



# Measurement of cardiovascular and pulmonary function endpoints and other physiological effects following partial or complete substitution of cigarettes with electronic cigarettes in adult smokers

Carl D. D'Ruiz<sup>a,\*</sup>, Grant O'Connell<sup>b,\*\*</sup>, Donald W. Graff<sup>c</sup>, X. Sherwin Yan<sup>d</sup>

<sup>a</sup> Clinical Study Consultant, Fontem Ventures, Greensboro, NC, USA

<sup>b</sup> Fontem Ventures, Scientific and Regulatory Affairs, Amsterdam, The Netherlands

<sup>c</sup> Celerion, Lincoln, NE, USA

<sup>d</sup> Lorillard Tobacco Company (formerly), Greensboro, NC, USA

## ARTICLE INFO

### Article history:

Received 23 November 2016

Received in revised form

31 March 2017

Accepted 1 May 2017

Available online 3 May 2017

### Keywords:

E-cigarette

Cardiovascular effects

Pulmonary effects

Exclusive and dual use

Harm reduction

Adverse effects

Physiological effects

## ABSTRACT

Acute changes in select physiological parameters associated with cardiovascular physiology (systolic and diastolic blood pressure (BP) and heart rate (HR)), pulmonary function (FVC, FEV1, and exhaled CO and NO) and adverse events were measured in 105 clinically confined subjects who were randomized into groups that either completely or partially switched from conventional cigarettes to e-cigarettes or completely discontinued using tobacco and nicotine products altogether. Use of the e-cigarettes for five days under the various study conditions did not lead to higher BP or HR values, negative respiratory health outcomes or serious adverse health events. Reductions in BP and HR vital signs were observed in most of the participants that either ceased tobacco and nicotine products use altogether or switched completely to using e-cigarettes. Pulmonary function tests showed small but non-statistically significant improvements in FVC and FEV1 measurements in most use groups. Statistically significant ( $p < 0.05$ ) benefits associated with smoking reduction were also noted in exhaled CO and NO levels. All study products were well tolerated. The study findings suggest that there are potential cardiovascular and pulmonary function benefits when smokers switch to using e-cigarette products. This further reinforces the potential that e-cigarettes offer smokers seeking an alternative to conventional tobacco products.

© 2017 Fontem Ventures B.V. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Electronic cigarettes (e-cigarettes) are becoming an increasingly popular alternative to conventional tobacco cigarettes among smokers worldwide. E-cigarettes are battery-powered devices that deliver vaporized nicotine, propylene glycol and/or glycerol and flavorings to users from an “e-liquid”. E-cigarettes do not contain tobacco, require combustion or generate side-stream emissions but simulate the visual, sensory, and behavioral aspects of smoking which conventional nicotine replacement therapy products do not (Nelson et al., 2015; Nides et al., 2014; Hajek et al., 2014a,b). E-cigarettes have also been found to deliver sufficient levels of

nicotine to satisfy users (Vansickel and Eissenberg, 2013; Polosa et al., 2014; McNeill et al., 2015; Goniewicz et al., 2016) and there is also evidence that e-cigarettes can encourage quitting or cigarette consumption reduction even among those not intending to quit or rejecting other support (Caponnetto et al., 2013; McRobbie et al., 2014; McNeill et al., 2015).

In recent years, a credible and accumulating body of scientific evidence has shown that e-cigarettes are less harmful than smoking conventional tobacco cigarettes and may substantially reduce harm (e.g. Royal College of Physicians, 2016; Nutt et al., 2014). Public Health England, after reviewing all currently available evidence on the subject, concluded that it was reasonable to estimate that e-cigarettes are approximately 95% less harmful than smoking cigarettes (McNeill et al., 2015). While the precise percentage is difficult to quantify, such estimates are supported by previous studies which have reported reduced or undetectable levels of select harmful or potentially harmful constituents (HPHCs) in e-cigarette aerosols when assessed following machine-based aerosol

\* Corresponding author. Clinical Study Consultant, Greensboro, NC, USA.

