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Acute effects of heated tobacco smoking: a single-center study

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Abstract

The idea of heated tobacco products (HTPs) is to deliver nicotine to the consumer by heating the tobacco rather than burning it, possibly causing less release of many harmful and potentially harmful chemical constituents, including carbon monoxide (CO). This prospective observational study targets studying the acute effects of HTPs regarding exhaled CO, serum cotinine level, and pulmonary function. A total of 91 participants were included; 46 current traditional cigarette smokers were instructed not to smoke for a minimum of 12 hours before the study (not following the smoking cessation program) and then divided into two groups. Group 1 contained 23 participants who smoked their usual cigarette brands, and Group 2 consisted of 23 participants who smoked the I-Quit-Ordinary-Smoking tobacco sticks. Group 3 is the control group, including 45 normal healthy non-smoker participants. All participants were subjected to the subsequent thorough medical history and clinical examination, followed by assessment of the following parameters before smoking as well as 5 minutes after smoking (either heated tobacco or traditional cigarettes according to their groups): oxygen saturation (SpO_2), heart rate (HR), measurement of exhaled CO, spirometry, and blood sample for serum cotinine level (which was assessed 5 minutes as well as 30 minutes after smoking). The study's findings showed that after smoking cigarettes, the amount of CO in the air was higher (mean 32.83±16.73 standard deviation) than after smoking heated tobacco, which was statistically significant. Serum cotinine levels also went up after smoking in both groups, but they were slightly higher after HTPs than after conventional cigarettes (CCs). Spirometry and SpO_2 levels went down after smoking in groups 1 and 2, while HR levels went up after smoking in both groups, with a p-value of less than 0.001. We concluded that the HTPs have acute respiratory and cardiovascular effects similar to CCs but with less exhaled CO.

Key words: heated tobacco, exhaled CO, serum cotinine, IQOS.

Introduction

Tobacco smoke arises from usual cigarettes contains several dangerous chemical components like nicotine, arsenic, benzene, carbon monoxide, heavy metals, and tobacco-derived nitrosamines. Tobacco smoking is greatly accompanied by the development of lung inflammation of the airways and lung parenchyma leading to respiratory diseases such as asthma, Chronic Obstructive Pulmonary Disease (COPD), interstitial lung disease, and lung cancer. Also, it is accompanied by oxidative stress and cardiovascular diseases like stroke and myocardial infarction [1]. The idea of heating tobacco without combustion and smoke is called “Heat-Not-Burn" tobacco. IQOS is one of the recent heat-not-burn tobacco products, first introduced in Italy and Japan. IQOS is known as a new mixed product between conventional and electronic cigarettes, and it provides another method to decrease the quantity of harmful constituents in comparison to conventional cigarettes by its new technology [2]. In conventional cigarettes, tobacco combustion leads to release nicotine with other HPHCs including CO.

On the contrary, products that do not need combustion to deliver nicotine (such as nicotine replacement therapies - NRTs, smokeless tobacco, electronic cigarettes) release less HPHCs, including CO. So, non-combustible nicotine devices are offered for reducing harm from smoking [3]. Our research intends to assess the acute effects of heated tobacco smoking regarding exhaled CO level, serum Cotinine level, and pulmonary functions.

Materials and Methods

This is a prospective observational analytical study that was carried out from November 2021 to October 2022. Ninety-one participants were included with simple randomization using a table created by a computer software program, and divided into three groups as follows, Group 1 included 23 subjects of current cigarette smokers who were instructed not to smoke for a minimum 12 hours before the study, then after assessment were allowed to smoke one cigarette of their usual brands. Group 2 included 23 subjects of current cigarette smokers who were instructed not to smoke for at least 12 hours before the study, then after assessment were allowed to smoke one IQOS tobacco stick. Group 3 as a control group included 45 normal healthy subjects with no history of any type of smoking. The study was approved by the ethics committee with IRB Code No. (MD-337-2021) in 20/2/2022. Written informed consent was obtained from all participants before enrollment in the study. The inclusion criteria were: i) both sexes, ii) above 20 years old iii) current regular traditional cigarette smokers who are defined as subjects who smoke 1 cigarette/day during the last 30 days with at least 5 pack-years. (Brinkman index BI) [4]. The exclusion criteria were: i) any subjects using IQOS or electronic cigarettes (EC), any shisha smokers, ii) any subjects with

