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Research Article

Conventional cigarette and electronic nicotine delivery systems exacerbate high-fat diet-induced inflammation and oxidative stress

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Abstract

Objectives: There is a community habit that conventional cigarette or electronic nicotine delivery systems (ENDS) are used after meals. Also, they tend to consume a high-fat diet (HFD). The effects of this behavior on health remain unclear. Our study focuses on oxidative stress and inflammation in HFD-fed rats model exposed to conventional cigarettes and ENDS.

Methods: Twenty-four male rats were equitably separated into the following four different groups: (1) NDC: normal diet and fresh air control, (2) HFDC: HFD and fresh air control, (3) HC: HFD+conventional cigarette, and (4) HE: HFD+ENDS. Conventional cigarettes and ENDS were exposed to the same nicotine dose of 12 mg/mL/group. Oxidative stress markers comprising malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), as well as inflammation markers comprising interleukin (IL)-1β, IL-6, tumor necrosis factor-α, and high sensitivity C-reactive protein were assayed after 6 weeks of treatment. Statistical analysis of one-way ANOVA with post hoc test was performed.

Results: HFD independently increased MDA and IL-6; simultaneously, it decreased SOD, CAT, and GSH. Both conventional cigarettes and ENDS exposure significantly increased entire inflammation markers and MDA, simultaneously decreasing SOD, CAT, and GSH compared to the normal and HFD control rats. Furthermore, a significant difference was observed between conventional cigarettes and ENDS-exposed groups.

Conclusion: This study revealed that ENDS is less harmful than conventional cigarettes. Nevertheless, both exposures significantly exacerbated oxidative stress and inflammation in HFD-fed rats, potentially leading to related diseases.

Keywords: Cigarette, electronic nicotine delivery systems, inflammation, oxidative stress, rats

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Electronic cigarettes or electronic nicotine delivery systems (ENDS) have been used extensively in smoking cessation programs, but also in people who have never smoked [1]. The ENDS trend is increasing in adolescents and young adults [2]. In Indonesia, which has the worst tobacco control regulations in Southeast Asian countries, ENDS is freely sold, cheap, and easy to find in retail vape stores, online stores, and social media with various concentrations of nicotine [3]. Although some online stores require age verification, this can still be circumvented. Accordingly, a previous study reported that underage and young adults could access ENDS from online and retail stores [4].

There is a common misconception about the perception that ENDS is considered safer than conventional cigarettes because the aerosol produced is less harmful, less addictive, and more popular nowadays [5]. In fact, ENDS liquid contains harmful chemicals such as propylene glycol (PG) and vegetable glycerin (VG) as the main constituents and nicotine and flavorings as additional constituents [6].

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On the other hand, obesity prevalence continues to increase yearly; however, an increase in prevalence is more common in rural communities than in urban ones [7]. This result is caused by a lack of knowledge and behavior toward the need for balanced nutrition, which is more common in rural communities associated with low education levels [8]. Eating behavior appears to play an important role in obesity as well. A systematic review concluded that adolescents in Indonesia had not received adequate nutrition; they tended to consume excessive amounts of high-sodium and high-fat diets (HFD) [9]. It is well known that HFD contributes to obesity, cardiovascular, and cerebrovascular diseases involving oxidative stress and chronic inflammation [10].

In community habits, especially in Indonesia, conventional cigarettes or ENDS are usually used after meals as a recreational behavior. This will increase the possibility of adverse effects due to HFD consumption. However, no studies evaluate the effect of this behavior. We hypothesized that exposure to conventional cigarettes and ENDS would exacerbate the adverse effects of HFD consumption. This study focuses on the effects of exposure to conventional cigarettes and ENDS on oxidative stress and inflammation in HFD-fed rats model. Our intervention uses the inhalation route and the same nicotine dose in ENDS liquid and conventional cigarettes to adjust real-life exposure to humans.

