Vitamin E acetate in bronchoalveolar-lavage fluid associated with electronic cigarette- or vaping product-associated lung injury

The USA is experiencing an ongoing outbreak of electronic cigarette (e-cigarette) or vaping-product-associated lung injury (EVALI). To date, it has affected more than 2 400 hospitalised patients. This disease has mainly affected young patients below the age of 40, with almost half of them requiring intensive care facilities.

Investigations into the causes of EVALI found that most of the patients had used tetrahydrocannabinol (THC)-containing e-cigarette products. Subsequent evaluation of the product fluids tested positive for vitamin E acetate. Vitamin E acetate is used in illicit THC-containing products to cut the amount of THC oil used.

The plausibility of vitamin E acetate as a culprit in EVALI has been linked to it causing surfactant dysfunction and the production of ketene on heating, which is a potential direct lung irritant. Secondly, the addition of vitamin E acetate to vaping fluid coincided with the start of the outbreak.

This study evaluated the presence of vitamin E acetate and other priority toxicants in the broncoalevolar-lavage (BAL) fluid of EVALI cases. The fluid was collected from 51 EVALI patients meeting confirmed case definitions as well as probable case definitions, based on the use of e-cigarettes in the 90 days prior to symptom onset, radiological features, exclusion of infectious causes or infection not deemed the major underlying cause and no evidence of an alternative plausible diagnosis.

BAL fluid from healthy non-smokers, exclusive nicotine e-cigarette or exclusive cigarette smokers was used as a health comparator group. Interestingly, urine THC biomarkers were positive in 25.6% of healthy participants but highest among those reporting exclusive smoking. Vitamin E as well as the other priority toxicants, namely plant oils, medium chain triglyceride oil, coconut oil, petroleum distillates and diluent terpenes were not found in the comparator group participants.

Detectable THC or its metabolites in the BAL fluid or reporting vaping of THC products within 90 days prior to onset of disease was noted in 94% of subjects. Vitamin E acetate was also found in 94% (n=48/51) of the EVALI patients. Coconut oil was found in one patient, and limonene (a diluent terpene) in one other. All three of the patients found to have no detectable vitamin E acetate in their BAL fluid were classified as probable cases, with coinciding diagnoses of unintentional multidrug overdose, coccidioidomycosis and methicillin-resistant *Staphylococcus aureus* pneumonia. This could reasonably explain the lung injury, and therefore they may not have been true EVALI cases.

Vitamin E acetate detected in the BAL fluid of EVALI patients provides evidence that e-cigarettes can deliver vitamin E acetate to the presumed site of injury in the lung. Widespread use of THC products in the USA, and the increased vitamin E acetate concentration found in products that came to the (illicit) market matching the timing of the outbreak, indicate that vitamin E acetate might be a causative agent in EVALI.

Additional studies are needed to examine the effects of inhaling vitamin E acetate in isolation, as well as its aerosol constituents from heating it.

There is yet to be a case reported outside of the USA, and this raises the question whether legalisation of e-cigarettes/cannabinoid products and/or their illicit use has contributed to the outbreak of EVALI. We need to be aware of the potential dangers of e-cigarette use, and the danger of not regulating their constituents.

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Afr J Thoracic Crit Care Med 2020;26(1):20. https://doi.org/10.7196/AJTCCM.2020.v26i1.058

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