

Electronic cigarette: A review

Vinay Mahishale

Professor, Department of Pulmonary Medicine, KLE University, J.N. Medical College, Belgaum, Karnataka, India

ABSTRACT

The principal addictive component of tobacco smoke is nicotine. The mechanisms of nicotine addiction are highly complex and are responsible for maintenance of smoking behaviour. Use of electronic cigarettes (E-cigarettes), devices that deliver a nicotine containing vapor has increased rapidly across the world. They are marketed as a “healthier alternatives” to conventional cigarettes. There is extensive debate over long-term safety and efficacy of these devices on public health. Studies show that the vapor generated from the E-cigarettes has a variable amount of nicotine and potential harmful toxins. Until robust research demonstrates the safety of E-cigarettes and efficacy in the treatment of tobacco dependence, their role as safe smoking cessation tool is unclear. This review highlights the recent data regarding E-cigarettes toxicity, impact on lung function, and efficacy in smoking reduction and cessation.

Key words: Electronic cigarette, electronic tobacco products, nicotine, smoking cessation

Introduction

Everyone should be aware of the undeniable facts that cigarette smoking is a leading cause of several serious medical diseases; that nicotine is a powerfully addictive substance, and despite the availability of several therapies that are approved by the various health agencies, the vast majority of smokers who try to quit having incredible difficulty maintaining abstinence. Once thought to be a “habit” or “custom,” cigarette smoking and other forms of tobacco use are now widely recognized as behaviors driven by nicotine addiction. It is an addiction to nicotine that compels many smokers to continue to use tobacco products even when they recognize its harmful effects and wish to quit.^[1] Cigarette smoke also exposes smokers to high concentrations of toxic combustion products that are

responsible for six of the eight leading causes of death worldwide, including ischemic heart disease, cerebrovascular disease, lower respiratory infections, chronic obstructive pulmonary disease, tuberculosis, and lung cancer.^[2] Although advances have been made in diagnosis and treatment of smoking-related diseases, cigarette smoking continues to cause an enormous burden of preventable disease and untimely mortality even into the 21st century.^[3] There is inexorable evidence that successful treatment of nicotine addiction improves mortality, regardless of age at cessation. In smokers unwilling or unable to quit, smoking reduction can improve some health outcomes and may eventually lead to cessation.^[4] Over the last 50 years, many treatment options for tobacco dependence have demonstrated insufficient success at decreasing initiation of cigarette use in nonsmokers and cessation in smokers. These include nicotine containing transdermal patches, nasal spray, gum, lozenges cigarette-shaped inhalers, nonnicotine pharmacotherapies and psychosocial interventions.^[5]

The most effective way to tobacco control is to get current smokers to quit and prevent nonsmokers from starting. The questions of how to get more smokers to quit and how to reduce harm among those who continue to smoke have

Access this article online

Quick Response Code:



Website:
www.amhsjournal.org

DOI:
10.4103/2321-4848.144334

Corresponding Author:

Prof. Vinay Mahishale, Department of Pulmonary Medicine, KLE University, J.N. Medical College, Belgaum - 590 010, Karnataka, India.
E-mail: pulmovinay@yahoo.com

been the subjects of public health debate for many years. For a number of years, tobacco and health researchers and policy makers considered the possibility of clean nicotine delivery devices that would satisfy nicotine craving and addiction in smokers, allowing them to stop smoking and thus avoid most if not all of the harm from cigarette smoking.^[6] The latest attempt at reduced harm products is a heterogeneous collection of battery-driven inhalers termed by the World Health Organization (WHO) as electronic nicotine delivery systems or more popularly as electronic cigarettes (E-cigarettes).^[7]