Materials and Methods

Animals' experiment

A total of 24 4-week-old male Wistar rats weighing 155±20 g were obtained from the Integrated Research and Testing Laboratory of Universitas Gadjah Mada, Yogyakarta, Indonesia. Before starting the treatments, all rats were acclimatized for a week under controlled conditions of temperature (22±2°C), relative humidity (50±10%), and a light/dark cycle of 12-h. The rats were housed in a polypropylene cage with two rats each and given regular feed and tap water *ad libitum*. Food intake was measured every day and body weight was measured every 7th day of the week. After acclimatization, the rats were randomized into four groups (six each) for 6 weeks of treatment, as follows:

1. NDC: normal diet and fresh air control
2. HFDC: HFD and fresh air control
3. HC: HFD+conventional cigarette
4. HE: HFD+ENDS.

All study protocols and procedures complied with national and international guidelines and were approved by The Ethics Committee of the Faculty of Medicine of Universitas Islam Indonesia, Yogyakarta, Indonesia (#7/Ka.Kom.Et/70/KE/III/2021).

HFD administration

Palm oil (Indofood, Jakarta, Indonesia) and quail eggs were obtained from a local market in Yogyakarta, Indonesia. HFD was prepared with a mixture of oxidized palm oil and quail egg yolk. It was administered 2 mL/rat orally, as described in a previous study [11].

Conventional cigarette, ENDS, and refill liquid

Commercially available conventional cigarettes (Gudang Garam, East Java, Indonesia), ENDS model mod (Dovpo, Guangdong, China), and refill liquid with oat milk blueberry flavored (Pahlawan Lima Tujuh, Jakarta, Indonesia) were used in this study. The detailed information and specification were described in a previous study [11].

Protocol of conventional cigarette and ENDS exposures

Conventional cigarettes and ENDS exposures were conducted using an exposure instrument that adjusted to real-life exposure to humans straight after HFD administration. A group of treated rats was exposed to 25 cycles per day, of which one cycle equals a 5-second puff, 30-second interval, and 30-second exhaust. They were administered the same dose of 12 mg/mL of nicotine. The instrument exposure and method in detail have been previously reported [11].

Blood collecting

After 12 h of the last exposure, the rats were fasted for another 12 h and continued to collect blood from the heart under general anesthesia using Zoletil® 50 (Virbac SA, Carros, France). The blood was collected and put in ethylenediaminetetraacetic acid contained tube, then centrifuged at 1073× g for 10 min at 4°C to obtain plasma for oxidative stress and inflammatory marker assays. The collected plasma samples were stored at −25°C and then assayed within the next day to less than 7 days.

Oxidative stress marker assay

Malondialdehyde (MDA) (Catalog #E-BC-K025-S) was assayed using commercially available reagent kits provided by Elabscience (Hubei, China) based on its reaction with thiobarbituric acid-reactive substances to produce the pink chromogen. It was then determined with a spectrophotometer at 532 nm. Superoxide dismutase (SOD) (Catalog #K335-100), catalase (CAT) (Catalog #K773-100), and glutathione (GSH) (Catalog #K261-100) activity were assayed by colorimetric method at 450, 570, and 340 nm, respectively, using a microplate reader and reagent kits provided by BioVision (CA, USA). Each oxidative stress marker assays standard protocol follows the respective manufacturer's guidelines.

Inflammatory marker assay

The expression of interleukin (IL)-1β (Catalog #E-EL-R0012), IL-6 (Catalog #E-EL-R0015), tumor necrosis factor (TNF)-α (Catalog #E-EL-R2856), and high sensitivity C-reactive protein (hs-CRP) (Catalog #E-EL-R3002) was assayed by micro-ELISA plate using sandwich-ELISA principle. These assays were used commercially available reagent kits and standard protocols provided by Elabscience (Hubei, China).

