Vaping increases susceptibility to coronavirus in mice

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The use of e-cigarettes, or vaping, causes serious damage to the lungs. After the novel coronavirus responsible for the respiratory disease COVID-19 emerged last year, there have been ongoing concerns about

how vaping might impact risk of infection and severity of symptoms. Some evidence shows an increased risk of COVID-19 among those who vape. Research also shows a higher COVID-19 mortality rate in men compared to women, and men are more likely to vape than women. However, there is no evidence to link these two observations.

New research from Jefferson sheds light on this by showing that exposure to e-cigarette vapor increases levels of the coronavirus receptor in the lungs of male mice, particularly when nicotine is present in the vapor. This could make it easier for the virus to infect. The findings were published in *Journal of Investigative Medicine* on April 29.

Using the spike-like protein on its surface like a key, the novel coronavirus binds to the angiotensin-converting enzyme 2 (ACE-2) receptor found in the lining of our airways, and unlocks its path into our lung cells.

"It's been shown that cigarette smokers have higher levels of ACE-2 in their lungs and that smoking is a known risk factor for developing lung disease and infection," says Pawan Sharma, Ph.D. and co-senior author of the study. "We wanted to see if a similar effect is seen with e-cigarettes or vaping, and whether any effects observed are different between male and females."

The researchers housed female or male mice in a box attached to an automated system that delivered precisely controlled amounts of e-cigarette vapor, with or without nicotine, for 30 min, twice a day for 21 days. Compared to control mice that breathed room air, mice exposed to e-cigarette vapor had inflammation of their lung tissue and reduced lung function, confirming the dangers of vaping. These effects were observed whether or not nicotine was added to the vapor, pointing to the inherently harmful nature of the chemicals found in e-cigarette vapor.

There was also an increase in the levels of the ACE-2 receptor in the lungs of vapor-exposed mice, male and female. Though this was not tested in the current study, higher levels of ACE-2 receptor could make it easier for the virus to enter the airways, increasing susceptibility to infection.

Interestingly, the presence of nicotine in the vapor further enhanced the increase in ACE-2 specifically in male mice.

The researchers are the first to demonstrate this potential sex-difference in the effect of vaping and nicotine exposure on ACE-2 levels in vivo. Though further research is needed to understand the complexity of risk factors for COVID-19, this result sheds light on important physiological differences that make one sex potentially more vulnerable.

"Our findings provide rationale for looking at the effect of vaping on ACE-2 levels in the lungs of humans," says Dr. Sharma. "If a similar induction of ACE-2 is seen, it provides further evidence for vaping being a risk factor for COVID-19 and can help us understand how to prevent and mitigate infection in this population."

More information: Vegi Naidu et al, Sex differences in the induction of angiotensin converting enzyme 2 (ACE-2) in mouse lungs after e-cigarette vapor exposure and its relevance to COVID-19, *Journal of Investigative Medicine* (2021). DOI: 10.1136/jim-2020-001768

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