."[2]

Current cigarette smokers and former smokers who stopped smoking in the past year are more likely to use e-cigarettes than former smokers who quit more than 1 year and those who never smoked. Approximately 3.7% of adults use e-cigarettes every day or some days, with use differing by age and race. Non-Hispanic white and non-Hispanic American Indian or Alaska Native have a significantly higher percentage of use (4.6% and 10.7%, respectively) compared with Hispanics (2.1%), non-Hispanic black (1.8%), or non-Hispanic Asian (1.5%). Men more than women use e-cigarettes (4.1% vs 3.4%) with greatest use in those 18 to 24 years old (5.1%) followed by 25 to 44 years old (4.7%). Persons 65 years or older use e-cigarettes more rarely (1.4%).[5] Nearly 20% of Americans aged 25 to 44 years currently use e-cigarettes.[6]

Health concerns for e-cigarette use have been minimized by reporting that ingredients and flavoring agents are "food grade" and "generally recognized as safe." What the consumer is not told is that flavoring agents, although safe for consumption as part of food, have no evidence for safety metrics with regard to inhalation. Results from recent studies (in vivo and in vitro) do not support the broad product safety claims by e-cigarette manufacturers. In sample testing, diacetyl and/or acetyl propionyl, associated with bronchiolitis obliterans, has been identified in some e-liquid products. Also found are heavy metals (mercury, cadmium, lead), known carcinogens, and teratogenic agents. The interaction effects of heat and e-liquid may also be problematic. Vaping e-liquid creates formaldehyde from degradation from heating of propylene glycol, which also results in pulmonary stress. Emerging evidence suggests that e-cigarette aerosols create oxidative stress in human lung epithelial cells and trigger an inflammatory response.[3]

In a recent report, exposure of human epithelial cells (the first line of defense against infection) to electronic vapor (EV) resulted in dose-dependent cell death. Epithelial cells, alveolar macrophages, and neutrophils had reduced antimicrobial activity against *Staphylococcus aureus* (SA). Mice exposed to EV for 1 hour per day for 1 month experienced suppression of host defenses as evidenced by increases in inflammatory markers, increased SA biofilm formation, and up-regulation of virulence genes. Methicillin-resistant SA exposed to EV also had increased biofilm formation in a dose dependent manner similar to those for tobacco smoking. Findings suggest

Author Affiliation: Nurse Researcher, Center of Nursing Excellence, Premier Health–Miami Valley Hospital, Dayton, Ohio.

The author reports no conflicts of interest.

Correspondence: Patricia Anne O'Malley, PhD, RN, CNS, Premier Health–Miami Valley Hospital, 1 Wyoming St, Dayton, OH 45409 (pomalley@premierhealth.com; pomalley5@woh.rr.com).

DOI: 10.1097/NUR.0000000000000259

SA becomes more virulent when exposed to EV. Finally, in a mouse model of pneumonia, EV increased methicillin-resistant SA virulence.[6]

Nicotine exposure with e-cigarettes is variable because of aerosolization and wide variance in product dose related to lack of quality standards and regulation. Surprisingly, serum cotinine levels are similar to those of tobacco smokers. Effects of secondhand exposure are unknown. While e-cigarette aerosol has fewer toxicants compared with cigarette smoke, whether e-cigarettes are less harmful is unknown. What is known is that e-cigarette aerosols can contain propylene glycol and/or glycerol also used in the theater industry and in aviation training and are known upper airway irritants. Aerosolized propylene glycol and glycerol cause mouth and throat irritation and dry cough and are associated with respiratory impairments.[2]

Limited evidence suggests that e-cigarette use may help in smoking cessation.[2] E-cigarettes possess characteristics that augment pharmacological and behavioral smoking-cessation interventions. E-cigarettes provide what nicotine replacement therapy (NRT) cannot, the action of smoking with nicotine replacement to mitigate withdrawal. While the efficacy of e-cigarettes for smoking cessation is unknown, limited evidence suggests that e-cigarettes may help reduce the number of cigarettes smoked and may be as effective as NRT with adverse events rates similar to NRT. Large randomized controlled trials are needed to establish e-cigarette use for smoking cessation.[7]

Millions of dollars of e-cigarette profit are in part due to the lack of tobacco signs of use. This may explain the sharp rise in e-cigarette use in high school and middle school children. However, hidden in this emerging vaping culture is an unspoken threat; e-cigarettes have great potential to become a powerful gateway to cigarette smoking, and e-cigarette use may be creating a new generation of nicotine addicts.[1,7]

Lack of research and regulatory guidelines for the manufacturing process has not been addressed over the past decade. However, on August 8, 2016, the Food and Drug Administration (FDA) enacted 81FR 28973, a final rule that extended the agency's ability to regulate all tobacco products including e-cigarettes. As part of this regulatory expansion, manufacturers will be required to report all ingredients and premarket review to obtain permission to market the product. Consumers will finally have access to actual ingredients in e-cigarettes.[1,8] In addition, the rule makes it illegal to sell in person or online to persons younger than 18 years.[8]

