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The Acute Effects of Water-pipe Smoking on the Cardiorespiratory System

Fahed Hakim, MD; Elias Hellou, BSc; Aviv Goldbart, MD; Rina Katz, MSc; Yedidia Bentur, MD; Lea Bentur, MD

Authors and Disclosures

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Abstract and Introduction

Abstract

Objective: There are limited data on the acute effects of water-pipe tobacco smoking, commonly known as water-pipe smoking (WPS), on cardiopulmonary parameters. This study evaluated the acute effects of a single 30-min session of WPS on carboxyhemoglobin (COHb) levels, pulmonary function test results, vital signs, fractional exhaled nitric oxide (Feno) levels, and exhaled breath condensate (EBC) cytokine levels in volunteers in a domestic, open-air, group smoking setting.

Methods: This prospective study evaluated the above-noted outcome parameters before and after 30 min of WPS. The primary outcome parameter was the change in COHb levels.

Results: Forty-five volunteers (30 men, 15 women), aged 32.35 ± 15.33 years, were recruited. After one session of WPS, the COHb levels rose significantly, from 1.47% ± 0.57% (median 1.4) to 9.47% ± 5.52% (median 7.4), $P < .001$. Systolic and diastolic BP levels significantly increased after smoking (systolic, 119.52 ± 12.07 mm Hg vs. 131.98 ± 17.8 mm Hg; diastolic, 74.84 ± 7.89 mm Hg vs. 82.98 ± 12.52 mm Hg, respectively; $P < .001$). Heart rates increased from 80.39 ± 9.92 beats/min to 95.59 ± 17.41 beats/min, $P < .001$; and respiratory rates increased from 14.36 ± 1.63 breaths/min to 16.68 ± 2.24 breaths/min, $P < .001$. There were decreases in forced expiratory flow between 25% and 75% of FVC, peak expiratory flow rate, Feno levels, percentage of eosinophils in peripheral blood, and 8-isoprostane levels in EBC.

Conclusions: This study shows that one session of WPS causes acute biologic changes that might result in marked health problems. It adds to the limited evidence that WPS is harmful and supports interventions to control the continuing global spread of WPS, especially among youth.

Introduction

Smoking with a water pipe (WP), also known as a hookah, shisha, goza, narghile, and hubble-bubble, has been practiced extensively for about 400 years. Water-pipe tobacco smoking, commonly known as water-pipe smoking (WPS), is considered by the public to be less harmful than cigarette smoking, leading to tolerance of this practice. It has been claimed that > 100 million people worldwide smoke WPs daily. Initially, WPS was common mainly in the Middle East, Turkey, India, and Pakistan. With globalization and immigration from these countries, WPS spread to Western countries, notably among youth. It has been estimated that 20% to 40% of college students in the United States have experienced WPS. A recent study found that WP use was not restricted to any single racial, ethnic, or cultural group.[1] Among the reasons for the growing popularity of WPS are low cost; easy access; the social interaction that accompanies it; the sweetened, flavored, and aromatic tobacco that can mask the taste of tobacco; the misperception of its impact on health, including the idea that WPS is less addictive than cigarette smoking; and the lack of public health warnings on the use of WPs.[2]

While there is a large amount of data regarding the acute and chronic effects of cigarette smoking, there is a paucity of data regarding WPS. The tobacco used in WPS ("moasel") typically weighs 10 to 20 g per session and contains 30% tobacco and 70% honey or molasses. Burning charcoal is placed above the tobacco, separated by a piece of perforated tin foil. Several types of charcoal can be used; the most common are lump charcoal and briquettes containing wood by-products, hydrocarbons, and other chemicals. During inhalation, air heated by the burning charcoal passes through the tobacco and vaporizes it, producing smoke. The types of charcoal and tobacco used affect the combustion product content. Most smoking sessions last 30 min to several hours. WP smoke contains harmful constituents, including nicotine, carbon monoxide, carcinogens, tar, and heavy metals.[3]