Nature of Nicotine Addiction and Smokeless Tobacco Products

The principal addictive component of tobacco smoke is nicotine. The mechanisms of nicotine addiction are highly complex which include at least two important reward pathways: One mediated directly and immediately by stimulation of dopamine release in the shell of the nucleus accumbens, secondly indirectly after more sustained use through release of dopamine in the nucleus accumbens core in response to stimuli associated with nicotine administration.^[8] The cigarette is an effective instrument for delivering nicotine to the body. Burned tobacco produces vaporized nicotine that is easily entrained into the lungs. Within 10-15 s of puffing on a cigarette, nicotine is absorbed into the bloodstream of smokers and travels to the brain. The swiftness of absorption is an important determinant of the addictiveness of the drug. Nicotine exerts its effects by binding to nicotinic cholinergic receptors in the brain. Nicotine affects a number of neurotransmitter systems, including the dopamine system, which is critical in experiencing pleasure, arousal, and mood modulation. With chronic nicotine exposure, neuroadaptation occurs, such that more nicotine is required to deliver the same neurochemical effect. As the brain becomes tolerant, nicotine is needed in higher concentration to maintain normal brain functioning. In this situation, stopping smoking is associated with deficient neurotransmitter release which leads to withdrawal symptoms like irritability, anxiety, problems getting along with people, difficulty in concentrating, increased hunger, excess eating and weight gain. Nicotine addiction is thus sustained by a combination of positive effects related to pleasure and arousal and the need to continue to take nicotine to avoid the unpleasant effects of nicotine withdrawal.

It is essential to note that, nicotine addiction is also associated with conditioning. Smoking often becomes connected with specific behaviors, such as drinking a cup of coffee, alcohol consumption, talking on the phone, driving a car, and/or

after meals. Conditioning of these behaviors become cues for smoking and contribute to maintained smoking. Smoking also facilitates nicotine dependence through sensorimotor factors associated with the act of smoking. The factors include the smoking process, the smell, taste, and feel of the cigarette smoke.

Nicotine is the essential element of addiction to tobacco but that most of the harm to the health comes from combustion of tobacco, it is logical to consider the use of noncombusted sources of nicotine as a way to reduce the harm from cigarette smoking. The idea that noncombusted sources of nicotine as a way to reduce the harm from cigarette smoking has led to the development of many Smokeless Tobacco Products as well as Potentially Reduced -Harm Nicotine Delivery Products. These include oral tobacco products, such as snus and dissolvable tobacco. Since, the risks of traditional smokeless tobacco are much lower than those of cigarette smoking, these were used as an aid to smoking cessation. However, these products were later withdrawn from the market due to concerns of safety as these have been associated with diseases of the oral cavity, oral cancers, pancreatic cancers, cardiovascular diseases and reproductive problems.^[9] Then, the search for clean nicotine delivery systems that would satisfy nicotine craving and promote the smoking cessation lead to the development of E-cigarettes.

Electronic Cigarette

Electronic cigarettes are battery powered devices that convert nicotine containing liquid into a vapor that can be inhaled. In recent years, multiple companies have introduced variety of brands of E-cigarettes. This device was invented by Ruyan Group (Holdings) Limited, China in 2003, and the company patented E-cigarettes in Canada in 2004.^[10] E-cigarettes consist of a plastic tube, electronic heating element, liquid nicotine cartridge, and a lithium battery and atomization chamber with a membrane to suspend ingredients. Some E-cigarettes contain a light emitting diode in the tip, which illuminates when the user inhales (or “vapes”), giving the appearance of the burning end of a conventional cigarette. Chemicals introduced into the liquid vehicle produce aromas and flavors of tobacco, chocolate, mint, fruit, and coffee.^[11]

Electronic cigarette were developed with the goal of mimicking the conventional cigarette without the considerable harmful effects of tobacco smoke. They are often marketed as the healthier version of the conventional cigarette. The device aerosolizes nicotine, so that it is readily absorbed into the respiratory tract and then enters the bloodstream, resulting

in a near immediate nicotine reward in the central nervous system. Propylene glycol: A chemical used to generate artificial “smoke” for theatrical productions — is added to the liquid vehicle to stimulate the appearance of using “real” cigarette. The concentration of nicotine varies both across different manufacturers and within the same brand. Cartridges vary in their nicotine content from no nicotine to 16-18 mg/cartridge. Cost of the E-cigarette varies according to the brand and country in which it is sold. Surveys have shown that sales of E-cigarette have increased as consumers buy for a variety of reasons, such as trying to quit smoking, preventing exposure to smoke, being allowed to smoke in smoke free zones, better flavor, for smoking without generating irritation and harmful second hand smoke.