The final rule was published in the *Federal Register* on May 10, 2016, and describes the deeming regulations which permit the FDA to regulate any tobacco product for human consumption including e-cigarettes, as well as any future products that meet the legal definition of "tobacco product" including electronic nicotine delivery systems such as e-cigarettes and "vape pens." Product premarket reviews will be mandatory. However, the FDA is delaying enforcement for 12, 18, or 24 months after August 8, 2016. Because of the limits of FDA authority and the slow process for rulemaking, state and local governments retain authority to implement policies to protect community health.[9,10]

Some have questioned the need for tightening regulations in light of so little evidence. What about adults using e-cigarettes as a bridge to quit smoking? Are e-cigarettes a recreational drug or a therapy? Do e-cigarettes help persons reduce smoking? Uncovering the long-term effects of e-cigarettes will be difficult related to the small numbers of regular e-cigarette users and very low number of persons who are regular users and never smoked.[8]

What to do about use of e-cigarettes for smoking cessation? Probably, recommend e-cigarettes are not the first choice. However, if available drug therapies are not effective, and the patient desires to try e-cigarettes after education, then support of patient cessation efforts is key while the research continues. Recreational use and concomitant use with smoking tobacco should be strongly discouraged. Pregnant women should be counseled to avoid e-cigarettes because risks to the fetus are unknown.[3,8]

Tobacco consumptions is a leading cause of mortality in the world linked to cancer, heart disease, chronic obstructive pulmonary disease, and numerous neurological and neurodegenerative diseases.[3] In the United Kingdom, e-cigarettes are a widely accepted tool to quit smoking and preferable to NRT. Limited evidence suggests that the e-cigarette nicotine dose and pattern of use may influence quit rates.[8] Regulation, monitoring, and research will address these important issues: the safety of e-cigarettes and if e-cigarettes are another bridge to smoking cessation.

References

1. Kim JJ. The FDA E-cigarette regulations on public health policy. Health eSource. American Bar Association. 2015–2016;12(10). http://www.americanbar.org/publications/aba_health_esource/2015-2016/june/ecigarette.html. Accessed September 19, 2016.
2. Callahan-Lyon P. Electronic cigarettes: human health effects. *Tob Control*. 2014;23:ii36–ii40.
3. Kaisar M, Prasad S, Liles T, Cucullo L. A decade of e-cigarettes: limited research & unresolved safety concerns. *Toxicology*. 2016; 365:67–75.
4. Zhu S, Sun J, Bonnevie E, et al. Four hundred and sixty brands of e-cigarettes and sixty brands of e-cigarettes and counting: implications for product regulation. *Tob Control*. 2014;23(suppl 3): iii3–iii9.
5. Schoenborn C, Gindi R. Electronic cigarette use among adults: United States 2014. NCHS Data Brief. US Department of Health and Human Services. Centers for Disease Control and Prevention, National Center for Health Statistics. No. 217, October 2015. http://www.cdc.gov/nchs/data/databriefs/db217.pdf. Accessed September 22, 2016.

6. Hwang J, Lyes M, Sladewski K, et al. Electronic cigarette inhalation alters innate immunity and airway cytokines while increasing the virulence of colonizing bacteria. *J Mol Med*. 2016;94(6):667–679.
7. Franck C, Budlovsky T, Windle S, et al. Electronic cigarettes in North America. History, use, and implications for smoking cessation. *Circulation*. 2014;129:1945–1952.
8. Abbasi J. FDA extends authority to e-cigarettes: implications for smoking cessation? *JAMA*. 2016;316(6):572–574.
9. The Deeming Regulation: FDA Authority Over E-Cigarettes, Cigars, and Other Tobacco Products. *Tobacco Control Legal Consortium*. http://publichealthlawcenter.org/sites/default/files/resources/tclc-fda-deemingreg-regulation-authority-2016.pdf.
10. Department of Health and Human Services. Food and Drug Administration 21 CFR Parts 1100, 1140, and 1143 deeming tobacco products to be subject to the federal food, drug, and cosmetic act, as amended by the Family Smoking Prevention and Tobacco Control Act; restrictions on the sale and distribution of tobacco products and required warning statements for tobacco products; final rule. *Fed Regist*. May 10, 2016;81(90): 28974–29106.

Instructions:
- Read the article. The test for this CE activity can only be taken online at http://www.nursingcenter.com/ce/CNS. Tests can no longer be mailed or faxed.
- You will need to create (its free!) and login to your personal CE Planner account before taking online tests. Your planner will keep track of all your Lippincott Williams & Wilkins online CE activities for you.
- There is only one correct answer for each question. A passing score for this test is 13 correct answers. If you pass, you can print your certificate of earned contact hours and access the answer key. If you fail, you have the option of taking the test again at no additional cost.
- For questions, contact Lippincott Williams & Wilkins: 1-800-787-8985.

Registration Deadline: February 28, 2019

Disclosure Statement:
The authors and planners have disclosed that they have no financial relationships related to this article.

Provider Accreditation:
Lippincott Williams & Wilkins, publisher of *Clinical Nurse Specialist* will award 1.5 contact hours for this continuing nursing education activity.

Lippincott Williams & Wilkins is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 1.5 contact hours. Lippincott Williams & Wilkins is also an approved provider of continuing nursing education by the District of Columbia, Georgia, and Florida, CE Broker #50-1223. Your certificate is valid in all states.

Payment:
- The registration fee for this test is $17.95.