Table 1. Body weight and food intake in control and treated rats

	NDC	HFDC	HC	HE
Baseline body weight (g)	146.33±5.47	155.83±4.92	147.50±7.77	149.50±9.59
Final body weight (g)	271.83±14.72	268.33±29.29	256.00±12.13	256.17±14.30
Baseline food intake (g/day)	13.88±0.19	13.67±0.52	13.93±0.08	13.88±0.17
Final food intake (g/day)	18.59±0.09	18.27±0.88	16.11±1.02[a]	16.67±1.42[a]

[a]: Statistically significant ($p<0.05$) compared to the NDC group using the Mann–Whitney U test. Values were presented as the mean±standard deviation (n=6). NDC: normal diet control; HFDC: high-fat diet control; HC: HFD+conventional cigarette; HE: HFD+ENDS

Statistical analysis

Data analyses were performed using SPSS version 25 software (IBM, IL, USA). Shapiro–Wilk test was performed for the normality test. Values were presented as the mean±standard deviation (n=6). Differences between groups were made using one-way ANOVA with Tukey's post hoc test or Kruskal–Wallis followed by Mann–Whitney U as a post hoc test for nonparametric data. Pearson correlation was also performed to analyze the general correlation between oxidative stress and inflammatory markers. A p-value less than 0.05 was considered statistically significant.

Results

Effect of conventional cigarette and ENDS exposures on body weight and food intake

There was no significant difference between the groups in the initial measurement. However, the rats exposed to conventional cigarettes and ENDS recorded a significant reduction in final food intake compared to the control group (Table 1).

Effect of conventional cigarettes and ENDS on oxidative stress markers

The oxidative stress of rats was assessed by measuring MDA, SOD, CAT, and GSH in plasma. MDA is a reactive compound of lipid peroxidation due to oxygen free radicals' reactions. As presented in Figure 1a, the administration of HFD demonstrated significantly increased MDA levels compared to the control rats. Moreover, this MDA increase was exacerbated with conventional cigarettes, followed by ENDS compared to HFD-only-administered rats. Figure 1b-d depicts the activity of antioxidant enzymes against oxidative stress. A significant decrease in SOD and CAT activities was demonstrated in the HFD-administered group compared to the control group. Conventional cigarettes and ENDS exposures decreased SOD, CAT, and GSH activities more than rats administered HFD. In addition, a significant harmful effect on exacerbating oxidative stress markers was documented in the group exposed to conventional cigarettes than ENDS.

Effect of conventional cigarettes and ENDS on inflammatory markers

The effect of conventional cigarettes and ENDS on inflammatory markers was assessed by determining IL-1β, IL-6, TNF-α, and hs-CRP expressions, as presented in Figure 2. Administration of HFD for 6 weeks resulted in a significant increase only in IL-6 compared to the control group of rats. However, conventional cigarettes and ENDS increased all assessed inflammatory markers in exposed rats compared to the HFD-only-administered rats. Moreover, conventional cigarettes also demonstrated a greater effect in exacerbating inflammatory markers than ENDS.

Correlation between oxidative stress markers and inflammatory markers

The general correlation between oxidative stress and inflammation was analyzed as presented in Table 2. There was a significantly strong positive correlation between MDA levels and all inflammatory markers. Further, significant strong negative correlations were identified between antioxidant enzymes and all inflammatory markers.

Discussion

The major finding of this *in vivo* study was that HFD administration caused systemic oxidative stress through lipid peroxidation and, to some extent, this process also induced inflammation. Further, the inhalation route of conventional cigarettes and ENDS exposure exacerbate those negative effects. To the best of our knowledge, this is the first study revealing oxidative stress and inflammation following conventional cigarettes and ENDS using an exposure instrument adjusted to real-life exposure to humans.

As well as conventional cigarettes, ENDS liquid contains nicotine in addition to VG and PG constituents. Moreover, in the heating process of ENDS, during the heat-not-burn state able to reach a high temperature (>200°C) and then produce toxic aldehydes such as acetaldehyde, formaldehyde, and acrolein [12, 13]. This process may differ from other studies that administered nicotine through the parenteral route.

In the present study, the food intake of both exposed groups was significantly less than the control group. In turn, it resulted in a lighter mean weight in the exposed group, although the results were not statistically significant compared between groups. The effects of exposure to conventional cigarettes and ENDS on body weight were in accordance with a previous study on mice [14]. Meanwhile, in supporting our finding, a

