CHEST

More to Add to E-Cigarette Regulations

Unified Approaches

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ABBREVIATIONS: CDC = Centers for Disease Control and Prevention; FDA = Food and Drug Administration

E-cigarette is an electronic nicotine delivery system (or device) designed for smoking cessation, which has been shown to be more effective than nicotine replacement therapy.[1] The Committee for Advertising Practice[2] issued regulations in 2015 requiring disclosure of contents and discouragements of nonsmokers and youth. Public Health England announced that vaping only poses a small portion of risks of smoking and contributes to 20,000 new quits per year. Meanwhile, a meta-analysis indicated ineffectiveness of e-cigarettes in smoking cessation.[3] It is also unclear whether the cessation effect is a consequence of partial replacement with e-cigarettes making the smokers dual users.[4] Nonetheless, the popularity of e-cigarettes has increased drastically. According to the World Health Organization,[5] the number of vapers worldwide has increased from 7 million in 2011 to 41 million in 2018 (World Health Organization global report on trends in prevalence of tobacco smoking 2000-2025). Whereas both the Food and Drug Administration (FDA) and US Surgeon General officially declared teenage usage of e-cigarettes an epidemic in 2018, the use of e-cigarettes doubled in high school students (3.6 million using regularly),[6] promoting openness to tobacco smoking and nicotine addiction to result in damage in brain development.[4] In August 2019, the first case of e-cigarette use-related death emerged in Illinois. As of November 5, 2019, the Centers for Disease Control and Prevention (CDC) reported 39 deaths among the 2,051 cases of e-cigarette-related lung injuries occurring in the United States. CDC laboratory testing of BAL fluid samples (or samples of fluid collected from the lungs) from 29 patients with e-cigarette, or vaping, product use-associated lung injury (EVALI) submitted to CDC from 10 states found vitamin E acetate (an additive used to produce e-cigarettes or vaping products) in all of the BAL fluid samples. This is the first time a potential chemical of concern in biologic samples from patients with EVALI was detected. An important aspect to consider is that a number of the flavoring products used are purchased from the black market. Additionally, approximately 78% of the victims used tetrahydrocannabinol, an active ingredient of marijuana. Acute respiratory distress syndrome, lipoid pneumonia, and viral-like pneumonia have been observed in tetrahydrocannabinol-e-cigarette users.[7] Close examination of lung biopsies of 17 recent cases (13 men; median age, 35 years) indicates that most showed acute airway-centered injury, often with severe bronchiolitis accompanied by marked mucosal edema, sloughing of bronchiolar epithelium, and peribronchiolar organization.[8] Clinical presentations included shortness of breath, cough, chest pain, and GI symptoms of nausea, vomiting, diarrhea, and abdominal pain.[8]

Most e-cigarettes contain nicotine, the levels of which are still high enough to be toxic.[4,9] Nicotine-free e-cigarette products remain toxic because of solvent decomposition (ie, acrolein from glycerol) and flavoring additives.[4] Of note, acrolein contributes to the development of COPD.[4] Many identified components from e-cigarette vaporization are potential carcinogens, including acrolein, toxic metals (cadmium, chromium, lead, manganese, and nickel), and organic compounds

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such as propylene oxide formed from propylene glycol, a compound not present in tobacco cigarettes.[4] Exposure of mice to e-cigarette resulted in inflammation and reduced clearance of bacterial and viral particles.[4] Several studies have further demonstrated increased oxidative stress, impaired alveolar macrophage function, and nicotine-independent dysfunction of lung innate immunity in response to e-cigarette use.[4,10,11] In view of the recent lung injury cases, the US government has considered restricting sales of flavoring e-cigarettes since September 11, 2019. On September 18, 2019, India approved an executive order banning vaping products, including the production, manufacturing, import and export, sale, distribution, and advertising related to e-cigarettes. These decisions are supported by earlier studies indicating that flavoring additives are potentially pathogenic, and contain cytotoxic aldehydes that are recognized as primary irritants of the respiratory tract mucosa.[4] In a study where 41 e-cigarette refill fluids were examined for cytotoxicity to human pulmonary fibroblasts, human embryonic stem cells, and mouse neural stem cells, it was noted that cytotoxicity was related to the flavoring chemicals.[4]

Despite concerns with the safety of e-cigarettes, regulatory policies on e-cigarettes have been lagging since its marketing in 2005. The American Thoracic Society/European Respiratory Society/American College of Chest Physicians[12] and the American Heart Association[13] cited concerns regarding ineffectiveness of e-cigarettes in smoking cessation and the potential adverse effects of e-cigarettes in the 2014 recommendations. They collectively urged restricted use until the health impacts of e-cigarette exposure are fully understood. In the United Kingdom, nicotine-containing e-cigarettes have been regulated either as tobacco-related products, or as licensed medicines since 2016.[14] In the United States, the FDA established rules on e-cigarette regulations in 2016, with a series of timelines starting in August 2016 (http://fdaregs.info/fda-deeming-regulations/timeline/). Initial regulations in the August 2016 release include the following: (1) no new products can enter the market without FDA authorization; (2) prohibition to sell to customers $\leq$ 18 years of age; (3) a photo identification is required for everyone $<$ 27 years of age; and (4) prohibition to sell e-cigarettes using a vending machine. On August 8, 2018, the FDA released new regulations to request Premarket Tobacco Applications from all products on the market. On August 8, 2019, the FDA requested the manufacturers to report Harmful and Potentially Harmful Constituents. Simultaneously (July 2019), the World Health Organization released recommendations on e-cigarettes (WHO Report on the Global Tobacco Epidemic, 2019) urging countries to (1) define regulation of e-cigarettes in legislation; (2) apply existing tobacco control laws to e-cigarettes; (3) note impacts of e-cigarettes on smoking among youth and renormalization of smoking in society; 4) ban advertising and flavoring of products to deter use by youth; and (5) consider policies to make products unattractive to young people.

To complement existing policies and to respond to the recent e-cigarette-related lung injury outbreak since August 2019, we propose to implement additional regulations on e-cigarettes. The proposed actions include the following: (1) request the manufacturers to clearly label the packaging with nicotine-dependent and -independent toxicities; (2) request all media to drop advertising of e-cigarettes and set up educational programs to prevent use of e-cigarettes among youth; (3) set up legal regulations and penalties on sales without approval of governmental agencies and/or to the underaged youth; (4) set up professional monitoring and reporting systems of e-cigarette use as a smoking cessation tool and its related health consequences; and (5) increase tax on e-cigarette sales to further help prevent access of young people. We speculate that through implementations of these unified approaches, the harmful effects of e-cigarettes can be maximally prevented, whereas the potential benefits of e-cigarettes in smoking cessation in the presence of professional assistance can be preserved.

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