\*\* Corresponding author.

E-mail addresses: [carldruid@gmail.com](mailto:carldruid@gmail.com) (C.D. D'Ruiz), [grant.oconnell@fontemventures.com](mailto:grant.oconnell@fontemventures.com) (G. O'Connell), [Donald.graff@celerion.com](mailto:Donald.graff@celerion.com) (D.W. Graff), [xyan1209@gmail.com](mailto:xyan1209@gmail.com) (X.S. Yan).

generation (Goniewicz et al., 2014; Tayyarah and Long, 2014). Furthermore, studies of the major biomarkers of HPHCs or other chemicals in e-cigarette aerosols, have indicated substantially (9–450 times) lower levels compared to the smoke from cigarettes, cigars, hookah and other conventional tobacco cigarettes (Goniewicz et al., 2014; Hecht et al., 2015).

Two recent human studies measuring urine, blood and exhaled breath biomarkers of exposure to cigarette smoke toxicants and carcinogens in smokers who switched from tobacco cigarettes to e-cigarettes further support and extend the harm reduction potential of e-cigarettes by reporting that substituting tobacco cigarettes with e-cigarettes may significantly reduce exposure to HPHCs and numerous toxicants and carcinogens otherwise present in tobacco cigarettes (Goniewicz et al., 2016; O'Connell et al., 2016). More specifically, Goniewicz et al., 2016 showed that smokers who switched from tobacco cigarettes to e-cigarettes, were able to obtain similar levels of nicotine, but experienced statistically significant reductions in 12 out of 17 measured urinary biomarkers of exposure (BoE) of tobacco smoke, with mean nitrosamine levels declining in all subjects by 64% by the end of the second week of product use. Reductions in levels of exhaled toxic gases such as carbon monoxide were also noted.

Similarly, O'Connell et al., 2016, reported that smokers who completely substitute conventional tobacco cigarettes with e-cigarettes are able to obtain similar levels of nicotine but experience substantial reductions (29–95%) to numerous harmful toxicants reported to be significant contributors to smoking-associated disease risks. Together, both studies observed significant reductions in exposure to a total of 25 out of 30 tobacco-related human toxicants classified by FDA as HPHCs (USFDA, 2012) or by the International Agency for Research on Cancer (IARC) as Group 1 human carcinogens (e.g., tobacco-specific nitrosamines such as Nicotine-derived nitrosamine ketone (NNK); 1-3-butadiene; benzene; and ethylene oxide) (IARC, 2016) in smokers who either completely or partially replaced their tobacco cigarettes with e-cigarettes. The results of these studies provide biological evidence which shows that switching from tobacco cigarettes to e-cigarettes, in the short-term, provides smokers with comparable levels of nicotine, while also reducing their exposure to a variety of toxicants, otherwise present in tobacco cigarettes, which are believed to contribute to smoking related disease. This is encouraging as public health authorities such as the US Surgeon General suggest that reducing exposure to HPHCs found in tobacco smoke and discontinuing tobacco cigarette smoking can reduce the risks associated with diseases such as lung cancer, heart disease and emphysema (USDHHS, 2014).

To date, the scientific literature associated with the potential effects of e-cigarettes on cardiovascular and respiratory or lung function is growing and suggests that e-cigarettes may be less harmful than tobacco smoking. For example, a previous study comparing the immediate effects of tobacco cigarette and e-cigarette use on left ventricular (LV) myocardial function found that smoking one tobacco cigarette led to significant acute myocardial dysfunction, while the e-cigarette, which contained 1.1% nicotine, had no acute adverse effects on cardiac function (Farsalinos et al., 2014a). It was reported that smoking the tobacco cigarette led to important hemodynamic consequences, such as significant elevations in heart rate (HR), systolic and diastolic blood pressure (BP), but use of the e-cigarette only resulted in a slight increase in diastolic blood BP. Another clinical study (Yan and D'Ruiz, 2015) investigating the acute effects of e-cigarettes on BP and HR in comparison to tobacco cigarette smoking reported similar results. The study reported increases in systolic, diastolic BP and HR following acute use of both tobacco cigarettes and e-cigarettes, however, the increases associated with e-cigarette use were minimal and not clinically significant as compared to those of the

cigarette smokers.