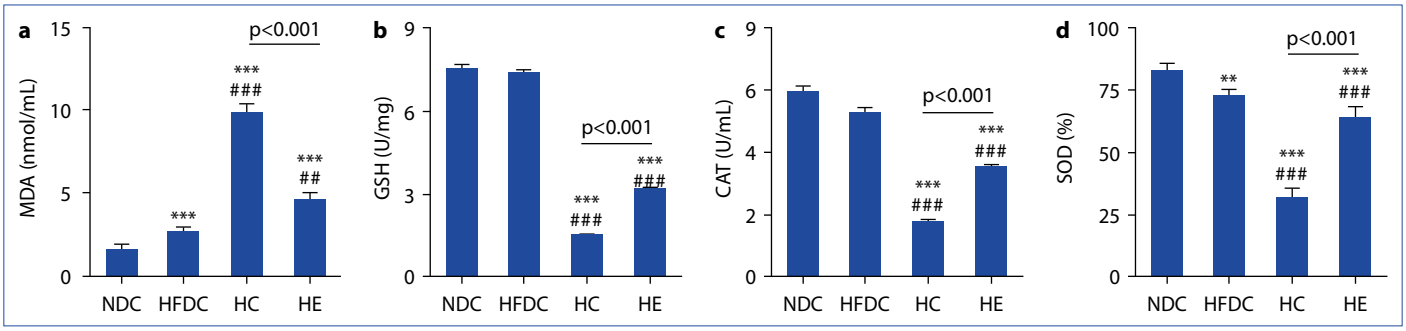

Figure 1. (a) MDA level and (b) SOD, (c) CAT, and (d) GSH activities after conventional cigarette and ENDS exposures. Values were presented as the mean±standard deviation (n=6).

**: p<0.01; ***: p<0.001 versus NDC group. ##: p<0.01; ###: p<0.001 versus HFDC group. NDC: Normal diet control; HFDC: High-fat diet control; HC: HFD+conventional cigarette; HE: HFD+ENDS; MDA: Malondialdehyde; GSH: Glutathione; CAT: Catalase; SOD: Superoxide dismutase.

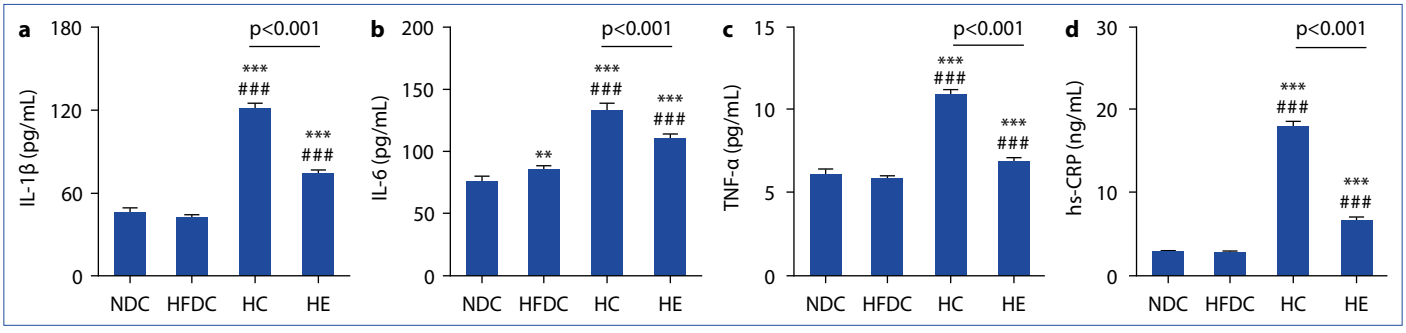

Figure 2. (a) IL-1β, (b) IL-6, (c) TNF-α, and (d) hs-CRP expressions after conventional cigarette and ENDS exposures.

Values were presented as the mean±standard deviation (n=6). **: p<0.01; ***: p<0.001 versus NDC group. ###: p<0.001 versus HFDC group. NDC: Normal diet control; HFDC: High-fat diet control; HC: HFD+conventional cigarette; HE: HFD+ENDS; IL-1β: Interleukin-1β; IL-6: Interleukin-6; TNF-α: Tumor necrosis factor-α; hs-CRP: High sensitivity C-reactive protein.

previous study among adolescents reported that cigarettes and BMI had a negative relationship, in which moderate and heavy smokers had a relatively low BMI compared to light and non-smokers [15].