Estimates of the equivalence between cigarette smoking and WPS vary between two and 10 cigarettes for occasional and daily WPS, respectively,[4] and 100 cigarettes for 200 puffs per WPS session.[5] Only a few studies have investigated the acute effects of WPS on cardiorespiratory parameters. Two studies reported markedly different increases in carboxyhemoglobin (COHb) levels after WPS.[6,7] Two studies evaluated vital signs after WPS, but female subjects were not included.[8,9] The acute effects on pulmonary function test results, fractional exhaled nitric oxide (Feno) levels, eosinophil levels, and exhaled breath condensate (EBC) parameters were studied in cigarette smokers but not WP smokers.[10]

Our hypothesis was that WPS can affect multiple parameters, similar to cigarette smoking. It is assumed that determination of the short-term effects of WPS can assist in understanding its long-term effects. The objective of our study is to evaluate the short-term effects of a single, 30-min session of WPS on COHb levels and cardiorespiratory and airway inflammatory parameters in volunteers.

Materials and Methods

Subjects

The study was approved by the Institutional Review Board, Rambam Health Care Campus (number 0219-09) and registered at ClinicalTrials.gov (identifier NCT01157832). Each subject read and signed an informed consent form prior to enrollment. Eligible subjects were older than 18 years and had previously smoked from WPs. Exclusion criteria included any chronic lung disease, pregnancy or lactation in women, acute illness during the previous 2 weeks, corticosteroid treatment, WPS in the previous 24 h, smoking cigarettes in the previous 6 h, and exposure to fire or massive smoke in the previous 24 h.

Setting

The study was conducted in an outpatient setting on an open-air balcony. All WPs were prepared by one of the investigators (E. H.). The WPs were of similar size, and all subjects smoked 10 g of double-apple-flavored moasel of the same brand (Nakhla; El Geish St. Cairo, Egypt). The tobacco was lit with the same instant-light charcoal disks (Bright Star Charcoal, 3.5 cm diameter and 1 cm width; Nakhla group). Subjects were instructed to smoke at their own regular pace and pattern.

Evaluation

All parameters were evaluated before and after a 30-min session of WPS. Laboratory evaluation was carried out blindly.

Vital Signs and Visual Analog Score: Systolic and diastolic BP levels were measured using an Omron HEM-712 C BP monitor (Houston, Texas). Heart and respiratory rates were measured manually. Each patient recorded his or her general feeling on a scale of one (worst) to 10 (best).

Spirometry: Spirometry was performed in accordance with the American Thoracic Society/European Respiratory Society Task Force, using a KoKo spirometer (nSpire Health, Inc; Louisville, Colorado). Each maneuver was repeated for at least three technically acceptable forced expiratory flow volume curves; the best results were used for analysis.[11]

Carboxyhemoglobin and CBC Count: COHb levels were measured in venous blood samples using an Illex cooximeter (IL-682; Instrument Laboratory; Lexington, Massachusetts). CBC counts were analyzed using an automated hematology flow cytometer (Coulter-STKS; Beckman Coulter; Miami, Florida).

Fractional Exhaled Nitric Oxide: Feno levels were measured using a portable electrochemical analyzer (NIOX MINO; Aerocrine AB, Smidesvägen, Sweden)[12] according to American Thoracic Society recommendations. The measurement procedure included a deep inhalation to total lung capacity followed by an exhalation for 10 s at a mouth flow rate of 50 mL/s and a pressure of 10 cm H_2O.[13]

