Journal of Addiction Research and Adolescent Behavior
Charl H. Woo, J Addiction Research and Adolescent Behavior
Doi:10.31579/2688-7517/002

Research Article Open Access

Efficacy of Vaping as a Nicotine Replacement Therapy for Smoking Cessation among Adults: A Review of the Literature

Nida R. Augustine [1], Charl H. Woo [2*], Driscoll H. Augustine[2]. Cristóbal S. Berry-Cabán[3].

[1] Augusta University Medical Center, Augusta, GA USA.
[2] 82nd Airborne Division, Fort Bragg, NC, USA.
[3] Department of Clinical Investigation, Womack Army Medical Center, Fort Bragg USA.

***Corresponding Author:** Charl H. Woo, 82nd Airborne Division, Fort Bragg, NC, USA. **E-mail: charl.h.woo2.mil@mail.mil**

Received date: May 17, 2018; Accepted date: July 19, 2018; Published date: July 26, 2018.

Citation this Article: Nida R. Augustine, Charl H. Woo, Driscoll H. Augustine, Cristóbal S. Berry-Cabán, Efficacy of Vaping as a Nicotine Replacement Therapy for Smoking Cessation among Adults: A Review of the Literature. J. Addiction Research and Adolescent Behavior, **Doi:**10.31579/2688-7517/002

Copyright: © 2018 Charl H. Woo. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Introduction

Nicotine replacement therapies have been on the market for several years in the form of patches and gums. Each has proven to be safe modalities, however, their efficacy resulting in cessation is modestly effective with long term quit rates around 20%. Since quitting smoking is difficult, some smokers have turned to e-cigarettes.

Methods

An extensive search of literature between 1 January 2010 and 31 December 2017 was conducted to identify scientific literature that referenced vaping, electronic cigarettes, and nicotine replacement. A literature search was conducted using several online databases: PubMed, Google Scholar, and Science Direct. After screening for eligibility and removing duplicate citations, we were left with 206 unique citations.

Discussion

After reviewing the literature we found only 2 randomized control trials published on the efficacy of e-cigarettes in smoking cessation. Studies that examine cessation trends conclude that those persons most successful in quitting entered the studies with the intention to stop using traditional combustible tobacco.

Conclusion

In the absence of clear data on the health consequences of e-cigarette use and their efficacy for smoking cessation the goal for patients should be to avoid dual use of e-cigarettes and combustible tobacco use as that could prolong harmful exposure to tobacco smoke. Therefore, based on our review the most effective potential e-cigarette used as a smoking cessation tool would be the use of one with the lowest non-modifiable voltage that with no or very low nicotine combined with a nicotine patch. This would reduce the thermal degradation products from the solvent and other components as well as the known carcinogenic degradation products of nicotine while still providing the habitual benefit that e-cigarettes provide.

Keywords: Vaping, Electronic Cigarettes, Nicotine Replacement

Introduction

Since the 1960s great effort has been made to inform the public about the harmful health effects of cigarette smoking in an attempt to promote cessation and prevent new users [1]. Despite gaining ground with these efforts, cigarette smoking remains the leading cause of preventable mortality worldwide and produces substantial morbidity costs [2, 3]. A lifelong smoker has a 50% chance of dying prematurely from smoking complications and it is the exposure to toxins in tobacco smoke that directly contributes to smoking related diseases [4, 5].

Evidence shows that successful treatment of nicotine addiction improves mortality, despite age at cessation [2, 5-7]. The extreme hazards of smoking stress the importance of patient-physician discussion that is a significant factor in tobacco cessation [8, 9]. Discussion alone and other methods such as "cold turkey" have proven to have low efficacy at cessation which has led to the development nicotine replacement therapy to help augment cessation [8].

