

Electronic Cigarettes: Impact on Lung Function and Fractional Exhaled Nitric Oxide Among Healthy Adults

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Abstract

Electronic cigarettes (e-cigarettes) are rapidly becoming an alternative form of nicotine consumption worldwide and a disruptive element in the global health diplomacy. This study aimed to investigate the impact of e-cigarettes on lung function and fractional exhaled nitric oxide (FeNO) among young healthy male adults. Sixty apparently healthy male volunteers were recruited and divided into two groups. Group 1 (e-cigarette-exposed group) consisted of 30 males who were daily e-cigarette users (age 27.07 ± 6.00 [mean \pm SD] years). Group 2 (control group) consisted of 30 males who were not e-cigarette users (age 25.90 ± 7.72 [mean \pm SD] years). Both groups were neither current nor former traditional tobacco users. Age, ethnicity, height, weight, and socioeconomic status were considered using a matched design to investigate the impact of e-cigarette use on lung function and FeNO. The lung function test parameters that were found to be significantly decreased in e-cigarette users compared to their control group were forced expiratory volume in the first second (FEV₁), forced expiratory ratio (FEV₁/FVC), forced expiratory flow—25% (FEF_{25%}), forced expiratory flow—50% (FEF_{50%}), forced expiratory flow—75% (FEF_{75%}), forced expiratory flow—25%–75% (FEF_{25%–75%}), and forced expiratory flow—75%–85% (FEF_{75%–85%}). FeNO was also decreased in e-cigarette users, but it did not reach the level of significance. The use of e-cigarettes significantly impaired various lung function parameters and the pattern of impairment exhibited a peripheral obstructive airway involvement. These findings have a general message for the global health community on the potential harm of e-cigarettes on lung function.

Keywords

e-cigarette, lung physiology, pulmonary function, FeNO

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Electronic cigarettes, also known as e-cigarettes and e-shisha, are a relatively new nicotine delivery method, which originated in China in 2003 (Henningfield & Zaatari, 2010; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, & Voudris, 2013; Xu, Guo, Liu, Liu, & Wang, 2016). Electronic Nicotine Delivery Systems (ENDS) is a broad term that encompasses any electronic device that heats a nicotine-containing solution (e-liquid) to create an aerosol. These devices aerosolize a liquid that contains various chemical elements including glycol, vegetable glycerin, propylene, ethylene glycol, polyethylene glycol mixed with variable percentages of nicotine, metabolites of nicotine, and allied impurities

(Hahn et al., 2014; Lim & Shin, 2013; Lopez et al., 2015). Despite significant apprehensions from public health authorities, e-cigarette use is more prevalent among adolescents and currently gaining more popularity (Farsalinos, Tomaselli, & Polosa, 2018; Meo & Asiri,

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2014), with mixed perceptions of harmfulness (Camenga et al., 2016). E-cigarette use is steadily spreading among the youth, especially in high-income and urban populations around the globe (Camenga et al., 2016). The e-cigarette industry is growing rapidly and may catch up with the conventional tobacco industry by the year 2023 (Besaratina & Tommasi, 2014). The current worldwide e-cigarette market is estimated to be worth about \$10B (Besaratina & Tommasi, 2014), and that number is only rising with the gain in popularity of ENDS around the world. Globally, approximately 200 e-cigarette brands and 7,700 e-cigarette flavors are currently being marketed (Allen et al., 2016).

The progressive use of e-cigarettes and other vaping products poses a growing risk to public health (Rohde et al., 2018). The rising use of e-cigarettes has been a topic of great controversy with much speculation both in the medical and public arenas over the potential risks. The possibilities of health hazards from long-term e-cigarette use cannot be ignored due to the inhalation of the various e-liquid ingredients (Rohde et al., 2018). ENDS use has been gaining more popularity in the Middle East café culture and becoming a fashionable alternative to tobacco smoking. E-cigarettes are also being used as an aid to decrease or even quit tobacco smoking, although their impact on the user's health has not been fully assessed. Research and regulatory efforts have commonly focused on the traditional cigarette-smoking industry, while little research has been conducted on e-cigarettes and their industry. Most of the studies conducted do not consider the physiological factors, which have considerable influence on the conclusions, such as age, gender, weight, height, ethnicity, and socioeconomic status. The purpose of this study was to investigate the impact of using e-cigarettes on lung function and fractional exhaled nitric oxide (FeNO) among healthy male young adults.