Exhaled Breath Condensate: EBC samples were collected in RTubes[14] (Respiratory Research; Charlottesville, Virginia) according to the manufacturer's instructions and European Respiratory Society recommendations.[15] The collected EBCs were stored at −80°C until analysis, which was performed within 3 months. Samples were analyzed for nitrotyrosine and 8-isoprostane, which are markers of oxidative stress. Nitrotyrosine levels were determined using a specific immunoassay with a commercially available kit (Nitrotyrosine-EIA; Oxis Research; Portland, Oregon), and 8-isoprostane levels also were determined using a commercially available immunoassay kit (Cayman Chemical; Ann Arbor, Michigan). All samples were assayed in duplicate and at two dilutions, at plate reader absorbance (450 nm for nitrotyrosine, 420 nm for 8-isoprostane). The results were analyzed using a four-parameter logistic curve fit. The intraassay and interassay variability for nitrotyrosine and 8-isoprostane were < 10%; specificity was 100%. The limit of detection of the assays was 2.1 pg/mL for nitrotyrosine and 5 pg/mL for 8-isoprostane.

Statistics

The sample size was determined using Win Episcope 2 software for paired tests (Learning Technology Section, College of Medicine & Veterinary Medicine, The University of Edinburgh; Edinburgh, Scotland). The primary outcome was COHb concentration; pulmonary function tests results, vital signs, and Feno and EBC cytokine levels were considered secondary outcome parameters. Seven subjects were required to demonstrate an increase in COHb concentration from 2% to 3.5% with 95% confidence and 80% power. The sample size was increased to a minimum of 20 patients to allow detection of an increase of 10% in respiratory rate and systolic and diastolic BP levels. The power analyses for the other parameters were not predetermined.

Statistical analysis was performed using a paired Student *t* test for parametric values and a Wilcoxon test for nonparametric values. Since multiple outcome parameters were evaluated, the *P* value was also adjusted using a Bonferroni correction.

A general linear model of repeated measures was performed to find categorical (gender) predictors that are in relation to the difference before and after WPS for the 15 dependent variables. For EBC levels, analysis of variance was used, followed by Neuman-Keuls post hoc tests, whenever appropriate.

Results are expressed as mean ± SD, median, and range. A P value < .05 was considered statistically significant; when a Bonferroni correction was used, a P value < .0033 (P < .05 divided by the 15 parameters evaluated) was considered significant.

Results

Forty-five subjects (30 men, 15 women) were included; their characteristics are presented in Table 1.

Table 1. Characteristics of Subjects Participating in the Study

Subject Characteristic	Value
Sex, male (female)	30 (15)
Age, mean ± SD (range), y	32.35 ± 23.36 (18.3–65.1)
BMI, mean ± SD (range)	24.14 ± 4 (17.8–33.5)
Cigarettes smokers	8
Exclusive WP smokers	37
Occasional WP smokers	17
Regular WP smokers	28
Daily smoking of WPs	10
Smoking duration > 60 min/session	21

Values given are No. unless otherwise indicated. Exclusive = subjects who smoke a WP only; occasional = subjects who smoke a WP on occasions and less than two times a week; regular = subjects who smoke a WP more than three times a week; WP = water pipe.

The vital signs before and after one session of WPS are shown in Table 2.

Table 2. Vital Signs Before and After WPS

Characteristic	Before WPS	After WPS	*P* Value[a]
Heart rate, beats/min	80.39 ± 9.92 (80, 60–117)	95.59 ± 17.41 (92, 60–141)	< .0001
Systolic BP, mm Hg	119.52 ± 12.07 (120, 99–145)	131.98 ± 17.8 (130.5, 72–186)	< .0001
Diastolic BP, mm Hg	74.84 ± 7.89 (74, 53–97)	82.98 ± 12.52 (84.5, 26–106)	< .0001
Respiratory rate, breaths/min	14.36 ± 1.63 (14, 12–18)	16.68 ± 2.24 (16, 14–25)	< .0001

Data are shown as mean ± SD (median, range). WPS = water-pipe smoking.

[a] Bonferroni correction for multiple comparisons (n = 15); $P < .0033$ was considered as statistical significance.