Furthermore, Farsalinos et al., 2016 investigated changes in BP and HR in smokers who reduced or quit smoking by using e-cigarettes for a 12-month period in a randomized control trial. The study reported that smokers (with elevated BP at baseline) who reduced smoking or quit smoking by switching to e-cigarettes experienced statistically significant reductions in systolic BP after 1 year. Similar changes in BP from baseline were observed in quitters who stopped using e-cigarettes compared to quitters who still used e-cigarettes. In addition, Benowitz and Burbank, 2016 investigated the cardiovascular safety of nicotine within the context of short-term e-cigarette use and concluded that the cardiovascular risks of nicotine from e-cigarettes are low in healthy users. It was also reported that while it is possible that people with established cardiovascular disease (CVD) might incur some increased risk from e-cigarette use, the risk is much less than that of smoking. Interestingly, the investigators also noted that in contrast to cigarette smoking which results in an arterial spike of nicotine, e-cigarette use is more intermittent and results in lower and more stable nicotine levels without arterial spikes. Moreover, this effect may possibly reduce the intensity of the pharmacologic effects associated with nicotine and subsequently result in less cardiovascular stress or impact for e-cigarette users as compared to conventional tobacco smokers.

Very few investigations exist which have focused on the effects of e-cigarettes on lung function. Most of the studies and surveys conducted to-date indicate that the use of e-cigarettes leads to a near normalization in toxic-levels of exhaled carbon monoxide (Farsalinos and Polosa, 2014; Polosa, 2015) and do not appear to support negative respiratory health outcomes under acute use conditions (Flouris et al., 2013; Polosa, 2015). It has also been recently suggested by Polosa, 2015 that smokers with preexisting asthma and COPD may benefit from regular e-cigarette use. Evidence for this is based on emerging medical case reports, which showed significant improvements in quality of life and reductions in the number of pulmonary disease exacerbations in patients who quit tobacco smoking on their own by switching to e-cigarettes (Caponnetto et al., 2011) and on the findings from a large internet survey of regular e-cigarette users diagnosed with asthma or COPD which largely corroborate the medical case report findings (Farsalinos et al., 2014b). In general, the internet survey showed that improvements in the symptoms of asthma and COPD were reported by 65.4% and 75.7% of the survey respondents diagnosed with pulmonary disease, respectively. Furthermore, it was also reported that after switching, the use of pulmonary disease medications was reported to have stopped in 18.4% of the respondents with asthma and COPD. Worsening conditions after switching were only reported by 1.1% of the asthmatics and 0.8% of the COPD respondents.

Moreover, findings from the first long-term (1 year) investigation of changes in spirometric indices and respiratory symptoms in smokers who reduced or quit smoking by switching to e-cigarettes also indicate e-cigarette use may have beneficial effects in relation to respiratory outcomes (Cibella et al., 2016). The study reported that smokers who quit smoking and substantially reduced their exposure to harmful cigarette smoke toxicants by switching to e-cigarettes, experienced a steady and progressive normalization of peripheral airways function, as measured by forced expiratory flow from 25% to 75% of vital capacity, (FEF<sub>25–75%</sub>) improvements from baseline. Improvements in respiratory symptoms were also noted.

Currently, further information is needed to augment our understanding of the impacts of acute e-cigarette use on key physiological parameters associated with cardiovascular and respiratory function. This information, together with the emerging evidence that has been presented above, will provide further insight as to

Download English Version:

<https://daneshyari.com/en/article/5561331>

Download Persian Version:

<https://daneshyari.com/article/5561331>

[Daneshyari.com](https://daneshyari.com)