Nicotine, one of the more well-known harmful chemicals in cigarettes, provides the main addictive characteristic of cigarettes [7]. This is why some form of nicotine replacement is often needed for cessation. Nicotine replacement therapies (NRTs) have been on the market for several years in the form of patches and gums [10, 11]. Each has proven to be safe modalities, however, their efficacy resulting in cessation is modestly effective with long term quit rates around 20%. Since quitting smoking is difficult, some smokers have turned to e-cigarettes [12].

In the United States, the use of e-cigarettes has increased since 2010, corresponding to an increase in marketing for the products [13, 14].

Web-based consumer surveys of adults reported that between 2010 and 2013, ever use of e-cigarettes increased from 3.3% to 8.5% of all adults, while current use (use in the past 30 days) increased from 1.3% to 1.9% [15].

E-cigarettes provide the patient with the continued social aspect of smoking but with less nicotine and carcinogen exposure. This allowance of the continued habit combined with a safer metabolite profile, in conjunction with behavior therapy, makes the argument that e-cigarettes are a better tool for cessation [14, 16-18].

The following paper examines the use of e-cigarettes as an efficient method to quit smoking.

Methods

An extensive search of literature between 1 January 2010 and 31 December 2017 was conducted to identify scientific literature that referenced vaping, electronic cigarettes, and nicotine replacement. A literature search was conducted using several online databases: PubMed, Google Scholar, and Science Direct. These databases were selected to capture potential literature from many sources. For example, PubMed is a national Library of Medicine's database that has literature from the life and behavioral sciences. Google Scholar captured the behavioral and mental health sciences. Science Direct provided broad coverage of both the biological and social sciences.

Various keyword searches were conducted that searched PubMed and Google Scholar. Boolean operators were included to ensure that the searches were precise and that all relevant information was collected.

The initial keyword searches yielded 211 citations. Hand-search and initial screening was conducted under the direction of the primary investigator. Topical journals and books were examined as well as a review of the final selection reference lists. The Cochrane Database of Systematic Reviews also was searched with no date limit and that search yielded 1 new result. After screening for eligibility and removing duplicate citations, we were left with 206 unique citations. Three investigators independently reviewed the list of titles and abstracts for relevance.

The following discusses relevant evidence that electronic cigarettes may be an aid to smokers in stopping their smoking.

Discussion

Structure of an Electronic Cigarette. E-cigarettes include a diverse group of devices that allow users to inhale an aerosol that typically contains nicotine, flavorings, and other additives. E-cigarettes vary widely in design and appearance, but generally operate in a similar manner and are composed of similar components (Figure 1). A key challenge for surveillance of the products and understanding their patterns of use is the diverse and nonstandard nomenclature for the devices [13]. These devices are referred to, by the companies themselves, and by consumers, as "e-cigarettes," "e-cigs," "cigalikes," "e-hookahs," "mods," "vape pens," "vapes," and "tank systems, among others [13, 14]."

Figure 1: Diversity of e-cigarette products

Reproduced from U.S. Department of Health and Human Services, Office of the Surgeon General. *E-cigarette use among youth and young adults: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services 2016.

The electronic cigarette is a battery powered device that aerosolizes nicotine with no combustion involved as in a traditional tobacco cigarette. Instead of combustion, a battery powered heating element vaporizes the liquid followed by an immediate cooling to form an aerosol or mist that is inhaled by the user. At this stage, a light-emitting diode (LED) turns on to signify mist formation and the passage of air through the chamber [19]. There are over 7,000 different e-liquids and they come in a variety of flavors containing a carrier substance, most commonly propylene glycol, and nicotine (Figure 2) [20, 21].