Oxidative stress evaluation revealed that the HFD administration led to increased MDA levels and decreased SOD and CAT activities. This finding is consistent with a previous study [16]. The increase in oxidative stress is likely associated with decreased antioxidant enzyme activities. Exposure to conventional cigarettes and ENDS demonstrated an exacerbated effect of oxidative stress, with lower SOD, CAT, and GSH activities and higher MDA levels than in HFD-only groups.

Conventional cigarettes caused significantly lower antioxidant enzyme activity and higher lipid peroxidation than ENDS. This finding is consistent with a recent study in which ENDS causes a milder dysregulation of oxidative stress in kidney tissue than conventional cigarettes [17]. Another study by Sanders et al. [18] reported that exposure to conventional cigarettes causes lung injury mediated by receptors for advanced glycation end products, thereby triggering oxidative stress and nuclear factor erythroid 2-related factor 2 (Nrf2) compensation, although this compensation is inadequate. Thus, this condition led to the activation of alveolar macrophages and increased susceptibility to emphysema. In supporting available evidence, our finding indicates that the harmful effects caused by conventional cigarettes are greater than ENDS, even though they are in the same nicotine concentration.

The ENDS blueberry flavored oat milk refill liquid used in our study potentially has a role in causing oxidative stress. This is supported by Muthumalage et al. [19], who revealed that flavors in the refill liquid produced significant levels of H_2O_2 equivalents, contributing to the increase in reactive oxygen species (ROS) upon acute ENDS exposure. Further, these flavorings also induce a cytotoxic response on cell viability and an increase in IL-8, and combining several flavors will increase the harmful effect.

Table 2. Pearson correlations between oxidative stress and inflammatory markers after conventional cigarette and ENDS exposures

	IL-1β	IL-6	TNF-α	hs-CRP
MDA	0.971[b]	0.946[b]	0.961[b]	0.985[b]
SOD	−0.947[b]	−0.943[b]	−0.950[b]	−0.968[b]
CAT	−0.962[b]	−0.980[b]	−0.903[b]	−0.937[b]
GSH	−0.945[b]	−0.967[b]	−0.847[b]	−0.884[b]

Results were presented as Pearson correlations. [b]: Statistically significant (p<0.001). ENDS: Electronic nicotine delivery systems; IL-1β: Interleukin-1β; IL-6: Interleukin-6; TNF-α: Tumor necrosis factor-α; hs-CRP: High sensitivity C-reactive protein; MDA: Malondialdehyde; SOD: Superoxide dismutase; CAT: Catalase; GSH: Glutathione

The current study demonstrated that conventional cigarette and ENDS exposures enhance increases in IL-1β, IL-6, TNF-α, and hs-CRP expressions than in HFD-only-administered. However, a previous study suggested that exposure to conventional cigarettes for 4 weeks increased IL-1β and IL-6, while ENDS did not [20]. Contrary to our results that those pro-inflammatory cytokines increased, it might be due to inflammation that has previously been induced by HFD. Thus, both exposures have an exacerbating effect, with a greater impact found in conventional cigarettes than ENDS.

Cigarette smoking is well-understood and involved in inflammatory processes [21]. Furthermore, evidence regarding ENDS is also rising along with its popularity and widespread use [22]. An *in vitro* study by Gellatly et al. [23] suggested that the liquid without nicotine increased IL-6 and intracellular mucin but not the liquid with nicotine, in contrast to our study, which was exposed to 12 mg/mL nicotine of ENDS liquid. In agreement with our findings, another study on human alveolar macrophages indicated ENDS with nicotine increased IL-6, C-X-C motif chemokine ligand 8, monocyte chemoattractant protein-1, and matrix metalloproteinase-9 expressions compared to controls [24].

The hs-CRP is an inflammatory marker predicting cardiovascular disease [25]. Thus, increased hs-CRP expression in both exposed groups indicated that conventional cigarettes and ENDS are potentially associated with cardiovascular disease. A review by the American Heart Association summarized that ENDS could increase blood pressure and heart rate, cause endothelial cell dysfunction, and induce oxidative stress [26]. Similar results to our study were also reported that exposure to conventional cigarettes and ENDS with and without nicotine for 18 weeks significantly increased hs-CRP and TNF-α expressions [27]. Another study among Korean populations also supports this finding, increased expression of hs-CRP experienced by ENDS users similar to conventional cigarette users [28]. The cardiovascular effects of ENDS might be associated with the chemicals in liquids, such as nicotine, PG, VG, and flavors, as demonstrated previously by Carll et al. [29].