Significant increases in systolic and diastolic BP (≤ 186 mm Hg and 106 mm Hg, respectively), heart rate (≤ 141 beat/min), and respiratory rate (≤ 25 breaths/min) were observed. The visual analog scores of general feeling showed a significant decrease, from a median of 10 (9.68 ± 0.64) to 7 (6.95 ± 1.98) ($P < .0001$), even though subjects reported they enjoyed smoking. Pulmonary function test results (Table 3) revealed no changes in FVC, FEV_1, and FEV_1/FVC, but decreases in forced expiratory flow between 25% and 75% ($FEF_{25\%–75\%}$) and peak expiratory flow rate (PEFR) were found ($P = .045$ and $P = .0004$, respectively).

Table 3. Pulmonary Function Test Results Before and After WPS

Pulmonary Function	Before	After	*P* Value[a]
FVC, L	4.07 ± 0.86	4.09 ± 0.92	NS
FVC, % predicted	0.91 ± 0.09	0.91 ± 0.09	NS
FEV_1, L/s	3.51 ± 0.77	3.47 ± 0.82	NS
FEV_1, % predicted	93 ± 0.1	92 ± 0.1	NS
FEV_1/FVC	0.86 ± 0.05	0.85 ± 0.06	NS
$FEF_{25\%–75\%}$, L	3.98 ± 1.13	3.76 ± 1.12	.045
$FEF_{25\%–75\%}$, % predicted	0.90 ± 0.18	0.85 ± 0.17	.040
PEFR, L	7.34 ± 1.89	6.67 ± 1.93	.00043
PEFR, % predicted	0.83 ± 0.14	0.75 ± 0.15	.00032

Data are shown as mean ± SD. $FEF_{25\%–75\%}$ = forced expiratory flow between 25% and 75% of FVC; NS = not significant; PEFR = peak expiratory flow rate. See Table 2 for expansion of the other abbreviation.
[a]Bonferroni correction for multiple comparisons (n = 15); $P < .0033$ was considered as statistical significance.

The changes in laboratory parameters before and after WPS are presented in Table 4.

Table 4. Laboratory Parameters Before and After WPS

Parameter	Before	After	*P* Value[a]
COHb, %	1.47 ± 0.56 (1.4, 0.7–3.3)	9.49 ± 5.52 (7.4, 3.4–26)	< .0001
Hemoglobin, g/dL	14.08 ± 1.96 (14, 8.8–17.6)	14.24 ± 1.86 (14.4, 9.07–17.4)	.059
Eosinophils, count/μL	0.24 ± 0.2 (0.169, 0.06–0.77)	0.24 ± 0.20 (0.15, 0.03–0.84)	.588
Eosinophils, %	3.03 ± 2.25 (1.84, 0.6–8.32)	2.86 ± 2.09 (1.9, 0.4–7.66)	.018
Feno, ppb	6.64 ± 3.37 (5, 5–20)	6.20 ± 2.68 (5, 5–15)	.038
8-Isoprostane in EBC, pg/mL	87.41 ± 4.16 (88.3,78.03–93.1)	83.84 ± 9.47 (85.6, 54.68-92.35)	.043
Nitrotyrosine in EBC, pg/mL	8.64 ± 1.40 (8.72,6.80–11.90)	9.36 ± 1.94 (7.42,6.30–13.10)	.40

Data are shown as mean ± SD (median, range). COHb = carboxyhemoglobin; EBC = exhaled breath condensate; Feno = fractional exhaled nitric oxide; ppb = parts per billion. See Table 2 for expansion of the other abbreviation.
[a]Bonferroni correction for multiple comparisons (n = 15); $P < .0033$ was considered as statistical significance.