uncontrolled comorbidities such as renal failure, or heart failure, iii) if there is any current active infectious lung disease. All participants were evaluated as regards complete medical history with special concern to personal history (demographics such as age, and sex), smoking index, exposure history (second-hand smoking), history of any chronic diseases or comorbid conditions, physical examination, SpO_2 and heart rate (HR), CO level measured by CO Check Pro device which is a handheld portable battery-operated device used for assessing the concentration of CO in the exhaled breath and calculating the percentage of % COHb in the blood, it requires a single exhaled breath into the device to display CO results in parts per million (PPM) and %COHb, and spirometry by Master Screen PFT 2012, CareFusion 234 GmbH, Germany (V-781267-057 version 03.00); During the test, the patients sat upright, and a clip was placed on their nose. They were then instructed to insert the mouthpiece, clamp it between their teeth, and close their lips tightly around it to form a proper seal. The patient was asked to breathe normally through the transducer, achieving tidal breathing, before taking in a deep, full breath and exhaling as forcefully and quickly as possible for as long as they could. Graham et al., 2019 [5]. A blood sample was taken for serum Cotinine level as a baseline value , the used kit is an Enzyme-Linked Immunosorbent Assay (ELISA). COTININE is added to the wells pre-coated with COTININE monoclonal antibody. After incubation, a biotin-conjugated anti-human COTININE antibody is added and binds to human COTININE. Then Participants of group 1 smoked their usual brand of cigarettes, while those of group 2 smoked the IQOS tobacco cigarette for up to 14 puffs (around 5–6 min). For each subject, a new tobacco cigarette was used as IQOS includes a charger, a holder, and tobacco sticks (Heets). The tobacco stick is "heated" with an electronically controlled heating blade (less than 350 ^{o} C). The participants of group 3 were controllers. After that, all participants of (groups 1 & 2) were exposed again to the above steps (including measurements of serum cotinine level 5 min and 30 min after smoking).

Statistical analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Analysis included mean, standard deviation, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. The non-parametric Mann-Whitney test was used for comparing quantitative variables. For assessing serial measurements within each patient, the non-parametric Friedman fort and Wilcoxon signed rank test were applied [6]. For comparing categorical data, a Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency was less than 5 [7]. The Spearman correlation

coefficient was used to evaluate correlations between quantitative variables [8]. P-values below 0.05 were considered statistically significant.

Results

The age range of the participants was from 21 to 71 years with a mean age of 47.54 years (± 10.89 SD), 46 males (100%), and all of them were cigarette smokers, while the age range of the control group was from 22 to 66 years with a mean age of 43.44 years (± 13.06 SD), males (91.1%) and most of them with no special habits of medical importance (94.3%), 3 of them were exposed to secondhand smoke.

A statistical significance was found in the pre-smoking measurements of spirometry between groups 1 & 2 (Table 1). The post-smoking exhaled CO (Table 1) was elevated in group 1 more than in group 2 with a statistical significance, the heart rate also increased and SpO_2 decreased in both groups post-smoking compared to the pre-smoking values but with no statistical significance.

Also, our study shows an increase in post-smoking Cotinine after 5 min and after 30 min in both groups with no statistical significance. The percentage of change % in serum cotinine level from the baseline after 5 min.(mean 22.19 ± SD 39.08) and after 30 min.(36.98 ± SD 63.84) was more in those who smoked the heated tobacco products than those who smoked the cigarette(mean 9.79 ± SD 24.75 after 5 min) (mean 8.73 ± SD 23 after 30 min) but with no statistical significance **.**

In Table 2, the measurements of spirometry decreased post-conventional cigarette smoking without statistical significance except for peak expiratory flow (PEF). The exhaled CO level increased post-conventional cigarette smoking, SpO_2 decreased, and HR increased all with a statistical significance.

Spirometry measurements decreased post-heated tobacco product smoking without statistical significance except for PEF and FEF25% which was decreased with statistical significance (Table 2) also showed that the exhaled CO level didn't increase after heated tobacco product smoking (pre-smoking mean of 10.74 ± 5.70 SD), (post smoking mean of 10.30 ± 5.23 SD) , decreasing SpO_2, and increasing HR with statistical significance.

There was a negative correlation between smoking index (pack/year) and spirometric measures but with no statistical significance except with FVC (P value 0.029) and a positive correlation with exhaled CO without statistical significance.

Discussion

The study included 46 male smokers (100 %) as all our cases were males with mean age 47.54 (±10.89 SD), and the predominance of the male sex among the participants may be

attributed to the habits and traditions of our society. This was also found by Pataka et al. [2] who evaluate 50 male non-smokers healthy and current smokers with no co-morbidity regarding the acute effects of IQOS on pulmonary function and all subjects in that study were males with a mean age of 38.8 (±11.09 SD). However, our study participants were not in line with the studies conducted by Rabenstein et al. [9], Vukas et al. [10], and Majek et al. [11], in which both sexes were included with a mean age of 26.5, 32, 30 and 23 respectively.