Methods

Study Design and Participants

This cross-sectional study was conducted in the Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia, during the period September 2016–September 2017. The study was steered in accordance with the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board, Ethics Committee, College of Medicine Research Centre, King Saud University, Riyadh, Saudi Arabia (17/0593).

After obtaining the ethical committee approval, the two coinvestigators handed out questionnaires that screened the participants from the various suburbs in the city of Riyadh. These investigators mainly focused

on cafés and university grounds and invited e-cigarette users to participate in the study. E-cigarette users were recruited based on their voluntary participation and matched according to age, gender, nationality, and relative socioeconomic status. Written consent was obtained from all the participants, and they were given the opportunity to read the research objectives and the freedom to join or withdraw from the research at any time.

Exclusion Criteria

Initially, 300 participants were interviewed and clinical history and physical examinations were conducted; 60 (30 e-cigarette users and 30 control) were selected. The exclusion criteria were well standardized. Participants with any acute or chronic respiratory diseases such as chronic bronchitis, emphysema, bronchiectasis, asthma, and cystic fibrosis were excluded. Subjects with anemia, diabetes mellitus, and malignancy, and also those who were current or former traditional cigarette smokers, shisha smokers, and users of other tobacco products were not included. Participants who had undergone a vigorous exercise forty minutes per day and five days in week or worked in an industry that generates dust or fumes were also excluded from the study (Meo, 2006; Meo, Al-Drees, Al Masri, Al Rouq, & Azeem, 2013).

After the selection process, from the original 300 participants, 30 e-cigarette users, who were using nicotine-containing e-liquid daily for at least the past 6 months and 30 male matched controls who had never tried e-cigarettes, regular cigarettes, or shisha took part in the lung function assessment and FeNO analysis.

The two groups were matched for age, height, weight, ethnicity, and socioeconomic status. The mean age of the exposed group (ENDS users) and control group (non-e-smokers) was 27.07 ± 6.00 (mean \pm SD) and 25.90 ± 7.72 years, respectively.

Spirometry

Spirometry was conducted using SPIROVIT SP-1 (Schiller, Switzerland) to assess lung function test parameters including forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), forced expiratory ratio (FEV₁/FVC), peak expiratory flow (PEF), forced expiratory flow—25% (FEF_{25%}), forced expiratory flow—50% (FEF_{50%}), forced expiratory flow—75% (FEF_{75%}), forced expiratory flow 25%–75% (FEF_{25%–75%}), and forced expiratory flow 75%–85% (FEF_{75%–85%}).

Well-defined procedures were applied in conducting the various lung function test parameters, and guidelines were followed based on the official statement of the

Table 1. Comparison of Anthropometric Parameters Between Electronic Cigarette Users and Their Matched Control Group.

Parameters	Electronic cigarette users group (n = 30)	Control group (n = 30)	Level of significance
Age (years)	27.07 ± 6.00	25.90 ± 7.72	.51
Height (cm)	174.80 ± 6.67	176.9 ± 6.65	.22
Weight (kg)	87.20 ± 23.94	90.07 ± 18.66	.60
Body mass index	28.46 ± 7.29	28.84 ± 5.97	.82

Note. Values are presented as mean ± SD.

American Thoracic Society Standardisation of Spirometry (Miller et al., 2005). All participants were instructed not to eat or drink any kind of hot or cold beverages for at least 2 hours before testing. They were also asked not to use their ENDS device at least an hour before testing. Participants were given detailed descriptions of the tests and encouraged to practice the test process before taking the pulmonary function test. The tests were performed in the standing position with a nose clip at the fixed time of the day (2:00–4:00 pm) to minimize the diurnal variations. Separate new sterile mouthpieces for each individual were used to prevent any cross infections.