The median COHb concentration increased from 1.4% (1.47% ± 0.56%) to 7.4% (9.49% ± 5.52%) ($P < .001$). The post-WPS COHb concentration was 10% to 15% in 10 subjects, 15% to 20% in one subject, and > 20% in three subjects (≤ 26%). The individual changes in COHb concentration are displayed in Figure 1. The percentage of eosinophils, but not the total eosinophil count, decreased ($P = .018$). The total eosinophil count decreased only in those patients whose WBC count also decreased (n = 16) ($P = .003$). The analysis of EBC was performed for only 20 subjects (prior to and following WPS). The other 25 EBC samples were broken during transportation using liquid nitrogen rather than dry ice. The 8-isoprostane concentrations decreased after WPS ($P = .043$). The changes in $FEF_{25\%–75\%}$ rates, PEFRs, percentage of eosinophils, Feno levels, and 8-isoprostane levels were insignificant after applying a Bonferroni correction. Gender analysis showed significant difference only in post-WPS COHb concentrations (10.44% ± 6.32% and 6.84% ± 4.6% in women and men, respectively; $P = .044$) (Fig 2).

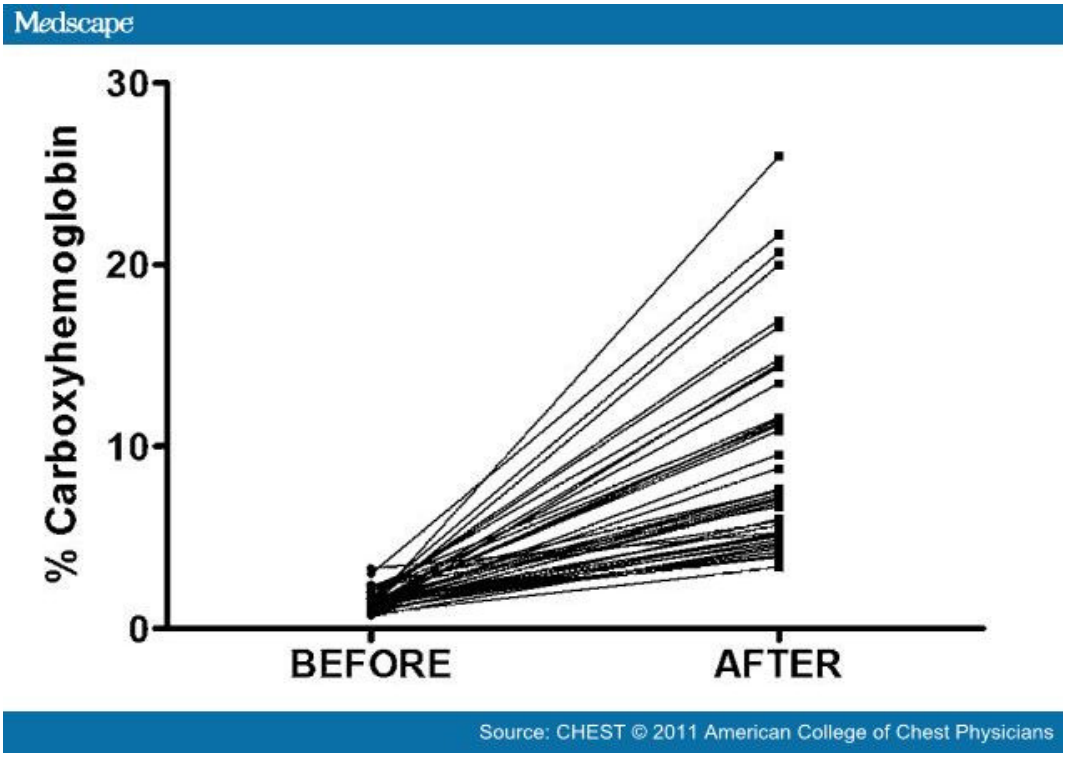

Figure 1. Carboxyhemoglobin (COHb) concentrations before and after water-pipe smoking (WPS).