The exhaled CO level increased post-conventional cigarette smoking with statistical significance with a p-value <0.001 (pre-smoking mean of 9.83 ±4.41 SD and post-smoking mean of 32.83 ± 16.73 SD) which was more than group 2 (who smoked heated tobacco product) with a mean of 10.74 (±5.70 SD) as described in Table 1. This is in line with Pataka et al. [2] as in both groups**,** after IQOS use the amount of exhaled CO was found within the range of CO exposure found in non-smokers (4.12 ± 1.66 in the non-smoker group) (4.9 ± 3.6 in the smoker group), and was lower than the announced levels of smokers in Deveci et al. study [12]. Also, in Majek et al. [11], there was a significant rise in exhaled CO in the T group (traditional cigarette smokers), from 6 ppm to 11 ppm just following smoking with a slow decline 30 min after to 9, with no return to the baseline value ($p < 0.01$). while in H group (HTP users) the baseline value was 4 ppm and was 4 ppm immediately after smoking.

Along the same line, the observations from studies on the chemical composition of heated tobacco cigarettes and smoke they produce revealed not only that combustion occurs when using HTP, but also the presence of CO [13], However, the concentration of CO emitted during the use of HTPs was approximately one-hundredth of that emitted by conventional combustion cigarettes.

The same findings were found by Maloney et al. that own-brand cigarettes increased exhaled carbon monoxide concentration [14], but IQOS did not. Also, Zhang et al. concluded that levels of exhaled CO among HTP users were lower than CC users [15].

Serum cotinine level increased post-conventional cigarette smoking with statistical significance and the rate of raising in the first 5 min was more than that in the remaining 25 min as shown in the curve in Figure 1 but in Figure 2 it increased post-heated tobacco products smoking with statistical significance and the rate of raising in the first 5 min is almost the same in the remaining 25 min.

The slope of the nicotine curves in the initial phase of consuming of nicotine-containing products indicates their addictive potential. It is assumed that cigarettes are addictive due to quickly delivery of nicotine into the bloodstream and subsequently to the brain. So, if other nicotine delivery products exhibit similar kinetics, they could potentially be just as addictive, although other factors play important roles as well. Nicotine addiction is recognized as a

complex issue, with psychosocial and biogenic factors, for example, should also be taken into consideration.

Another study shows that the nicotine delivery by heated tobacco products was significantly less than that by traditional cigarettes. [10]

Also in Hardie et al. [16], which estimated nicotine pharmacokinetics and subjective effects of two HTPs compared with traditional cigarettes, it was found that nicotine uptake was much more for the cigarette (Cmax = 22.7 ng/mL) than for either HTP (8.6 and 10.5 ng/mL). In the same line with the previous one, Phillips-Waller et al. found that IQOS delivers less nicotine (median Cmax 8.3) than cigarettes (median cmax 12.9) [17].

Also, two more studies showed the same findings, Maloney et al. [14], and Goldenson et al. [18]. The first one concluded that among smokers, IQOS provided lower nicotine levels compared to cigarettes, with Cmax values of 20.4 ng/mL and 12.7 ng/mL for cigarettes and HTP 1, respectively. The second study found that the delivery of nicotine was highest for combustible cigarettes, followed by IQOS 18 mg/g, with Cmax values of 24.83 ng/mL and 13.68 ng/mL for cigarettes and HTP 1, respectively.

Contrary to our findings, Brossard et al. found that maximum nicotine concentration (Cmax) and area under the curve from the beginning of product use to the last measurable concentration (AUC0-last) were comparable between THS and CC, with Cmax ratios ranging from 88 to 104% and AUC0-last ratios between 96 to 98% [19].

Regarding the spirometric measures post-cigarette smoking in our study (group 1), we found that measurements of spirometry decreased without statistical significance except for PEF which was decreased with a statistical significance p-value of 0.021 although PEF may not be considered a measure of response as it is highly dependent on the patient effort and cooperation. Pre smoking mean was 54.89 ± 20.83 SD and post smoking mean was 50.90 ± 22.38 SD (Table 2). These results are in line with previous studies as in Kougias et al. [20], who found that mid-to-small size pulmonary airways were firstly affected (FEF 25%, FEF 50%, FEF25–75%) in a dose-dependent manner, indicating significant subclinical inflammatory changes in the peripheral bronchial tree, not just in the larger airways.

Also, Unverdorben et al. [21], studied the acute effects of traditional cigarette smoking on pulmonary function. It was found that forced expiratory flow of 25% was significantly lower in conventional cigarette smoking than in electrically heated smoking systems and non-smoking and concluded that there were acute and reversible effects of traditional cigarette smoke exposures on mid to small-sized airways in a concentration -dependent manner. Another two studies Flouris et al. [22], and Chorti et al. [23] showed a decline in FEV1/FVC just after smoking traditional cigarettes.