ROS excess could induce transcription factors and pro-inflammatory genes, which in turn, induce inflammation. On the other hand, inflammation also increases the generation of ROS by inflammatory cells [30]. In concordance, positive correlations between MDA and analyzed inflammatory markers were demonstrated in our study. Furthermore, simultaneously, the antioxidant enzymes decreased significantly.

Conclusion

This study revealed that conventional cigarettes and ENDS exposures exacerbate oxidative stress and inflammation in HFD-fed rats. Although ENDS is considered safer than conventional cigarettes, both showed harmful health effects. Potentially causes various diseases related to oxidative stress and inflammation.

Conflict of Interest: The authors declare that there is no conflict of interest.

Ethics Committee Approval: The study was approved by The Universitas Islam Indonesia Faculty of Medicine Ethics Committee (No: 7/Ka.Kom.Et/70/KE/III/2021, Date: 19/03/2021).

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References

1. McMillen R, Klein JD, Wilson K, Winickoff JP, Tanski S. E-cigarette use and future cigarette initiation among never smokers and relapse among former smokers in the path study. Public Health Rep 2019;134(5):528–36. [CrossRef]
2. Vallone DM, Cuccia AF, Briggs J, Xiao H, Schillo BA, Hair EC. Electronic cigarette and JUUL use among adolescents and young adults. JAMA Pediatr 2020;174(3):277. [CrossRef]
3. Lian TY, Dorotheo U. The tobacco control atlas: ASEAN region. 5th ed. Bangkok: Southeast Asia Tobacco Control Alliance (SEATCA); 2021. p. 124–35.
4. Gaiha SM, Lempert LK, Halpern-Felsher B. Underage youth and young adult e-cigarette use and access before and during the coronavirus disease 2019 pandemic. JAMA Netw Open 2020;3(12):e2027572. [CrossRef]
5. Jiang N, Cleland CM, Wang MP, Kwong A, Lai V, Lam TH. Perceptions and use of e-cigarettes among young adults in Hong Kong. BMC Public Health 2019;19(1):1123. [CrossRef]
6. Song MA, Reisinger SA, Freudenheim JL, Brasky TM, Mathé EA, McElroy JP, et al. Effects of electronic cigarette constituents on the human lung: A pilot clinical trial. Cancer Prev Res 2020;13(2):145–52.
7. Oddo VM, Maehara M, Rah JH. Overweight in indonesia: An observational study of trends and risk factors among adults and children. BMJ Open 2019;9(9):e031198.
8. Scalvedi ML, Gennaro L, Saba A, Rossi L. Relationship between nutrition knowledge and dietary intake: An assessment among a sample of Italian adults. Front Nutr 2021;8(September):1–13.
9. Rachmi CN, Jusril H, Ariawan I, Beal T, Sutrisna A. Eating behaviour of Indonesian adolescents: A systematic review of the literature. Public Health Nutr 2021;24(S2):s84–97.
10. Lin X, Li H. Obesity: Epidemiology, pathophysiology, and therapeutics. Front Endocrinol (Lausanne) 2021;12(September):1–9.
11. Ismail NA, Nabila T, Ramadhani AS, Ahsani DN. Electronic and conventional cigarette exposure aggravate metabolic parameters in high-fat diet-induced rats. Open Access Maced J Med Sci 2022;10(A):841–7. [CrossRef]

