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Electronic cigarette exposure triggers neutrophil inflammatory responses

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Abstract

Background: The use of electronic cigarettes (e-cigs) is increasing and there is widespread perception that e-cigs are safe. E-cigs contain harmful chemicals; more research is needed to evaluate the safety of e-cig use. Our aim was to investigate the effects of e-cigs on the inflammatory response of human neutrophils.

Methods: Neutrophils were exposed to e-cig vapour extract (ECVE) and the expression of CD11b and CD66b was measured by flow cytometry and MMP-9 and CXCL8 by ELISA. We also measured the activity of neutrophil elastase (NE) and MMP-9, along with the activation of inflammatory signalling pathways. Finally we analysed the biochemical composition of ECVE by ultra-high performance liquid chromatography mass spectrometry.

Results: ECVE caused an increase in the expression of CD11b and CD66b, and increased the release of MMP-9 and CXCL8. Furthermore, there was an increase in NE and MMP-9 activity and an increase in p38 MAPK activation. We also identified several harmful chemicals in ECVE, including known carcinogens.

Conclusions: ECVE causes a pro-inflammatory response from human neutrophils. This raises concerns over the safety of e-cig use.

Keywords: Electronic cigarettes, COPD, Inflammation, Smoking, Neutrophils, MMP-9

Background

There are an estimated 13 million users of electronic cigarettes (e-cigs) worldwide [1]. E-cigs are used to help reduce or stop tobacco smoking [2]. However, it has been shown that toxic chemicals are present in e-cig vapour, such as formaldehyde and acrolein [3–5], casting doubt on the safety of using e-cigs.

Cigarette smoke extract increases the secretion of pro-inflammatory mediators from a range of different cell types including epithelial cells, macrophages and neutrophils [6–8]. Similarly, e-cig vapour exposure increases the release of inflammatory mediators from keratinocyte and alveolar epithelial cell lines [9]. Furthermore, e-liquid increases interleukin-6 secretion from bronchial epithelial cells [10]. This raises concerns over the potential of e-cigs to promote pulmonary inflammation in a similar manner to tobacco smoking.

Neutrophil numbers are increased in the lungs of chronic obstructive pulmonary disease (COPD) patients and increased numbers positively correlate with disease severity [11, 12]. Chemokine C-X-C motif ligand 8 (CXCL8) is a key neutrophil chemoattractant [13] and the levels of CXCL8 are increased in the lungs of COPD patients [14]. Cigarette smoke exposed neutrophils secrete CXCL8, which may lead to increased neutrophil recruitment to the lungs.

Neutrophils are involved in many aspects of COPD pathophysiology. For example, neutrophils release proteases such as neutrophil elastase (NE) and matrix metalloproteinase-9 (MMP-9) which cause tissue destruction resulting in emphysema [15]. Cigarette smoke stimulates NE and MMP-9 release from neutrophils [8, 16]. The levels of NE and MMP-9 are increased in the airways of COPD patients and the levels positively correlate with disease severity [17–19]. Moreover, COPD neutrophils demonstrate a higher level of activation compared to controls {Wright, 2016 #132}.

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