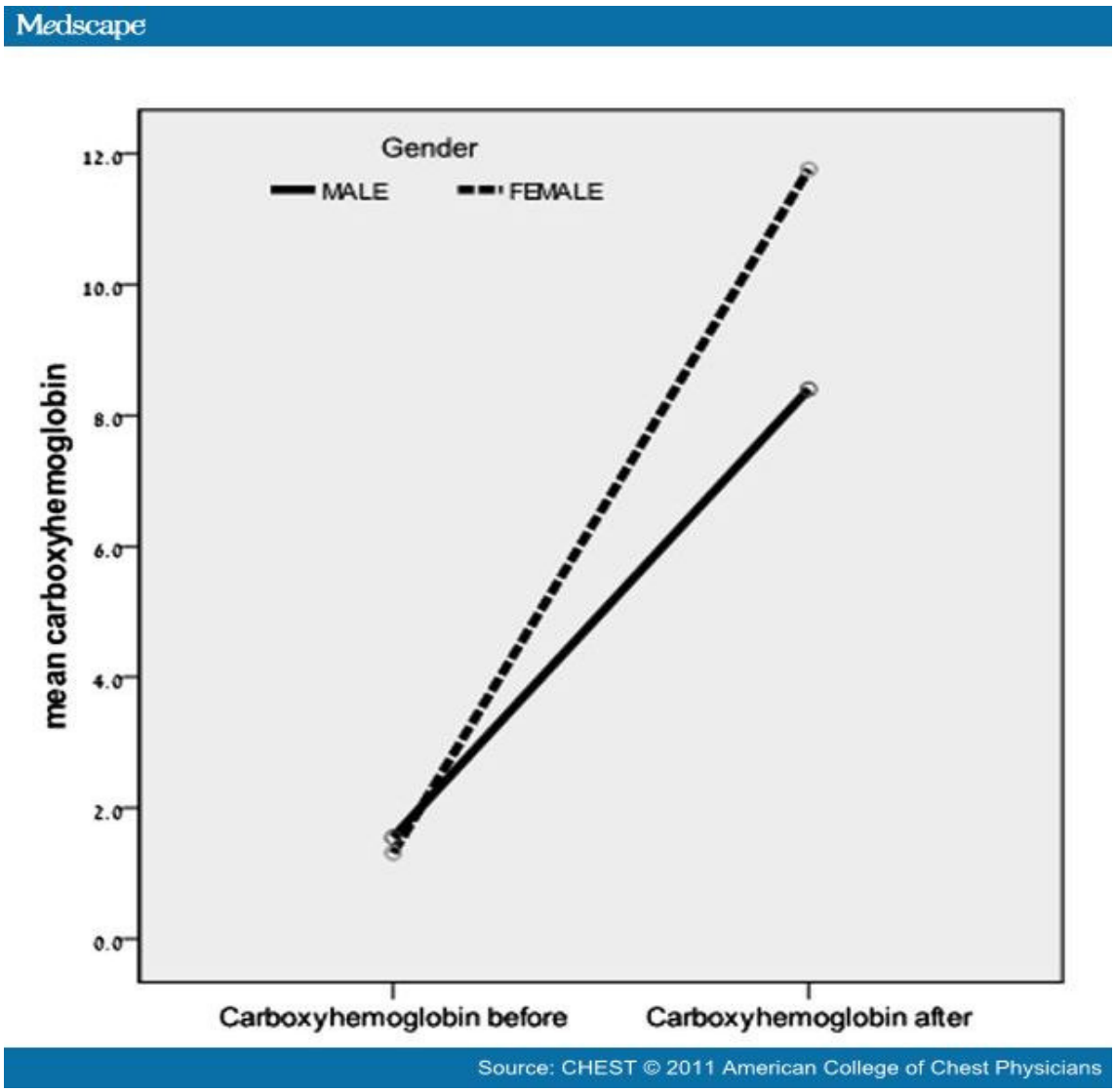

Figure 2. Gender difference in COHb concentrations before and after WPS. See Figure 1 legend for expansion of abbreviations.