Marketing of electronic cigarette

They are aggressively marketed as harmless alternatives to traditional tobacco smoking. Sales are increasing so rapidly that some analysts predict that they will surpass cigarette sales within a decade.^[12] More than 400 different E-cigarettes are currently marketed. Initially, E-cigarettes were manufactured by small companies. Now major tobacco companies have entered the marketplace. The marketing of E-cigarettes has been vigorous and has emphasized harm-reduction beliefs.^[13] Endorsements use beautiful and handsome models and celebrities with glamorous images so that they are attractive. The hard-line marketing activity of E-cigarette manufacturers and distributors is one of the core factors that may be responsible for the rapid increase of E-cigarette use in many countries. Another powerful marketing tactics of the E-cigarette industry include the use of internet websites and blogs to sell and promote their products. Internet blogs allow the industry to achieve two-way communication between themselves and existing/future consumer. The WHO and US Food and Drug Administration (FDA) have already addressed their concerns about the aggressive marketing activities of E-cigarette companies in their reports. Until conclusive scientific evidence of safety and efficacy of E-cigarettes is released, all marketing activities of the E-cigarette industry should be banned.^[14,15] Despite the viewpoints of the WHO and US FDA, the industry is quick to advertise that E-cigarettes can be an effective smoking cessation aid by employing “above-the-line” and “below-the-line” marketing policies.

Public health concerns of electronic cigarette

There is currently extensive debate in the public health community about the safety and benefits of E-cigarettes. All agree that E-cigarettes would be a health benefit if the population of conventional cigarette smokers all switched to E-cigarettes and stopped smoking cigarettes completely. However, this is far from reality. Many E-cigarette users

report smoking fewer cigarettes per day, while using E-cigarettes, but the health benefits of such reduction are not clear, and there is concern that the availability of E-cigarettes when one cannot smoke conventional cigarettes may impede quitting, resulting in more smokers and more population harm.^[16] There are also concerns about the potential toxicity of E-cigarettes, as information on the pharmacology, toxicology, and safety of E-cigarettes is limited. Available information suggest the presence of nicotine (including cotinine), tobacco specific impurities (anabasine, myosmine, β -nicotyrine), propylene glycol (rarely diethylene glycol), and tobacco specific nitrosamines (which include carcinogens) in commonly available brands of E-cigarettes.^[17-19] A recent study found that the effort required (vacuum desired) to smoke an E-cigarette is higher than that for conventional cigarettes.^[20] This effect was accentuated after a few puffs resulting in nonuniform nicotine delivery, leading to excessive inhalation of nicotine. Nicotine itself has some potentially harmful effects on cardiovascular hemodynamics (increased heart rate and blood pressure), may impair endothelial function, and may promote insulin resistance with a possible increased risk of type 2 diabetes. Propylene glycol in aerosol form can be a pulmonary irritant and increases dynamic airway resistance. E-cigarette use could be detrimental to people with asthma and chronic obstructive pulmonary disease. E-cigarettes generate particles of a size similar to cigarette smoke particles, and there are concerns that particles *per se* may have adverse health effects.^[16]

Nicotine has also been implicated in a number of cancers and concept of “third hand smoke.”^[21,22] It crosses the placenta and alters fetal gene expression and tissue development in a variety of organs.^[23] Its toxic effects have been documented in many organs, and it has been shown that nicotine binds to the airway epithelial cell nicotine receptor, producing physiological changes in airway epithelial cells similar to those found in cystic fibrosis.^[24] There is sufficient evidence about the toxicity of nicotine and the other components that have been found in E-cigarettes. Analysis of nicotine solutions used in E-cigarettes has been carried out which have revealed a range of other constituents including formaldehyde, acetaldehyde, and derivatives of benzene and benzodiazepine, raising the question of whether these solutions are suitably pure. The vapor produced by E-cigarettes also contains a range of toxins, including some nitrosamines, though at much lower levels than in tobacco smoke. However, it is far from clear that these compounds are safe or reliable as might reasonably be expected. On this basis, it seems clear that E-cigarettes containing nicotine should not be promoted as harmless alternatives to regular cigarettes.