12. Kaisar MA, Prasad S, Liles T, Cucullo L. A decade of e-cigarettes: Limited research & unresolved safety concerns. Toxicology 2016;365:67–75. [CrossRef]
13. Ogunwale MA, Li M, Ramakrishnam Raju MV, Chen Y, Nantz MH, Conklin DJ, et al. Aldehyde detection in electronic cigarette aerosols. ACS Omega 2017;2(3):1207–14. [CrossRef]
14. Mayyas F, Aldawod H, Alzoubi KH, Khabour O, Shihadeh A, Eissenberg T. Comparison of the cardiac effects of electronic cigarette aerosol exposure with waterpipe and combustible cigarette smoke exposure in rats. Life Sci 2020;251(April):117644. [CrossRef]
15. Jacobs M. Adolescent smoking: The relationship between cigarette consumption and bmi. Addict Behav Reports 2019;9(December 2018):100153.
16. Lasker S, Rahman MM, Parvez F, Zamila M, Miah P, Nahar K, et al. High-fat diet-induced metabolic syndrome and oxidative stress in obese rats are ameliorated by yogurt supplementation. Sci Rep 2019;9(1):20026. [CrossRef]
17. Dogan K, Saygin H, Yalman Y. The effects of electronic cigarettes on oxidative stress markers in the kidney tissues of wistar albino rats. Int J Med Biochem 2022;5(2):96–100.
18. Sanders KA, Delker DA, Hueckstead T, Beck E, Wuren T, Chen Y, et al. RAGE is a critical mediator of pulmonary oxidative stress, alveolar macrophage activation and emphysema in response to cigarette smoke. Sci Rep 2019;9(1):231.
19. Muthumalage T, Prinz M, Ansah KO, Gerloff J, Sundar IK, Rahman I. Inflammatory and oxidative responses induced by exposure to commonly used e-cigarette flavoring chemicals and flavored e-liquids without nicotine. Front Physiol 2018;8(January):1–13. [CrossRef]
20. Glynos C, Bibli SI, Katsaounou P, Pavlidou A, Magkou C, Karavana V, et al. Comparison of the effects of e-cigarette vapor with cigarette smoke on lung function and inflammation in mice. Am J Physiol Cell Mol Physiol 2018;315(5):L662–72.
21. Madani A, Alack K, Richter MJ, Krüger K. Immune-regulating effects of exercise on cigarette smoke-induced inflammation. J Inflamm Res 2018;11:155–67.
22. Masso-Silva JA, Byun MK, Crotty Alexander LE. Acute and chronic effects of vaping electronic devices on lung physiology and inflammation. Curr Opin Physiol 2021;22(Table 1):100447. [CrossRef]
23. Gellatly S, Pavelka N, Crue T, Schweitzer KS, Day BJ, Min E, et al. Nicotine-free e-cigarette vapor exposure stimulates IL6 and mucin production in human primary small airway epithelial cells. J Inflamm Res 2020;13:175–85. [CrossRef]
24. Scott A, Lugg ST, Aldridge K, Lewis KE, Bowden A, Mahida RY, et al. Pro-inflammatory effects of e-cigarette vapour condensate on human alveolar macrophages. Thorax 2018;73(12):1161–9.
25. Bassuk SS, Rifai N, Ridker PM. High-sensitivity C-reactive protein: Clinical importance. Curr Probl Cardiol 2004;29(8):439–93.
26. Qasim H, Karim ZA, Rivera JO, Khasawneh FT, Alshbool FZ. Impact of electronic cigarettes on the cardiovascular system. J Am Heart Assoc 2017;6(9):e006353.
27. Lan K, Zhang G, Liu L, Guo Z, Luo X, Guan H, et al. Electronic cigarette exposure on insulin sensitivity of apoe gene knockout mice. Tob Induc Dis 2020;18(August):3–8. [CrossRef]
28. Moon J, Lee H, Kong M, Kim H, Oh Y. Association between electronic cigarette use and levels of high-sensitivity C-reactive protein and uric acid. Asia Pac J Public Health 2020;32(1):35–41.
29. Carll AP, Arab C, Salatini R, Miles MD, Nystoriak MA, Fulghum KL, et al. E-cigarettes and their lone constituents induce cardiac arrhythmia and conduction defects in mice. Nat Commun 2022;13(1):6088. [CrossRef]
30. Mittal M, Siddiqui MR, Tran K, Reddy SP, Malik AB. Reactive oxygen species in inflammation and tissue injury. Antioxid Redox Signal 2014;20(7):1126–67. [CrossRef]