Discussion

This study evaluated the short-term effects of a 30-min single session of WPS on multiple cardiorespiratory parameters. This model is a relatively easy and sensitive method of investigating the specific effects of WP smoke on these parameters.[16]

The study showed that one session of WPS resulted in significant increases in COHb concentrations, systolic and diastolic BP levels, and heart and respiratory rates. Decreases were observed in PEFRs, the percentage of eosinophils in the peripheral blood, and levels of $FEF_{25\%–75\%}$, Feno, and 8-isoprostane in EBC. The following is a discussion of our findings in relation to long-term WPS, and short- and long-term cigarette smoking.

Carboxyhemoglobin

Our results showed that after WPS, COHb concentrations increased significantly to 9.49% ± 5.52% (> 20% in three subjects), with significantly greater increases in the subjects. A WPS session is generally a social event, puffing is intermittent, and smoking patterns vary. In our study, WPS was limited to 30 min using one charcoal disk. The subjects were instructed to smoke at their own regular pace and pattern. Instant-light charcoal disks are commonly used in WPS and are sold wherever WP tobacco is sold. The tobacco and charcoal used and the length and pattern of smoking mimicked realistic settings of WPS. The more traditional charcoal requires a small grill and longer lighting times.

A crossover study comparing presmoking and postsmoking COHb concentrations between WPS and cigarette smoking in 31 subjects found significantly higher COHb concentration after WPS (3.9% ± 2.5% vs. 1.3% ± 0.5%, respectively).[12] The lower COHb levels found in this study relative to our findings may be due to a difference in smoking pattern and a difference in the charcoal briquette used.[7,17]
Zahran et al[6] reported COHb concentrations of 10.1% ± 2.5% in 975 healthy men following 10 to 40 min of WPS, which is similar to our results. These concentrations were significantly higher than in cigarette smokers. Presession abstinence was not required, and the presmoking COHb concentrations and postsmoking range were not reported, unlike our study.
High levels of COHb (27.8% and 28.7%) after WPS necessitating hospital admission and oxygen treatment were reported in two cases.[18,19] In three of our subjects, COHb concentration ranged between 20% and 26%. These levels may require hospital admission, oxygen therapy, and hyperbaric oxygen therapy, especially in subjects who are symptomatic or susceptible. Moreover, individuals can smoke WPs more than once daily and for several hours, exposing them to potentially toxic COHb concentrations for marked durations. Long-term exposure to carbon monoxide can lead to chronic poisoning.[20]
The gender difference in COHb concentrations found in our study was not reported. This finding might be explained by differences in alveolar ventilation and smoking patterns. It is unknown whether higher concentrations of other constituents of WP smoke (eg, nicotine, tar, carcinogens) can be found in women. Greater susceptibility to the lung-damaging effects of cigarette smoking has been reported in women.[21] Mohammad et al[22] reported a greater proportion of chronic bronchitis among women associated with daily WP use.

Vital Signs
Two studies on 20 and 202 male healthy volunteers reported significant increases in heart rates and systolic and diastolic BP levels after WPS.[8,9] These findings are comparable to our results in both men and women. Similar increases in heart rates and BP levels were also reported in cigarette smokers. These hemodynamic changes were suggested to be mediated by nicotine, which activates the sympathetic nervous system with a release of norepinephrine, epinephrine, and vasopressin, or by nicotine's direct effect on the endothelium.[9] Excess sympathetic stimulation in cigarette smokers contributes to cardiovascular morbidity and mortality. It is suggested that chronic WPS may lead to similar cardiovascular morbidity.