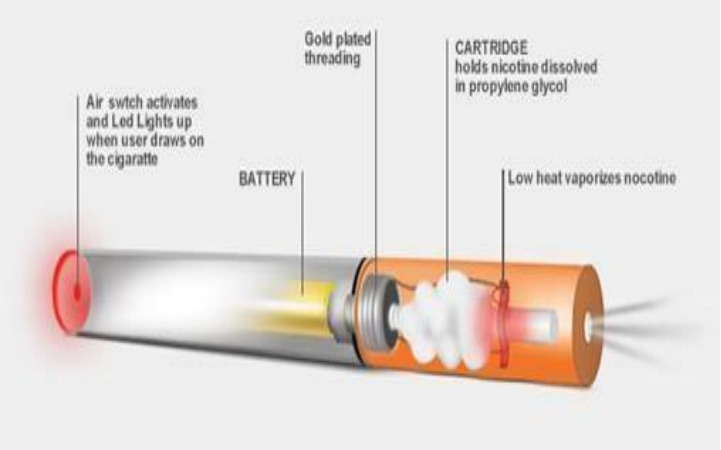

Figure 2: How e-cigarettes work.

Reproduced with permission from: http://ecigarettereviewed.com/about-e-cigs

Nicotine Content. The nicotine content in the liquid varies and is therefore not consistent in the doses aerosolized upon use. The amount of aerosol is directly proportional to the voltage leading some users to modify their experience by increasing voltage in order to attain a stronger nicotine hit [22].

Nicotine exposure from e-cigarette use, as from cigarette smoking, increases heart rate and produces measurable levels of blood cotinine, a nicotine metabolite [22-24]. The amount of nicotine delivered and the level of nicotine in the blood varies depending on nicotine concentration in the e-cigarette liquid, other components in the e-cigarette liquid, user experience, puffing intensity, device characteristics, and vaping technique [24]. Experienced e-cigarette users tend to take longer puffs and use the device more intensively compared with novice users [25]. Consequently, they have higher blood nicotine levels that more closely resemble the levels achieved by smoking conventional cigarettes. In less-experienced users, however, the nicotine delivered by e-cigarettes is consistently lower than nicotine delivered by conventional cigarettes [12].

One study analyzed 16 different e-cigarettes for their nicotine levels on use and 15 puffs of vapor were found to have a range of 0.5-15.4 mg nicotine. The traditional combustible tobacco cigarette contains 1.54-2.60 mg nicotine [6, 26, 27]. While, this variation makes e-cigarettes an inconsistent tool for cessation, if used carefully and correctly, it has the potential to be used as an effective NRT. Moreover, this mechanism of nicotine delivery provides the user with the oral stimulus similar to traditional tobacco smoking making it a better tool for cessation by the providing the habitual/behavioral need [10, 16, 28].

Toxin Profiles. Unfortunately, not just the positive similarities of combustible cigarettes are shared with e-cigarettes. As with cigarettes some degree of thermal degradation byproducts can form even though direct combustion does not occur [29, 30].

In both e-cigarettes and combustible cigarettes, toxicants and carcinogens found include tobacco-specific N-nitrosamines (TSNAs) and volatile organic compounds (VOCs) also known as carbonyl compounds. Volatile organic compounds include, but are not limited to, acrolein, acrylonitrile, 1,3 butadiene and ethylene oxide. Tobacco specific nitrosamines, acrylonitrile and 1,3 butadiene are potent lung carcinogens and major contributors to lung cancer risk while acrolein is a major contributor to harmful respiratory effects [23].

Traditional combustible tobacco cigarettes contain about 7,000 compounds with at least 70 carcinogens; among these carcinogens are formaldehyde, benzene, nitrosamines, free radicals, toxic gases and heavy metals [1, 2, 7, 26]. Volatile organic compounds are not only carcinogenic but have also been implicated to play a role in the development of cardiovascular disease [31]. In 2009, the U.S. Food and Drug Administration (FDA) detected low levels of the same nitrosamines and diethylene glycol in two brands of e-cigarettes [6]. Carbonyl compound acrolein has a concentration of 8.3-7.0 ug/cigarette in the combustible cigarette as compared to a concentration of 0.02-0.63 ug/cigarette in 15 puffs of an e-cigarette. Nitrosamine concentrations in a combustible cigarette range 0.005-0.19 ug/cigarette as compared to 0.00008-0.00043 ug in 15 puffs of an e-cigarette [6]. In general, the range of toxin exposure was 9-fold to 450 times higher in conventional cigarette smoke than in the vape of e-cigarettes [27].