Regarding the spirometric measures in group 2 (Table 2) , our finding is in line with Pataka et al. [2], which revealed that FEF 25%, FEF 50%, and PEF declined significantly after IQOS use, this study explained that the main conclusion was that pulmonary function was immediately decreased in all participants, both non-smokers and smokers, suggesting that IQOS may impact airways function even after just 5 min of use, potentially due to bronchospasm, mucosal edema, or even secretions. In contrast the study by Majek et al. [11], found no alterations in spirometric parameters between those smoking heated tobacco products and traditional cigarettes.

IQOS was evolved by Philip Morris International (PMI) as a "reduced harm" substitute to traditional smoking, aiming to substitute nicotine intake from combustible cigarettes. Moazed et al. [24], estimated industry data on the pulmonary and immunosuppressive effects of heated tobacco products under near-real-world conditions and also compared the participants with those who continued smoking CC. The industry data indicated no improvement in lung function after three months of switching to IQOS compared to those who continued smoking CC. Significant increase in FEV1/FVC were observed only in the group that abstained from smoking. This finding regarding improvement in lung function with smoking cessation is also found by Pezzuto and Carico, 2020 [25], who studied the benefit of smoking cessation over three months in terms of improvement of respiratory functional variables, and found improvement in oxygen desaturation index (ODI) , FEV1 , the walking test , the COPD Assessment Test (CAT) score , PaO2 and SaO2. A recent study by Sohal et al. [26], discovered that IQOS causes similar harmful effects on human airway epithelium and smooth muscle cells in vitro as the CC, due to changes in mitochondrial function, airway inflammation, and remodeling.

The findings shown in Table 2 were in line with Pataka et al. [2], which found that in the whole group of 50 participants, SaO2% decreased significantly after IQOS use. Also, Majek et al. [11] found that after the heated tobacco product smoking, there was a statistically significant decline in peripheral oxygen saturation from 99% at baseline to 98% 30 min after exposure. Also, significant rise in heart rate and blood pressure was observed after the traditional cigarette smoking group, group of heated tobacco products, and e-cigarette group, and concluded that using HTPs causes acute respiratory and cardiovascular health effects. The similar rise in heart rate and blood pressure after the use of HTPs and conventional tobacco may be attributed to the comparable nicotine levels in the two products. The increase in heart rate and blood pressure following HTP use aligns with former experimental research, such as the studies by Başaran et al. and Kopa and Pawliczak [27,28].

Our study showed a negative correlation between smoking index (pack/year) and spirometric measures but with no statistical significance except with FVC (P value 0.029) and a positive

correlation with exhaled CO without statistical significance. This is in line with Barthwal and Singh [29], who studied the early detection of COPD in asymptomatic smokers using spirometry and found that pulmonary function parameters are significantly less in smokers as compared to non-smokers. With higher smoking index, heavy smokers showed a greater decrease in lung function FVC and FEV1 as that with increasing age. Also, in Deveci et al. [12] there was a significant positive correlation between CO levels and both daily cigarette consumption and smoking duration in healthy individuals. The same finding was found by Gonzalez et al. [30], who elicited that CO in expiration significantly correlated with the number of cigarettes smoked.

In our study, the pre-smoking exhaled CO was elevated in the studied cases in comparison to the control group with statistical significance P value < 0.001. Also, pre-smoking serum cotinine level was elevated in the studied cases but with no statistical significance in Table 3, but the maximum cotinine level in our control group was 13.5 pg/ml which may be due to passive smoking or environmental exposure which were under-reporting which is in line with Wall et al. [31], who measured Cotinine in the saliva, serum and urine of passive smokers, nonsmokers and active smokers and found that mean urine cotinine level was somewhat elevated in passive smoker than a non-smoker.

Also in our control group, the maximum level of exhaled CO was 7 ppm which also may be due to passive smoking or environmental exposure (which were under-reporting as shown in Table 3, which is in line with Deveci et al. [12], who used a portable carbon monoxide monitor to compare the exhaled CO levels between established smokers and non-smokers, and found that passive smokers had higher mean exhaled CO levels than non-smokers, though the difference was not statistically significant (P>0.05). Similarly, Laranjeira et al. [32], elicited that environmental tobacco smoke is the likely cause of higher CO levels observed among passive smokers.

In the current study, all the spirometric findings of the cases were significantly lower than those of the control group, with a p-value of <0.001, as shown in Table 3. This is in line with Dutt et al. [33], showed that pulmonary function parameters are significantly reduced in smokers as compared to nonsmokers.