Fractional Exhaled Nitric Oxide

FeNO was recorded using Niox Mino, Aerocrine (Solna, Sweden). Measurement of FeNO in exhaled breath is now established as a simple, safe, noninvasive, and reliable marker for the assessment of respiratory inflammation severity. The FeNO device did not require recalibration during the test procedure as it was precalibrated from the manufacturer. Tests were conducted at a fixed time of day to lessen the diurnal variation (Stark et al., 2007). The well-defined procedures in executing FeNO test for the present study were based on the official statement of the American Thoracic Society/European Respiratory Society standardization procedure for FeNO measurements (Dweik et al., 2011).

Statistical Analysis

The results were analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0 for windows. Student's *t*-test was applied to test the difference of the means between the two quantitative variables. The level of significance was assumed at $p < .05$.

Results

The anthropometric parameters including age, height, weight, and body mass index (BMI) of ENDS users along with those of the matched control group are

displayed in Table 1. The mean age of the ENDS group was 27.07 ± 6.00 years and that of control was 25.90 ± 7.72 years; height of ENDS users was 174.8 ± 6.67 cm and that of control was 176.90 ± 6.65 cm; the weight of ENDS group was 87.20 ± 23.94 kg versus 90.07 ± 18.66 kg of control, and BMI of ENDS group was 28.46 ± 7.29 versus 28.84 ± 5.97 of control. The mean duration of using ENDS was 15.43 ± 2.70 months (mean ± SD). All the anthropometric parameters between the groups were nonsignificant.

The pulmonary function test parameters of ENDS users compared to their matched control are reported in Table 2. There was a significant decline in the lung function test parameters FEV₁; FEV₁/FVC ratio; FEF_{25%}; FEF_{50%}; FEF_{75%}; FEF_{25%–75%}; FEF_{75%–85%} among the ENDS group versus control. However, there was no significant difference in FVC and PEF between the two groups (Table 2, Figure 1). This study also identified that FeNO was decreased in ENDS users compared to their control participants, but it did not achieve the level of significance (Table 2, Figure 1).