The majority of e-cigarette users are current or former smokers that fall into two broad categories: those using them recreationally and those using them with the intention to quit [12, 31]. Both groups share a belief that e-cigarettes are a less harmful and less addictive alternative to traditional cigarettes; indeed, surveys have shown an increase in use among adult smokers from 10% in 2010 to 21% in 2011. Other surveys noted an increase in use from 1.8% of adult smokers in 2010 to 13% in 2013; a more dramatic increase yet [32]. E-cigarette use is more common among persons 30 to 60 years old [17]. This age range is also more likely to use of e-cigarettes as a dual use method in conjunction with traditional combustible cigarettes or use with other forms of NRT (i.e., patches or gum) [23].

Comparing the toxin profile of traditional NRTs and e-cigarettes with traditional cigarettes is important factor when examining tools for cessation. Shahab analyzed the presence of nicotine metabolites, tobacco-related carcinogens and toxicants among cigarette-only smokers and smokers and ex-smokers with long term e-cigarette use of NRT. They reported dual combustible cigarette-NRT users had low nicotine and cotinine levels (a nicotine metabolite) and that e-cigarette only users had nicotine levels around half that of combustible cigarette smokers. NRT only and e-cigarette only users had comparable TSNAs levels and each were significantly lower than users in the dual use groups and traditional combustible smoker only group. Of note from this analysis, e-cigarette only users had lower TSNA levels than all other groups and a 97% equivalent reduction when compared to combustible cigarette users [23].

While Shahab confirmed the known low toxin profile of traditional NRTs the study further highlighted that in some cases long-term NRT-only and e-cigarette-only use, was associated with substantially reduced levels of measured carcinogens and toxicants relative to cigarette-only smoking. Given this validation of a low risk metabolite profile in e-cigarettes their use in cessation therapy appears to make for a stronger alternative to patches and gum [23].

Nicotine replacement therapies and e-cigarettes are similar in their toxin profiles. NRTs have a better known safety profile given their longevity on the consumer market. However, e-cigarettes could be more useful as a cessation aid because they continue to provide the oral sensation of smoking thereby satisfying the already instilled biofeedback response of a long term smoker. In addition, being able to continue the social aspect of smoking as users can still partake with other smokers. This psychological dependency can be used as a tool to wean smokers from combustible tobacco use.

Shahab et al concluded that long term NRT only use or e-cigarette only use, among former smokers, exposed them to substantially lower levels of carcinogens as compared to traditional cigarettes [23].

Role in Cessation. The FDA has approved the use of nicotine as a cessation tool in the oral form, the transdermal form and inhaled form (nasal spray or oral inhaler) but not in the e-cigarette form [32]. Initially, the FDA attempted to regulate e-cigarettes as drug delivery devices however this was blocked by lawmakers as it was more appropriate to regulate them as tobacco related products and this could potentially hold e-cigarettes to the same regulations as combustible tobacco cigarettes in terms of sales and monitoring [31, 33, 34]. In 2014, the FDA reported that they would begin to regulate e-cigarettes however there is still a degree of variation among the contents of the vaporizing liquid [4]. In the future, standardizing and regulating e-cigarettes will also allow for robust longitudinal evaluations of their safety and efficacy [6]. Complete cessation of use of all tobacco products is still the best option to avoid harm [23].

There are currently only 2 randomized control trials published on the efficacy of e-cigarettes in smoking cessation. Bullen et al randomized 657 smokers to measure cessation rates among users of traditional NRTs versus e-cigarette smokers. Participants were given a 21mg nicotine patch, a placebo e-cigarette and a 16mg nicotine e-cigarette. After 6 months, self-reported cessation rates were comparable in placebo e-cigarette users and nicotine containing e-cigarette users. Although these rates were not statistically significant, cessation was reported in 7.3% of users of nicotine e-cigarettes, 4.1% in placebo e-cigarettes and 5.8% in nicotine patch users [12].