Conclusions

HTPs have acute respiratory and cardiovascular effects like CCs but with less exhaled CO than CCs, although these changes were relatively minor and not likely to be of major clinical significance, they should be a matter of concern about the long-term safety of the product. The slope of the nicotine curves during the initial phase of consuming of nicotine-containing products concludes the addictive potential of these products. More research is required to

evaluate both the short- and long-term effects of IQOS, mainly in patients with respiratory conditions.

This study offers a novel assessment of the acute respiratory and cardiovascular effects of HTPs compared to CCs. While previous research has predominantly focused on the chemical composition of emissions from HTPs , this study is among the first to directly compare exhaled CO levels post-smoking, revealing a significant reduction with HTPs. Despite this, both HTPs and CCs showed similar acute physiological effects, including increased serum cotinine levels and heart rate, along with decreased spirometry and oxygen saturation. These findings highlight the need to evaluate both chemical emissions and physiological outcomes to better understand the health implications of HTPs. Despite the valuable insights provided by this study, several limitations should be acknowledged; the study focused only on acute effects within a 30-minute timeframe post-smoking. Long-term studies are necessary to evaluate the chronic impact of HTPs on respiratory and cardiovascular health. Also Participants were limited to current smokers and healthy non-smokers, Including ex-smokers and individuals with pre-existing respiratory or cardiovascular conditions could provide a more comprehensive understanding of the effects of HTPs.

List of Abbreviations

BI: Brinkman index.
CAT: COPD Assessmnet Test
CCs: Conventional Cigarettes.
Cmax: Maximal Nicotine Concentration.
CO: Carbon Monoxide.
COPD: Chronic Obstructive Pulmonary Disease.
CO2: carbon dioxide.
EC: Electronic Cigarette.
eCO: Exhaled Carbon Monoxide.
FEF 25%: Forced Expiratory Flow of 25%.
FEF 50%: Forced Expiratory Flow of 50%.
FEF25–75%: Forced Expiratory Flow of 25%-75%.
FEV1: Forced Expiratory Volume in the first second.
FEV1/FVC: The ratio of Forced Expiratory Volume in the first one second to Forced Vital Capacity.
FVC: Forced Vital Capacity.
HPHCs: Harmful and Potentially Harmful Chemical Constituents.
HR: Heart Rate.
HTPs: Heated Tobacco products.
IQOS: I-Quit-Ordinary-Smoking.
MMEF: Maximum mid expiratory flow.
ODI : Oxygen Desaturation Index
PEF: Peak Expiratory Flow.
PEFR: Peak expiratory Flow Rate.
SpO_2: Oxygen Saturation.
% COHb: the percentage of carboxyhemoglobin.

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Table 1. Comparison between Groups 1 & 2 regarding pre-smoking and post-smoking pulmonary function test, exhaled CO, serum cotinine level, SpO_2, and heart rate.

	Group 1					Group 2					P-value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Pre- smoking											
FEV1/FVC	72.06	12.97	75.93	43.43	88.97	76.28	8.84	79.57	53.84	84.74	0.258
FEV1 %	60.36	26.81	57.00	15.30	105.00	78.79	18.89	84.00	42.30	106.00	0.018*
FVC %	66.51	24.13	64.00	28.40	110.00	84.23	15.73	86.00	46.90	118.00	0.018*
PEF L/s	54.89	20.83	56.00	19.00	101.00	66.41	21.06	64.00	28.80	114.00	0.119
FEF 25 %	47.28	26.15	47.00	5.00	104.00	65.38	26.06	63.00	20.70	116.00	0.032*
FEF 50%	48.36	31.22	45.00	6.20	110.00	71.40	31.06	77.00	21.10	119.00	0.021*
FEF75%	47.41	31.63	47.00	9.00	134.00	61.41	25.23	64.00	18.50	97.00	0.030*
MMEF25-75%	49.01	30.89	48.00	7.80	114.00	67.93	28.26	70.00	18.60	109.00	0.032*
Exhaled CO-level PPM	9.83	4.41	9.00	5.00	22.00	10.74	5.70	10.00	3.00	22.00	0.643
Serum Cotinine level(pg/ml)	7.49	4.65	6.90	1.80	21.40	11.51	14.05	7.00	1.50	55.40	0.725
SpO_2 %	96.83	1.37	97.00	93.00	98.00	97.43	0.90	98.00	95.00	99.00	0.141
HR	77.74	12.26	76.00	62.00	110.00	72.04	8.43	71.00	56.00	90.00	0.134
Post smoking											
FEV1/FVC	70.07	14.62	74.40	40.00	90.35	75.11	10.93	76.83	47.49	88.89	0.231
FEV1%	59.33	27.75	54.00	14.70	108.00	76.56	22.53	81.50	29.20	104.00	0.035*
FVC%	66.28	22.89	64.60	30.60	112.00	82.83	19.47	87.10	43.00	119.00	0.010*
PEF L/s	50.90	22.38	49.00	13.00	88.00	60.07	21.46	61.00	20.00	102.40	0.218
FEF25%	44.83	26.08	44.00	6.00	95.00	59.28	25.55	61.00	14.00	109.40	0.085
FEF50%	46.96	30.72	43.00	5.80	106.00	70.10	36.86	69.00	12.00	133.00	0.040*
FEF75%	51.99	40.75	41.00	6.90	160.00	60.37	31.24	62.00	11.90	129.00	0.166
MMEF25-75%	48.59	32.37	44.00	8.30	111.00	65.64	31.92	66.10	11.30	120.00	0.059
Exhaled CO-level PPM	32.83	16.73	27.00	15.00	74.00	10.30	5.23	9.00	3.00	21.00	< 0.001*
Serum Cotinine level after 5 mins of smoking (pg/ml)	8.03	4.97	7.00	1.70	21.40	12.43	14.22	8.30	1.60	53.50	0.356
Serum Cotinine level after 30 mins of smoking (pg/ml)	8.11	5.73	6.20	2.10	28.20	13.29	14.32	7.80	1.60	54.50	0.121
SpO_2	96.30	1.72	96.00	91.00	98.00	96.65	1.07	97.00	94.00	98.00	0.664
HR	92.00	13.08	88.00	72.00	117.00	87.65	10.38	88.00	68.00	110.00	0.415