Other concerns about E-cigarettes should also be considered. First, the use of these products could prolong actual smoking cessation period. Second, data are emerging to show that some users are not stopping cigarette use, but concurrently using E-cigarettes (“dual use”) in all the places where they would otherwise have been unable to smoke (e.g., restaurants, airports, and the workplace). Finally, and perhaps most challenging, is a very real possibility that E-cigarettes may serve as an initiation device for young people, who may in due course changeover to regular cigarettes when they reach the legal age to purchase those products because they are advertised as being safe, fashionable, and good tasting, often due to the addition of pleasant flavors.^[25] This might lead to the most important potential population harm of renormalization of cigarette smoking behavior, resulting in more youth initiation and fewer adults quitting smoking. Some E-cigarettes look like traditional cigarettes, and their widespread use would suggest that smoking behavior is socially acceptable. The most important factors for youth smoking initiation have friends who smoke and being exposed to smoking offers from close friends. Because of the increasing popularity of E-cigarettes, nonsmoking youth who have friends who use E-cigarettes are likely to be susceptible to initiate smoking E-cigarettes. In addition, the E-cigarette packaging may be attractive and fashionable to youth, who may be further tempted to try it. Compared with adult users who may decide to use E-cigarettes for the purpose of quitting, youth users are more likely to use E-cigarettes for the novelty factor. Another concern is the ability of the E-cigarette user to adjust the nicotine concentration, as youth users may not be aware that they can experience symptoms of nicotine addiction much more rapidly than adults. Therefore, it is important to understand youth users behaviors with E-cigarettes.^[26]

Electronic cigarettes and smoking cessation

Although E-cigarettes are aggressively promoted as smoking cessation aids, several recent studies of their effectiveness for cessation have been unconvincing. One randomized trial comparing E-cigarettes with and without nicotine with a nicotine patch found no differences in 6-month quit rates. Population-based, longitudinal studies have also not shown associations between E-cigarette use and quitting. A longitudinal, international study found that, although 85% of smokers who used E-cigarettes reported using them to quit, E-cigarette users did not quit more frequently than nonusers. Among US quit line callers, E-cigarette users were less likely to have quit at 7-month than nonusers.^[27-30] Many other studies comparing E-cigarettes to other forms of nicotine replacement therapy, failed in demonstrating E-cigarettes as a more effective tool than available FDA-approved nicotine

replacement therapies for smoking cessation. Until robust research demonstrates safety of E-cigarettes and efficacy in the treatment of tobacco dependence, their role as a harm reduction tool is uncertain.

It is evident from many studies that scientific proof regarding the human health effects of E-cigarettes is inadequate. Although E-cigarette aerosol may contain fewer toxicants than cigarette smoke, studies evaluating whether E-cigarettes are less harmful than cigarettes are inconclusive. Some evidence suggests that E-cigarette use may facilitate smoking cessation, but definitive data are lacking. No E-cigarette has been approved by FDA or any country as a cessation aid. Environmental concerns and issues regarding nonuser exposure exist. The health impact of E-cigarettes, for users and the public, cannot be determined with currently available information.^[28]

Future recommendations

Since, no long-term data demonstrating that E-cigarettes are a healthier alternative to conventional cigarettes, standardization and regulation of E-cigarette products is needed. A number of professional societies have produced guidelines and policy recommendations aimed at minimizing harms related to rapid E-cigarettes acceptance.^[31-33] Some of the recommendations are:

1. E-cigarettes should be regulated as tobacco products.
2. E-cigarettes should not be used in smoke-free areas.
3. Should be taxed at rates equivalent with conventional cigarettes and other tobacco products.
4. Candy and menthol flavors should be banned.
5. Sales to minors and internet sales should be regulated.
6. The packs of E-cigarettes should have warning labels, liquid cartridge chemical composition and nicotine content.

