Molecular Imaging of Pulmonary Inflammation: Claiming That Vaping Is More Harmful Than Smoking Is Unsupported

TO THE EDITOR: We read with interest the recent pilot study by Wetherill et al. (1). The authors used 18F-6-(1/2)(2-fluoropropyl)-4-methylpyridin-2-amine (18F-NOS) PET imaging to quantify inducible nitric oxide synthase expression to characterize oxidative stress and inflammation in the lungs of 5 electronic cigarette (EC) users, 5 tobacco cigarette (TC) smokers, and 5 controls who had never smoked or vaped. PET imaging showed much greater 18F-NOS nondisplaceable binding potential in the lungs of EC users than in TC smokers, but contrary to expectations, no difference between TC smokers and controls was found.

The reported absence of difference in 18F-NOS nondisplaceable binding potential between TC smokers and controls is inconsistent with the suggestion given by enhanced nondisplaceable binding potential on 18F-NOS imaging that there is oxidative stress and inflammation in the lungs, given that smoking causes both inflammatory responses and oxidative stress. This issue renders interpretation of the study’s findings invalid. In consideration of the very small sample size and low reproducibility of 18F-NOS PET imaging, the likelihood of chance findings is very high. There would have been more confidence in the interpretation if former smokers had been included in the study design; however, this was not done. Important confounders, such as allergies of the upper respiratory tract with inducible nitric oxide synthase upregulation and high levels of exhaled nitric oxide (2) and prior and present exposure to tobacco smoking among EC users (3)—who are typically either former smokers or dual users—were not taken into consideration. As it is impossible to decouple the lung health impact of EC aerosol emissions from prior tobacco smoke exposure, only long-term follow-up of exclusive EC users who have never smoked TCs in their life would have been a better-suited study design to verify potential harm caused by EC use. In a 3.5-y prospective clinical trial, daily exclusive EC users who had never smoked TCs did not exhibit any increase in exhaled nitric oxide (4).

Additionally, given the cross-sectional design of the study, the observed correlation between EC use and improved 18F-NOS PET imaging does not infer causation. The results of the study are inconsistent with the evidence that cigarette smoking reduces, not increases, inducible nitric oxide synthase expression and NO production from lung epithelial cells (5), as well as with the evidence that smoking is consistently linked to low levels of exhaled nitric oxide that return to normal after smoking is stopped (6–8).

Therefore, this pilot study does not support the argument that vaping is more harmful than smoking, and it contradicts clinical evidence showing that ECs may have some benefits in minimizing the harm caused by cigarette smoke and are unlikely to cause serious respiratory issues (3,4,9).

REFERENCES


DISCLOSURE

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REPLY: We thank Drs. Polosa, Spicuzza, and Palmucci for their interest and comments on our study. The team’s comments highlight evidence supporting traditional combustible cigarettes as a proinflammatory phenotype and the potential of electronic cigarettes for harm reduction as a tool for smoking cessation. Harm reduction represents an important strategy in public health, because smoking combustible nicotine cigarettes remains the largest preventable cause of death worldwide (1,2).

In our innovative pilot study, we found increased radiotracer binding of $^{18}$F-6-(1/2)(2-fluoropropyl)-4-methylpyridin-2-amine ($^{18}$F-NOS) in the lungs of electronic cigarette users compared with traditional combustible cigarette users (3). This unanticipated finding led us to conclude that electronic cigarette use leads to unique physiologic changes in the lungs, distinct from combustible cigarettes, including relatively increased inflammation in younger, otherwise healthy individuals. We neither concluded nor implied that vaping was more harmful than combustible cigarettes nor measured metrics of harm such as death or contribution to other diseases such as cancer, heart disease, or stroke.

Although there is evidence that electronic cigarettes can achieve cigarette quit rates superior to those for the nicotine patch (4), the long-term public health effects of electronic cigarettes, first introduced in the United States and the European Union in 2006, remain unclear (1,3). Given the decades of public health research documenting the various adverse outcomes that manifest after years of combustible cigarette smoking, including chronic obstructive pulmonary disease, cancer, and heart disease (6–8), it is important to acknowledge that electronic cigarettes are not harmless and could have long-term adverse health effects that are distinct from those associated with combustible cigarette use.

Electronic cigarettes are not unique to individuals trying to quit or who have quit smoking cigarettes. The Centers for Disease Control and Prevention report that 36.9% of individuals who vape also smoke combustible cigarettes and that 23.6% have never smoked combustible cigarette use. Harm reduction strategy for most of these individuals is not applicable; there is only the potential for harm. Thus, our study aimed to examine those who exclusively vape. How electronic cigarette use alters cardiopulmonary physiology and the local pulmonary cellular milieu remains unclear. In agreement with our study, there is growing evidence that electronic cigarette use results in a proinflammatory phenotype (11–15). We carefully excluded subjects with asthma or allergies and those taking medications that could temper inflammation. Additionally, we did not observe a decreased PET signal in conventional smokers or suggest that combustible cigarette use results in diminished pulmonary inflammation.

With the epidemic rates of electronic cigarette use among youth continuing to rise and most adult users not using electronic cigarettes for smoking cessation, the long-term public health consequences of this relatively new behavior cannot be dismissed because of the lack of long-term data.

REFERENCES

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