This table shows that there was statistical significance in the pre-smoking measurements of spirometry (FEV1, FVC%, FEF25%, FEF50%, FEF75%, MME F25-75%) between Group 1 and Group 2 . Regarding the post smoking finding the post smoking exhaled CO was elevated in Group 1 with a mean of 32.83 (±16.73 SD) more than Group 2 with a mean of 10.3 (±5.23 SD) with statistical significance. Also shows increase in post smoking Cotinine after 5 min and after 30 min in both groups but with no statistical significance between the two groups. The heart rate also increased in both groups post smoking but with no statistical significance between the two groups. The post smoking SpO2 in both groups decreased in relation to the pre smoking values but with no statistical significance between both groups. *significant $p<0.05$. FEV1/FVC, ratio of forced expiratory volume in the first second to forced vital capacity; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; PEF, peak expiratory flow; FEF 25%, forced expiratory flow of 25%; FEF 50%, forced expiratory flow of 50%; FEF 75%, forced expiratory flow of 75%; FEF 25-75%, forced expiratory flow of 25-75%; MMEF, maximum mid expiratory flow; CO, carbon monoxide; HR, heart rate; SpO_2, oxygen saturation.

Table 2. Comparison of pre and post-smoking pulmonary function test, exhaled CO, SpO_2, and HR in Group 1 and Group 2.

	Pre-smoking					Post-smoking					P-value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Group 1											
FEV1/FVC	72.06	12.97	75.93	43.43	88.97	70.07	14.62	74.40	40.00	90.35	0.068
FEV1 %	60.36	26.81	57.00	15.30	105.00	59.33	27.75	54.00	14.70	108.00	0.248
FVC%	66.51	24.13	64.00	28.40	110.00	66.28	22.89	64.60	30.60	112.00	0.782
PEF L/s	54.89	20.83	56.00	19.00	101.00	50.90	22.38	49.00	13.00	88.00	0.021*
FEF25% (L/sec)	47.28 (3.58)	26.15 (2.06)	47.00 (3.42)	5.00 (0.37)	104.00 (8.11)	44.83 (3.40)	26.08 (2.04)	44.00 (3.35)	6.00 (0.49)	95.00 (7.38)	0.114 (0.14)
FEF50%	48.36	31.22	45.00	6.20	110.00	46.96	30.72	43.00	5.80	106.00	0.573
FEF75%	47.41	31.63	47.00	9.00	134.00	51.99	40.75	41.00	6.90	160.00	0.484
MMEF25-75%	49.01	30.89	48.00	7.80	114.00	48.59	32.37	44.00	8.30	111.00	0.445
Exhaled CO-level PPM	9.83	4.41	9.00	5.00	22.00	32.83	16.73	27.00	15.00	74.00	< 0.001*
SpO_2 %	96.83	1.37	97.00	93.00	98.00	96.30	1.72	96.00	91.00	98.00	0.022*
HR	77.74	12.26	76.00	62.00	110.00	92.00	13.08	88.00	72.00	117.00	< 0.001*
Group 2											
FEV1/FVC	76.28	8.84	79.57	53.84	84.74	75.11	10.93	76.83	47.49	88.89	0.224
FEV1 %	78.79	18.89	84.00	42.30	106.00	76.56	22.53	81.50	29.20	104.00	0.065
FVC%	84.23	15.73	86.00	46.90	118.00	82.83	19.47	87.10	43.00	119.00	0.175
PEF L/s	66.41	21.06	64.00	28.80	114.00	60.07	21.46	61.00	20.00	102.40	0.02*
FEF25% (L/sec)	65.38 (4.81)	26.06 (1.99)	63.00 (4.55)	20.70 (1.54)	116.00 (8.51)	59.28 (4.36)	25.55 (1.93)	61.00 (4.17)	14.00 (0.96)	109.40 (8.37)	0.055 (0.045*)
FEF50%	71.40	31.06	77.00	21.10	119.00	70.10	36.86	69.00	12.00	133.00	0.503
FEF75%	61.41	25.23	64.00	18.50	97.00	60.37	31.24	62.00	11.90	129.00	0.281
MMEF25-75%	67.93	28.26	70.00	18.60	109.00	65.64	31.92	66.10	11.30	120.00	0.201
Exhaled CO-level PPM	10.74	5.70	10.00	3.00	22.00	10.30	5.23	9.00	3.00	21.00	0.101
SpO_2 %	97.43	0.90	98.00	95.00	99.00	96.65	1.07	97.00	94.00	98.00	0.002*
HR	72.04	8.43	71.00	56.00	90.00	87.65	10.38	88.00	68.00	110.00	< 0.001*