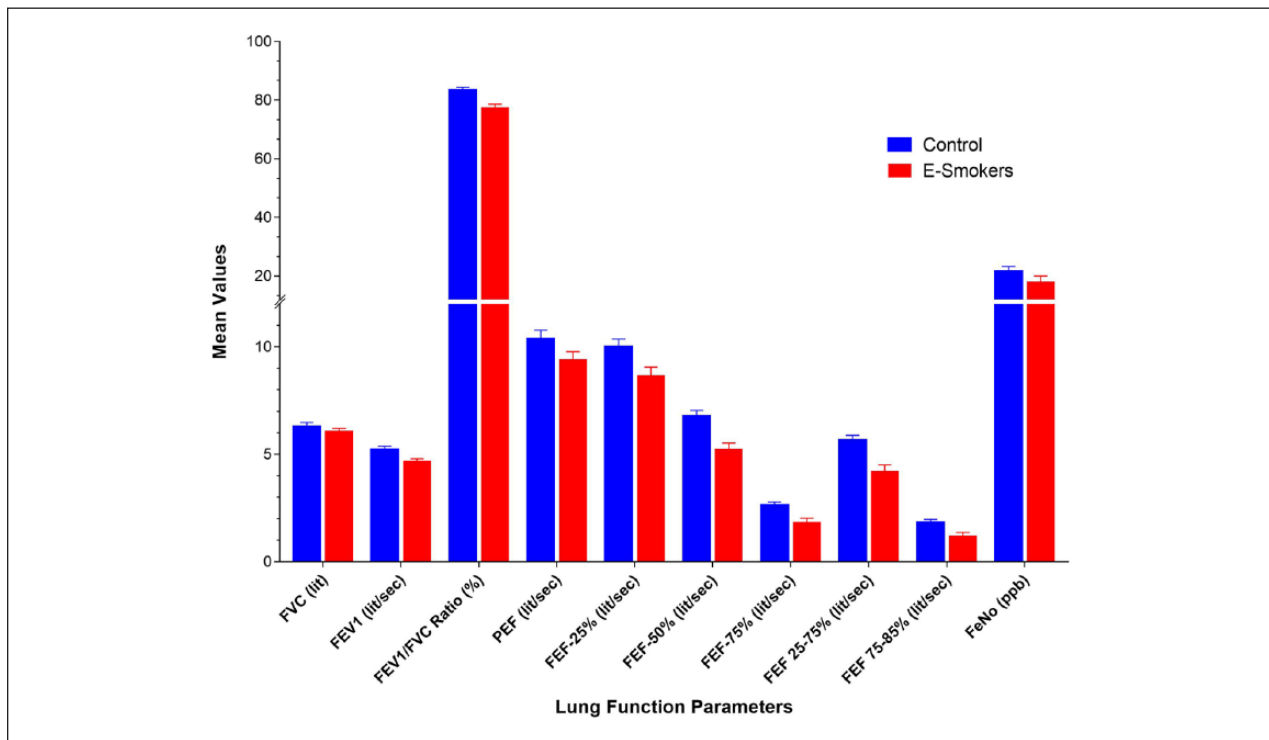
Discussion

This study is considered to be the first of its kind that presents an assessment of the impact of at least 6-month use of e-cigarettes on lung function and FeNO. In this study, a significant impairment in lung function parameters was observed in the ENDS group compared to control (Table 2, Figure 1). The reduced pattern of lung function test parameters exhibits peripheral obstructive airway impairment. In agreement with the findings presented in this study, Flouris et al. (2013) conducted a study on the acute effect of active and passive e-cigarette smoking on lung function. They concluded that short-term use of e-cigarettes generates smaller changes in lung function. Polosa (2015) monitored the lung function in a group of smokers who had quit tobacco smoking and after 3 months switched to e-cigarette smoking. The author reported a decrease in FEF_{25%} and FEF_{75%} and identified significant early signs of peripheral airway obstruction. Similarly, the present study findings are in accordance with those reported by Polosa (2015). The

Table 2. Comparison of Various Lung Function Parameters and FeNO Between Electronic Cigarette Users and Their Matched Control Group.

Parameters	Electronic cigarette users group (n = 30)	Control group (n = 30)	Level of significance
FVC (L)	6.06 ± 0.80	6.29 ± 1.08	.364
FEV ₁ (L/s)	4.68 ± 0.67	5.22 ± 0.83	.007
FEV ₁ /FVC ratio (%)	77.36 ± 7.19	83.39 ± 5.59	.001
PEF (L/s)	9.39 ± 2.07	10.39 ± 2.15	.071
FEF _{25%} (L/s)	8.66 ± 2.15	10.01 ± 1.84	.011
FEF _{50%} (L/s)	5.23 ± 1.60	6.78 ± 1.46	.001
FEF _{75%} (L/s)	1.82 ± 1.09	2.63 ± 0.84	.002
FEF _{25%-75%} (L/s)	4.21 ± 1.61	5.65 ± 1.27	.001
FEF _{75%-85%} (L/s)	1.20 ± 0.88	1.83 ± 0.70	.003
FeNO (ppb)	18 ± 11.05	21.67 ± 8.58	.156

Note. Vales are presented in mean ± SD. FeNO = fractional exhaled nitric oxide.

**Figure 1.** Comparison of lung function parameters and fractional exhaled nitric oxide (FeNO) between electronic cigarette users and their matched control participants.

present study identified that pulmonary function test parameters were decreased in ENDS users compared to their matched control and the pattern of lung function impairment showed peripheral obstructive airway involvement.

Contrary to the findings presented in this study, Vardavas et al. (2012) determined the effect of using e-cigarette for a period of 5 minutes on lung function parameters. They did not report reduction in lung function parameters FVC, FEV₁, and FEV₁/FVC ratio.