Further research investigating the effects of E-cigarettes must be conducted in order to convincingly determine the safety of this product. In addition, these studies should be conducted independently and should not be sponsored or funded by the E-cigarette industry.

Counseling of smokers and “vapers” about electronic cigarettes

The National Quit Line, physicians in smoking cessation clinics, school teachers, members of the family and other individuals who have opportunities to meet and counsel current smokers who want to quit should discourage the use of E-cigarettes as a smoking cessation aid until there is enough scientific evidence to support this claim. Following quick facts can be utilized by counselors to facilitate healthy behavioral change in smokers.^[21]

- E-cigarettes are not approved by FDA/Governments as quit smoking devices.
- The vapors from E-cigarettes are complex mixtures of chemicals, not pure nicotine. Whether inhalation of the complex mixture of chemicals in vapors is safe is unknown.
- There is no evidence that E-cigarette help smokers to quit smoking.
- There is increasing resistance to the use of E-cigarettes in public places and outright bans in a growing number of countries.
- The promotion of E-cigarette may communicate a message to children and adolescents that “vaping” is harmless inadvertently escalating the risk of nicotine addiction and tobacco use in a vulnerable population.
- Approved treatments for smoking cessation, proven safe and effective, are available.
- Long-term abstinence from tobacco use is a goal that has been achieved by millions of people without using E-cigarettes.
- Until more information about the safety of these devices becomes available, use of E-cigarettes cannot be recommended.
- Smoking cessation medications, conventional counseling strategies, including the 5 major steps to intervention “The 5 As”: (Ask, Advise, Assess, Assist, Arrange), and telephone quit lines are available in many countries for people who wish to quit.

1. their Operation. In: Report on the Scientific Basis of Tobacco Product Regulation: Third Report of a WHO Study Group. Geneva: World Health Organization; 2009.
8. Etter JF. Electronic cigarettes: A survey of users. *BMC Public Health* 2010;10:231.
9. Luo J, Ye W, Zendejdel K, Adami J, Adami HO, Boffetta P, *et al.* Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: A retrospective cohort study. *Lancet* 2007;369:2015-20.
10. Hon L. A non-smokable electronic spray cigarette (CA2518174). Available from: <http://www.wikipatents.com/CA-Patent-2518174/a-nonsmokable-electronic-spray-cigarette>. [Last accessed on 2014 Mar 18].
11. Yamin CK, Bitton A, Bates DW. E-cigarettes: A rapidly growing Internet phenomenon. *Ann Intern Med* 2010;153:607-9.
12. Purkayastha D. BAT ramps-up e-cigarette expansion as sales go up in smoke international business times, [2013 July 31]. Available from: <http://www.thefreelibrary.com/BATRamps-upE-cigaretteExpansionasSalesGoUpinSmoke.-a0338323170>. [Last accessed on 2013 Dec 13].
13. Noel JK, Rees VW, Connolly GN. Electronic cigarettes: A new ‘tobacco’ industry? *Tob Control* 2011;20:81.
14. World Health Organization, Study Group on Tobacco Regulation. Report on the Scientific Basis of Tobacco Product Regulation: Third Report of a WHO Study Group. Geneva: World Health Organization; 2010.
15. Westenberger BJ. US Food and Drug Administration evaluation of e-cigarettes. Available from: <http://www.fda.gov/downloads/Drugs/ScienceResearch/UCM173250.pdf>. [Last accessed on 2014 Jan 7].
16. Benowitz NL. Emerging nicotine delivery products. Implications for public health. *Ann Am Thorac Soc* 2014;11:231-5.
17. Westenberger BJ. US Food and Drug Administration Evaluation of E-cigarettes. Center for Drug Evaluation and Research, Division of Pharmaceutical Analysis. Rockville, MD: US Food and Drug Administration; 2009. Available from: <http://www.fda.gov/downloads/Drugs/ScienceResearch/CM173250.pdf>. [Last accessed on 2014 Jan 07].
18. Leondiadis L. Results of chemical analyses in NOBACCO electronic cigarette refills. Athens, Greece: Mass Spectrometry and Dioxin Analysis Laboratory, National Centre for Scientific Research (“Demokritos”); 2009.
19. Flouris AD, Oikonomou DN. Electronic cigarettes: Miracle or menace? *BMJ* 2010;340:c311.
20. Trtchounian A, Williams M, Talbot P. Conventional and electronic cigarettes (e-cigarettes) have different smoking characteristics. *Nicotine Tob Res* 2010;12:905-12.
21. Kuschner WG, Reddy S, Mehrotra N, Paintal HS. Electronic cigarettes and thirdhand tobacco smoke: Two emerging health care challenges for the primary care provider. *Int J Gen Med* 2011;4:115-20.
22. Brody JS. Transcriptome alterations induced by cigarette smoke. *Int J Cancer* 2012;131:2754-62.
23. Votavova H, Dostalova Merkerova M, Krejcik Z, Fejglova K, Vasikova A, Pastorkova A, *et al.* Deregulation of gene expression induced by environmental tobacco smoke exposure in pregnancy. *Nicotine Tob Res* 2012;14:1073-82.
24. Maouche K, Medjber K, Zahm JM, Delavoie F, Terryn C, Coraux C, *et al.* Contribution of a7 nicotinic receptor to airway epithelium dysfunction under nicotine exposure. *Proc Natl Acad Sci U S A* 2013 5;110:4099-104.
25. Britton J. Electronic cigarettes. *Thorax* 2013;68:904-5.