This table shows that the measurements of spirometry decreased post-conventional cigarette smoking (GROUP 1)without statistical significance except PEF that was decreased with statistical significance p value 0.021, and the exhaled CO level increased post conventional cigarette smoking with statistical significance p value <0.001 (pre smoking mean 9.83 ±4.41 SD)(post smoking mean 32.83 ±32.83SD) also showing decreased SpO2 , and increased HR post smoking with statistical significance p value <0.001.Regarding (GROUP 2) the measurements of spirometry decreased post heated tobacco product smoking without statistical significance except PEF and FEF25% that was decreased with statistical significance , and the exhaled CO level didn't increased after heated tobacco product smoking (pre-smoking mean of 10.74 ± 5.70 SD), (post smoking mean of 10.30 ± 5.23 SD), also showed decreasing SpO2, and increasing HR after smoking with statistical significance of p value <0.001.

Table 3. Comparison between the studied cases and the control group regarding the pre-smoking pulmonary function test, exhaled CO, serum Cotinine level, HR, and SpO2.

Pre-smoking	Cases					Control					P-value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
FEV1/FVC	74.17	11.18	77.45	43.43	88.97	84.33	5.93	83.73	72.80	99.54	< 0.001*
FEV1 %	69.57	24.75	74.85	15.30	106.00	93.06	10.79	90.00	72.00	127.60	< 0.001*
FVC%	75.37	22.04	77.00	28.40	118.00	92.76	12.85	89.90	75.00	138.30	< 0.001*
PEF L/s	60.65	21.52	60.00	19.00	114.00	81.52	16.62	79.00	57.00	126.50	< 0.001*
FEF25%	56.33	27.39	56.50	5.00	116.00	84.77	16.84	86.50	48.90	124.00	< 0.001*
FEF50%	59.88	32.92	61.00	6.20	119.00	93.08	17.55	93.00	56.00	131.40	< 0.001*
FEF75%	54.41	29.16	53.50	9.00	134.00	84.01	19.49	78.80	57.00	135.00	< 0.001*
MMEF25-75%	58.47	30.80	60.00	7.80	114.00	88.86	13.89	91.00	59.00	117.00	< 0.001*
Exhaled CO-level PPM	10.28	5.06	9.00	3.00	22.00	2.87	1.36	3.00	1.00	7.00	< 0.001*
serum Cotinine level(pg/ml)	9.50	10.54	6.90	1.50	55.40	5.99	2.65	5.60	1.40	13.50	0.120
SpO_2 %	97.13	1.19	97.50	93.00	99.00	97.53	1.01	98.00	96.00	99.00	0.130
HR	74.89	10.80	75.00	56.00	110.00	79.98	8.78	80.00	64.00	94.00	0.005*

This table showed that all the measurements of the spirometry were low in comparison to the control group with statistical significance of p value <0.001, and the pre-smoking exhaled CO was elevated in the studied cases in comparison to the control group with a statistical significance p-value of < 0.001. Also pre-smoking serum Cotinine level was elevated in the studied cases but with no statistical significance. *significant p<0.05. FEV1/FVC, ratio of forced expiratory volume in the first second to forced vital capacity; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; PEF, peak expiratory flow; FEF 25%, forced expiratory flow of 25%; FEF 50%, forced expiratory flow of 50%; FEF 75%, forced expiratory flow of 75%; FEF 25-75%, forced expiratory flow of 25-75%; MMEF, maximum mid expiratory flow; CO, carbon monoxide; HR, heart rate; SpO_2: oxygen saturation.