Caponnetto et al performed a 12 month prospective study among smokers who did not want to stop smoking. These participants were given e-cigarettes with 3 different doses of nicotine and while there was no significant difference in cessation among the groups, 8.7% reported abstaining completely from traditional cigarettes by the conclusion of the study [35].

All studies exploring use of e-cigarette for cessation have demonstrated efficacy in this capacity, even if it is by slowly decreasing the number of cigarettes smoked [16, 17]. Rahman et al reviewed 6 studies in a meta-analysis and found that among 1,242 smokers, 224 reported cessation after using nicotine enriched e-cigarettes for 6 months and use of e-cigarettes was also associated with a reduction in the number of cigarettes used. The users most successful at cessation with e-cigarettes were those who had used some concentration of nicotine [17].

Studies that examine cessation trends conclude that those persons most successful in quitting entered the studies with the intention to stop using traditional combustible tobacco [6, 18]. This indicates that behavioral support is a strong component no matter what the cessation modality. For long term smokers who are unprepared to give up combustible tobacco use, it is speculated that use of e-cigarettes might be associated with better long term and short term health outcomes [32]. Because lower levels of serum nicotine are detected in e-cigarette users as compared to combustible cigarette smokers, the addiction potential of e-cigarettes and other NRTs is very low. Similarly, the harmful second hand effects of e-cigarette vapor is several magnitudes less than exposure to second hand smoke of traditional cigarettes [18].

Multiple studies and analysis note that use of e-cigarettes is associated with smoking cessation and reduction however all analysis agree that more randomized control trials are needed to determine effectiveness in the long term and explore safety for use [23, 29, 30, 36]. Although we currently have limited long-term studies that prove e-cigarettes are effective as cessation tools, we know that e-cigarettes have similar or less harmful toxin profiles as compared to traditional NRTs [6, 17].

When patients ask about e-cigarettes as cessation tools, the primary care provider should use evidence based medicine to guide their suggestions and while e-cigarettes are likely as safe as nicotine patches and certainly safer than continuing to smoke traditional cigarettes, cessation is most successful alongside behavioral therapy and the intention to quit [12].

Conclusion

In the absence of clear data on the health consequences of e-cigarette use and their efficacy for smoking cessation the goal for patients should be to avoid dual use of e-cigarettes and combustible tobacco use as that could prolong harmful exposure to tobacco smoke. The high degree of modifiable settings makes some of the harmful variables difficult to not only control but also difficult to study. Therefore, based on our review the most effective potential e-cigarette used as a smoking cessation tool would be the use of one with the lowest non-modifiable voltage that with no or very low nicotine combined with a nicotine patch. This would reduce the thermal degradation products from the solvent and other components as well as the known carcinogenic degradation products of nicotine while still providing the habitual benefit that e-cigarettes provide.

While this still has the potential for long term effects that will need to be further examined with RCTs, it would likely be the best option for those who wish to use e-cigarettes as their cessation modality. Most studies continue to show that some level of continued nicotine exposure (whether in e-cigarettes or patches) is effective in aiding in cessation. Overall a good cessation program will require primary providers to be mindful of their patients as individuals and weigh the risk versus benefit in each case with respect to patient autonomy.

Trends to follow in the future will be the use of e-cigarettes by youth, particularly middle and high school age children as use in this population already appears to be on the rise [14]. The advertising of various flavors of tobacco makes e-cigarettes an attractive option for adolescents, especially as first time users. For now, there is limited evidence to support that e-cigarettes are being used by youth as a "gateway" to other tobacco products.

Information to counsel patients on what is known related to e-cigarettes is available from some medical societies' documents on e-cigarettes and from the American Heart Association policy statement that provides guidance on addressing e-cigarette use in clinical practice [37]. A report by the Surgeon General, "Know the risks, e-cigarettes and young people," includes information sheets that clinicians may use to educate adolescent and young adult patients as well as a tip sheet for parents [14].