However, in the present study, a significant reduction in lung function parameters including FEV₁, FEV₁/FVC ratio, FEF_{50%}, FEF_{75%}, FEF_{25%-75%}, and FEF_{75%-85%} was identified. The reason for inconsistent findings presented by Vardavas et al. (2012) is the use of e-cigarette for a period of 5 minutes.

The literature has presented evidence that e-cigarette users demonstrate an increase in airway resistance (Marini, Buonanno, Stabile, & Ficco, 2014; Palamidis et al., 2014). Some studies reported a decrease in specific airway

conductance and an increase in impedance and overall peripheral airway resistance (Marini et al., 2014). Gennimata et al. (2012) investigated the acute effect of e-cigarette smoking on lung function. The authors recruited 24 smokers and identified that using an e-cigarette for 10 minutes caused a significant increase in airway resistance.

Gennimata et al. (2012) reported that 10 minutes of e-cigarette use caused prompt airway obstruction. In another study, it was also documented that short-term and passive usage of one e-cigarette resulted in short-term lung obstruction (Chorti et al., 2012). Similarly, in the present study, a significant impairment in lung function parameters was identified and the pattern was peripheral obstructive airway lung impairment. The pathophysiological phenomenon could be that the increase in peripheral flow resistance is allied to the acute narrowing of the diameter of the peripheral airways, which could be due to confined mucosal edema, smooth muscle contraction, and bronchospasm or secretions.

In the present study, it was observed that FeNO level was decreased in the participants who used e-cigarettes, but the decline did not achieve significant levels when compared to the control. Vardavas et al. (2012) reported that using an e-cigarette for 5 minutes led to an immediate decrease in FeNO concentrations and increased the lung flow resistance within the experimental group. They reported immediate adverse physiological effects after short-term use similar to the effects seen with tobacco smoking. The authors also concluded that the use of an e-cigarette for 5 minutes causes an increase in impedance, peripheral airway flow resistance, and oxidative stress. The authors examined the short-term consequences of e-cigarette use on FeNO but did not take into account the long-term impact of at least 6-month use of e-cigarettes.

Marini et al. (2014) conducted a study on 25 participants and compared the short-term pulmonary effects between the use of e-cigarette and conventional tobacco cigarette through measuring the FeNO. The FeNO measured data shows that using electronic cigarettes both with and without nicotine causes reduction of FeNO in smokers. Their findings confirm that whatever the e-cigarette used and the nicotine content and the dose received smoking decreases FeNO. Another study also identified an immediate reduction in FeNO and increase in the release of the inflammatory signaling molecules upon inhalation (Schober et al., 2014).

Limitations

This study's limitations include the use of a small sample size, the male gender only, and 6 months duration of exposure to e-cigarette smoking. Moreover, it was not possible to calculate the dose response of e-cigarettes as there is no set "dose" for ENDS use and the dose inhaled varies in frequency, size, and depth of inhalation.

Conclusions

This article is the first study to report the relationships between the use of e-cigarettes and lung function and FeNO among healthy adults. The findings have a general message to the global health community. The use of e-cigarettes significantly impairs lung function, and the pattern of lung function impairment exhibited peripheral obstructive airway involvement. The present study, although modest in its size, scope, and conclusions, offers vital findings on the potential harm of e-cigarettes. Obviously, larger sample size studies are needed to examine the long-term use of e-cigarettes. Considering the current study findings, it is important to report that the use of the e-cigarettes does have adverse effects on an individual's lungs. However, in a pool of 300 participants, only 30 e-smokers were identified who had never smoked tobacco and directly used only e-cigarettes. Thus, it may be appropriate to monitor the growth of e-smoking among non-smokers, particularly given that this study provides more evidence of potential harm. It is essential to highlight the need to implement the policies such as higher taxes and workplace smoking bans, which would work well to decrease all kinds of smoking including e-cigarette use and its distribution across the globe.

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Declaration of Conflicting Interests

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