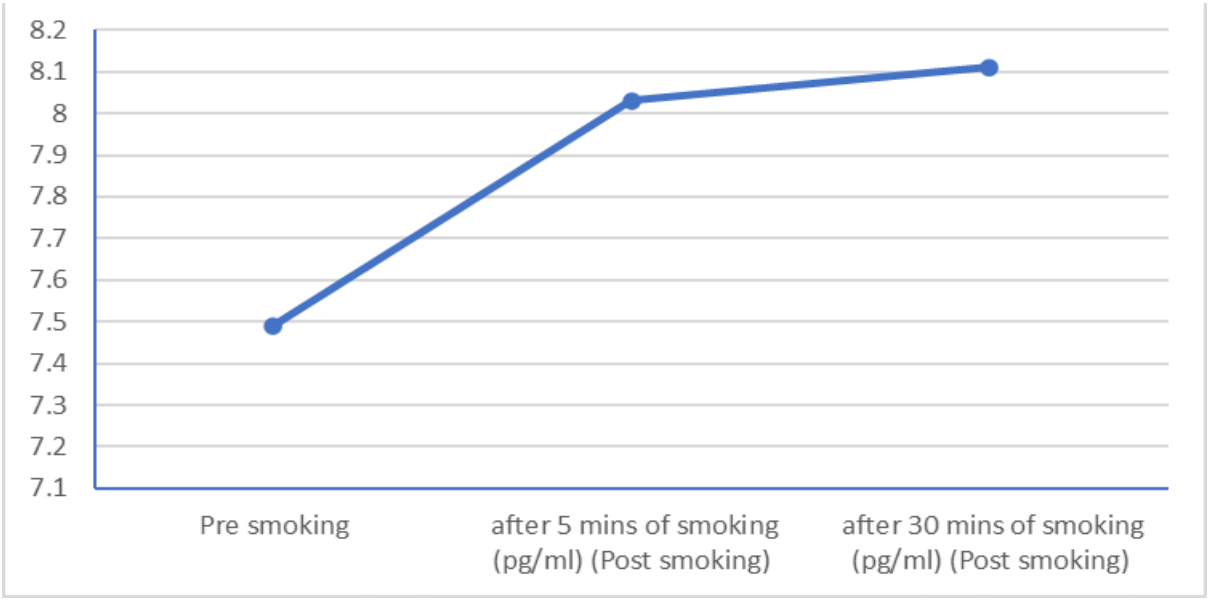

Figure 1. Serum cotinine level group 1 (pg/mL). Serum cotinine level increased post-conventional cigarette smoking with statistical significance and the rate of raising in the first 5 min was more than that in the remaining 25 min.

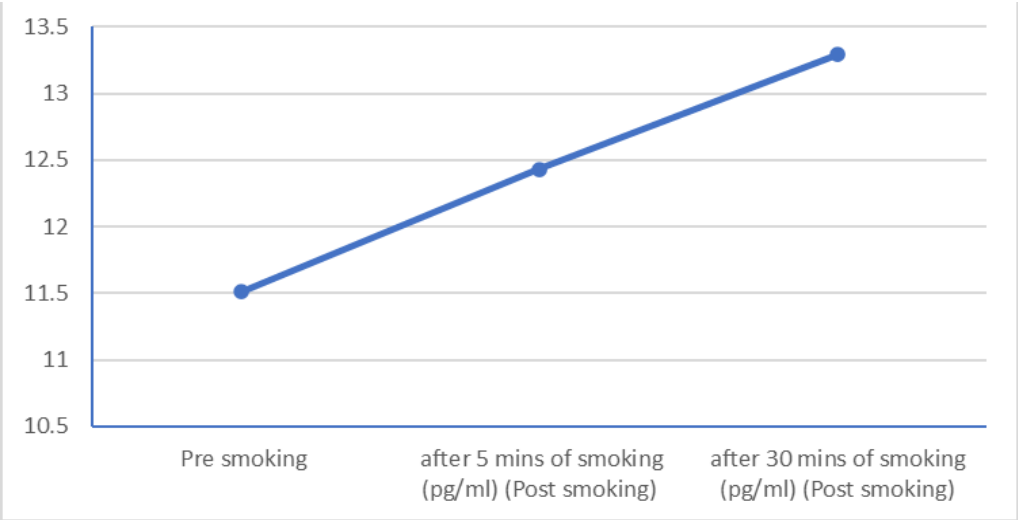

Figure 2. Serum cotinine level in group 2 (pg/mL). Serum cotinine level increased post-heated tobacco products smoking with statistical significance and the rate of raising in the first 5 min is almost the same in the remaining 25 min.