Disclaimer

The views expressed herein are those of the authors and do not reflect the official policy of the Department of the Army, Department of Defense, or the U.S. government.

References

1. U.S. Department of Health and Human Services,(2014 January), The Health Consequences of Smoking−50 Years of Progress. A Report of the Surgeon General. Rockville, MD: Public Health Service;
2. World Health Organization. WHO report on the global tobacco epidemic, 2017: Monitoring tobacco use and prevention policies. Geneva: World Health Organization; 2017. Contract No.: Licence: CC BY-NC-SA 3.0 IGO.
3. Johnson NB, Hayes LD, Brown K, Hoo EC, Ethier KA, (2014). CDC National Health Report: leading causes of morbidity and mortality and associated behavioral risk and protective factors−United States, 2005-2013. Morbidity and Mortality Weekly Report.;63(4):1-27.
4. Rom O, Pecorelli A, Valacchi G, Reznick AZ, (2015), Are E-cigarettes a safe and good alternative to cigarette smoking? Annals of the New York Academy of Sciences.;1340(1):65-74.
5. Benowitz NL, (2010). Nicotine addiction. New England Journal of Medicine.;362(24):2295-303.
6. Drummond MB, Upson D (2014). Electronic cigarettes. Potential harms and benefits. Annals of the American Thoracic Society.;11(2):236-42.
7. U.S. Centers for Disease Control and Prevention, U.S. National Center for Chronic Disease Prevention and Health Promotion,(2010) U.S. Office on Smoking and Health. How tobacco smoke causes disease: The biology and behavioral basis for smoking-attributable disease: A report of the Surgeon General. Atlanta Centers for Disease Control and Prevention.
8. Patnode CD, Henderson JT, Thompson JH, Senger CA, Fortmann SP,(2015). Behavioral counseling and pharmacotherapy interventions for tobacco cessation in adults, including pregnant women: A review of reviews for the US Preventive Services Task Force Interventions for Smoking Cessation. Annals of Internal Medicine;163(8):608-21.
9. Franck C, Filion KB, Kimmelman J, Grad R, Eisenberg MJ.(2016), Ethical considerations of e-cigarette use for tobacco harm reduction. Respiratory Research;17(1):53.
10. Silagy C, Mant D, Fowler G, Lodge M.(1994), Meta-analysis on efficacy of nicotine replacement therapies in smoking cessation. The Lancet;343(8890):139-42.
11. Fiore MC, Smith SS, Jorenby DE, Baker TB. (1994), The effectiveness of the nicotine patch for smoking cessation: a meta-analysis. JAMA;271(24):1940-7.
12. Bullen C, Howe C, Laugesen M. et al (2014) Electronic cigarettes for smoking cessation: a randomised controlled trial. Journal of Vascular Surgery;59(3):872.
13. Alexander JP, Coleman BN, Johnson SE, Tessman GK, Tworek C, et al (2016). Smoke and vapor: exploring the terminology landscape among electronic cigarette users. Tobacco regulatory science.;2(3):204-13.
14. U.S. Department of Health and Human Services, Office of the Surgeon General. E-cigarette use among youth and young adults: A report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services 2016.
15. King BA, Patel R, Nguyen KH, Dube SR.(2014) Trends in awareness and use of electronic cigarettes among US adults, 2010-2013. Nicotine & Tobacco Research.;17(2):219-27.
16. Kalkhoran S, Glantz SA.(2016), E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. The Lancet Respiratory Medicine.;4(2):116-28.
17. Rahman MA, Hann N, Wilson A, Mnatzaganian G, Worrall-Carter L.(2015),E-cigarettes and smoking cessation: evidence from a systematic review and meta-analysis. PloS One.;10(3):e0122544.
18. Nowak D, Jörres RA, Rüther T.(2014) E-cigarettes−prevention, pulmonary health, and addiction. Deutsches Ärzteblatt international.;111(20):349-55.
19. Brown CJ, Cheng JM.(2014) Electronic cigarettes: Product characterisation and design considerations. Tobacco Control.;23(suppl 2):ii4-ii10.
20. Zhu S-H, Sun JY, Bonnevie E, Cummins SE, Gamst A, et al.(2014), Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. Tobacco control.;23(suppl 3):iii3-iii9.
21. EcigaretteReviewed. What is an E-Cigarette? Tustin, CA: EcigaretteReviewed; 2017 [Available from: https://ecigarettereviewed.com/about-e-cigs.
22. Rowell TR, Tarran R.(2015)Will chronic e-cigarette use cause lung disease? American Journal of Physiology-Lung Cellular and Molecular Physiology.;309(12):L1398-L409.\
23. Shahab L, Goniewicz ML, Blount BC, Brown J, McNeill A, et al.(2017) Nicotine, carcinogen, and toxin exposure in long-term E-cigarette and nicotine replacement therapy users: a cross-sectional study. Annals of Internal Medicine.;166(6):390-400.
24. Vansickel AR, Eissenberg T.(2012) Electronic cigarettes: effective nicotine delivery after acute administration. Nicotine & Tobacco Research.;15(1):267-70.
25. Farsalinos KE, Spyrou A, Tsimopoulou K, Stefopoulos C, Romagna G,(2014). Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices. Scientific reports.;4:4133.