References

1. Tobacco Advisory Group of the Royal College of Physicians. Harm Reduction in Nicotine Addiction. London: Royal College of Physicians; 2007. Available from: <http://www.rcplondon.ac.uk/sites/default/files/documents/harm-reduction-nicotine-addiction.pdf>. [Last accessed on 2014 Jan 7].
2. World Health Organization. World Health Organization Fact Sheet 2009 — Tobacco; 2009. Available from: http://www.who.int/nmh/publications/fact_sheet_tobacco_en.pdf. [Last accessed on 2014 Jan 17].
3. Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, *et al.* 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 2013;368:351-64.
4. Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, *et al.* 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* 2013;368:341-50.
5. Rigotti NA. Smoking cessation in patients with respiratory disease: Existing treatments and future directions. *Lancet Respir Med* 2013;1:241-50.
6. Gray N, Henningfield JE, Benowitz NL, Connolly GN, Dresler C, Fagerstrom K, *et al.* Toward a comprehensive long term nicotine policy. *Tob Control* 2005;14:161-5.
7. World Health Organization Study Group on Tobacco Regulation. Tobreg Scientific Recommendation: Devices Designed for the Purpose of Nicotine Delivery to the Respiratory System in Which Tobacco is not Necessary for

26. Lee S, Kimm H, Yun JE, Jee SH. Public health challenges of electronic cigarettes in South Korea. *J Prev Med Public Health* 2011;44:235-41.
27. Polosa R, Caponnetto P, Morjaria JB, Papale G, Campagna D, Russo C. Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: A prospective 6-month pilot study. *BMC Public Health* 2011;11:786.
28. Callahan-Lyon P. Electronic cigarettes: Human health effects. *Tob Control* 2014;23 Suppl 2:ii36-40.
29. Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, *et al.* Efficiency and Safety of an eElectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PLoS One* 2013;8:e66317.
30. Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, *et al.* Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet* 2013;382:1629-37.
31. American Thoracic Society. ATS policy position: E-cigarettes, 2013. Available from: http://www.thoracic.org/advocacy/press-releases/ATS_Policy_Position_eCigarettes.pdf. [Last accessed on 2013 Dec 11].
32. American College of Physicians. Tobacco Control and Prevention: Policy Monograph. Philadelphia: American College of Physicians; 2010.
33. World Health Organization. Questions and answers on electronic cigarettes or electronic nicotine delivery systems (ENDS); July 9, 2013 Available from: http://www.who.int/tobacco/communications/statements/electronic_cigarettes/en/. [Last accessed on 2013 Dec 13].

How to cite this article: Mahishale V. Electronic cigarette: A review. *Arch Med Health Sci* 2014;2:184-9.

Source of Support: Nil, **Conflict of Interest:** None declared.

