CORRESPONDENCE

From Oncologist's Desk: Hemato-Oncological Aspect of Using Vaporizers, E-Cigarettes, and Other Electronic Nicotine Delivery Systems (ENDS)

Kamal Kant Sahu¹ · Ajay Kumar Mishra¹ · Amos Lal² · Ahmad Daniyal Siddiqui³ · George M. Abraham^{1,4}

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Dear Editor,

Electronic nicotine delivery systems (ENDS) like E-cigarettes are the smokeless and non-combustible alternative to conventional cigarette smoking, and have become increasingly popular in recent times. Since the time they came into existence, they have been surrounded by many controversies related to their ill-impact on health and wellbeing. On one side, youth today in increased numbers are engaging themselves with vaporizers and E-cigarettes in an attempt to either quit smoking or to have naïve experience, but at the same time the long-term effects of using these ENDS are yet to be known. Through this letter, we aim to raise our concern on the ill effects of E-cigarettes with special emphasis on their impact on hematological/oncological system.

As per Food and Drug Administration (FDA), United States (US) approximately there is 480,000 deaths per year in the U.S. alone from tobacco-associated cancers, emphysema, heart disease and stroke. Hence, every attempt should be made to educate and help the current smokers to quit smoking. Currently FDA has approved two remedies for smoking cessation: (A) *Nicotine based*, nicotine

replacement therapy (NRT) in the form of patch, gum, nasal spray, inhalers and lozenges and (B) *Non-Nicotine based*, drug therapy, bupropion and varenicline.

Though very popular amongst youth and smokers, vaporizers, E-cigarettes, and other electronic nicotine delivery systems (ENDS) are not FDA approved as smoking cessation tool. A typical device comprises of a vapor delivering/generating system and a fuel “E-liquid”. A typical E-liquid contains varied proportion and combination of nicotine, flavoring chemicals (Cinnamon, vanilla and butter flavoring chemicals and so on) and various volatile organic compounds (VOCs) like propylene glycol (PG) and vegetable glycerine (VG). Statistically, there are more than 500 E-cigarette brands with almost 8000 uniquely flavored E-juices available to consumers in the US alone and therefore practically it is difficult to keep a check on their compositions [1].

While it is claimed by various manufacturing industries that the nicotine content in E-liquid is lesser than in actual cigarette but there are ample reports of concentration high enough to cause nicotine intoxication and addiction [1, 2]. Many animal model studies have confirmed ill-effects of flavoring agents on lungs, bronchial lining, disrupting

✉ Kamal Kant Sahu
drkksahu85@gmail.com

Ajay Kumar Mishra
Ajay.Mishra@stvincenthospital.com

Amos Lal
Lal.amos@mayo.edu

Ahmad Daniyal Siddiqui
A.Daniyal.Siddiqui@stvincenthospital.com

George M. Abraham
George.Abraham@stvincenthospital.com

¹ Department of Internal Medicine, Saint Vincent Hospital, 123 Summer Street, Worcester, MA 01608, USA

² Division of Pulmonary and Critical Care Medicine, Mayo Clinic, 200 1st St SW, Rochester, MN 55905, USA

³ Division of Hematology and Medical Oncology, Saint Vincent Cancer and Wellness Center, 1 Eaton Place, Worcester, MA 01608, USA

⁴ University of Massachusetts Medical School, 55 N Lake Ave, Worcester, MA 01608, USA

mucociliary clearance by generating reactive oxygen species resulting in inflammation and subsequently tissue injury [3–5]. For instance, 2,3-pentanedione, an artificial butter flavoring agent has been found to be associated with bronchiolitis obliterans (BO) [6]. We reported recently a rare case of 40-year-old female who developed E-cigarette related organizing pneumonia [5]. Muthumalage et al. studied impact of E-cigarette flavoring chemicals at cellular level and reported a significant inflammatory, and oxidative response causing toxicity to leucocytes due to elevation of IL-8 and H₂O₂ levels [4].

Jain et al. in their study found that concentrations of heavy metals like cadmium, lead, and mercury in blood were no different among e-cigarette users vs conventional cigarette smokers or dual users of cigarettes and e-cigarettes. The heavy metals are well known for many systemic illnesses including anemia and carcinogenicity but needs more validation with regards to association with e-cigarette. Flach et al. in their review outlined the potential dangers of developing head and neck cancer associated with the use of E-cigarettes [7]. McConnell et al. recently studied the impact of nicotine (comprised of both cigarettes and e-cigarettes) on glioblastoma multiforme. Nicotine promotes neural tumor cell proliferation, likely through EGFR and/or CY2B1 pathways and McConnell et al. discussed the adverse effects of nicotine on glioblastoma and chemotherapy drug resistance (e.g. cytochrome-P450-metabolized agents, including BCNU) [8].

Twohig et al. recently reported a case of e-cig induced methemoglobinemia [9, 10]. They found two E-liquid toxins vanillin and propylene glycol as the cause of methemoglobinemia in their case. Cessation of E-cigarette led to complete resolution of methemoglobinemia.

Similar to conventional second hand smoking, passive vaping related to E-cigarette also poses threat of developing vaping related lung disorders and possibly cancer. Carcinogenicity of the vapor released depends on multiple factors: type of device, E-liquid composition and ingredients, temperature, technique and so on. Few of the studies have even found E-cigarettes to be more addictive than conventional smoking [11]. Any discovery in medical world aims towards betterment of society. Many drugs, therapies, procedures despite having proven benefits still could cause untoward side effects [12, 13]. As a responsible part of society, governing medical organisations need to take the challenge revolving around E-cigarettes seriously.

Current stand of FDA: E-cigarettes are not approved by the FDA for smoking cessation and does not authorize their safety or efficacy for smoking cessation. Following are the most updated recommendations of FDA on ENDS based on the available literature:

- FDA prohibits sales to individuals aged < 18 years,
- FDA prohibits sales in vending machines except in adult-only venues, and also bans distribution of free samples.
- FDA does not restrict the promotion of e-cigarettes; however, any false or misleading information is a punishable offense.
- All e-cigarette manufacturers must submit to FDA the report that their products meet the standards fixed by FDA of providing a net public health benefit.
- FDA bans E-cigarette use on airplanes

In conclusion, while the rough road for ENDS seems to be endless considering the fact that newer studies are suggesting them not to be risk free. However, general population by virtue of ignorance continue to use ENDS and related products fearlessly. Currently, there are close to 200 clinical trials (ClinicalTrial.gov) in various phases and results of them would give us more insight to this topic.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Statement The article doesn't contain participation of any human being and animal.

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