26. Djordjevic MV, Stellman SD, Zang E.(2000) Doses of nicotine and lung carcinogens delivered to cigarette smokers. Journal of the National Cancer Institute.;92(2):106-11.
27. Goniewicz ML, Kuma T, Gawron M, Knysak J, Kosmider L.(2013), Nicotine levels in electronic cigarettes. Nicotine & Tobacco Research.;15(1):158-66.
28. Kruger J, O'Halloran A, Rosenthal AC, Babb SD, Fiore MC.(2016) Receipt of evidence-based brief cessation interventions by health professionals and use of cessation assisted treatments among current adult cigarette-only smokers: National Adult Tobacco Survey, 2009–2010. BMC Public Health.;16(1):1-10.
29. Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH.(2015) Hidden formaldehyde in e-cigarette aerosols. New England Journal of Medicine.;372(4):392-4.
30. Sleiman M, Logue JM, Montesinos VN, Russell ML, Litter MI, et al.(2016), Emissions from electronic cigarettes: key parameters affecting the release of harmful chemicals. Environmental science & technology.;50(17):9644-51.
31. Rahman MA, Hann N, Wilson A, Worrall-Carter L(2014). Electronic cigarettes: patterns of use, health effects, use in smoking cessation and regulatory issues. Tobacco induced diseases.;12(1):21.
32. Dinakar C, O'Connor GT.(2016) The health effects of electronic cigarettes. New England Journal of Medicine.;375(14):1372-81.
33. Kowitt SD, Goldstein AO, Schmidt AM, Hall MG, Brewer NT.(2017) Attitudes Toward FDA Regulation of Newly Deemed Tobacco Products. Tobacco Regulatory Science.;3(4):504-15.
34. Cobb NK, Abrams DB. The FDA,(2014) e-cigarettes, and the demise of combusted tobacco. New England Journal of Medicine.;371(16):1469-71.
35. Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, R, 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(6):1-12.
36. Mishra A, Chaturvedi P, Datta S, Sinukumar S, Joshi P, et al (2015). Harmful effects of nicotine. Indian journal of medical and paediatric oncology: official journal of Indian Society of Medical & Paediatric Oncology.;36(1):24.
37. Bhatnagar A, Whitsel LP, Ribisl KM, Bullen C, Chaloupka F, Piano MR, et al.(2014) Electronic cigarettes: a policy statement from the American Heart Association. Circulation.;130(16):1418-36.