Pulmonary Function Tests
Our study showed acute decreases in $FEF_{25\%–75\%}$ levels and PEFRs after 30 min of WPS. Several studies evaluated the long-term but not short-term effects of WPS on pulmonary function tests. Most of them reported similar or even greater impairment of pulmonary function parameters after long-term WPS compared with cigarette smoking.[23] Cigarette smoking was not found to have a short-term effect on FEV_1 in 15 subjects; other measures of spirometry were not reported.[10]
Peripheral Blood Eosinophils
We found a decrease in the percentage of eosinophils; the total eosinophil count decreased only in subjects who exhibited a concomitant decrease in their total WBC count. Several studies reported that cigarette smoking acutely decreases peripheral blood eosinophil counts.[10] The suggested mechanisms for the decrease in eosinophils caused by cigarette smoke include a direct (apoptotic) effect by toxic substances[24] and antiinflammatory substances such as carbon monoxide.[25] We were unable to find a report on the effect of WPS on peripheral blood eosinophils.

Fractional Exhaled Nitric Oxide
A decrease in Feno levels (P = .038) after WPS was found in our study. Several studies reported reduced levels of Feno after both short- and long-term cigarette smoking.[26] Possible mechanisms include downregulation of endothelial and inducible nitric oxide synthase, and rapid conversion of nitric oxide to peroxynitrite by reactive oxygen and

nitrogen species.[27,28] The clinical importance of the small decrease in Feno levels is questionable.

Exhaled Breath Condensate

According to our study, 8-isoprostane levels decreased after 30 min of WPS, while nitrotyrosine levels remained unchanged. The measurement of EBC is an emerging, relatively simple, and noninvasive method used for sampling the lower respiratory tract for biomarkers of airway inflammation and oxidative stress.[29] This technique has been used to evaluate the acute effects of cigarette smoking on various inflammatory markers in EBC.[30,31] Oxidative stress and airway inflammation together form a vicious cycle that is responsible for the disease progression in patients with COPD. The degree of oxidative stress can be assessed using compounds that generally result from lipid peroxidation (8-isoprostane) or nitrative stress (nitrotyrosine).[32] These two EBC parameters are more likely to be immediately affected. Increased levels of 8-isoprostane and a negative correlation between FEV_1 and nitrotyrosine levels were reported in patients with COPD.[32,33] Balint et al[33] reported unchanged nitrotyrosine levels after cigarette smoking, similar to our results.

The levels of 8-isoprostane decreased after WPS. Montuschi et al[34] reported increased 8-isoprostane levels 15 min after acute cigarette smoking, while Papaioannou et al[31] did not find any change in healthy cigarette smokers. Our finding of a decrease in 8-isoprostane levels after WPS was unexpected. This may be explained by the high levels of carbon monoxide, a potent antiinflammatory agent.[35] The small sample size precludes drawing firm conclusions on the mechanism for this observation.

The marginal statistically significant changes in PEFRs, percentage of eosinophils, and levels of $FEF_{25\%–75\%}$, Feno, and 8-isoprostane became insignificant after applying a Bonferroni correction. While the Bonferroni correction controls the probability of a type-1 error (α error), this correction ordinarily comes at the cost of increasing the probability of a type-2 error (β error). Therefore, these parameters require evaluation in a larger sample size.

The main limitation of our study includes the relatively small sample size, which was calculated based on changes in COHb concentrations and vital signs. Analyses for other parameters may have been underpowered. The study included only healthy volunteers rather than subjects with cardiovascular and pulmonary diseases. We assessed exposure to carbon monoxide indirectly and did not assess exposure to other smoke constituents known to exert health effects (eg, aldehydes, polycyclic aromatic hydrocarbons, nicotine). Because of technical problems, EBC analysis was performed only in 20 patients and no assessment of other EBC parameters (eg, other cytokines, pH) was performed. We evaluated the effect only after 30 min and did not aim to assess possible reversibility of these changes after several hours.

Summary

Our study demonstrates that one session of WPS caused significant cardiorespiratory changes in healthy volunteers. These changes were similar or even greater than those reported in cigarette smoking. Larger studies, including the evaluation of the short-term and long-term effects of WPS, are required. The results of our study add to the limited evidence that WPS is harmful and support interventions to control the continuing global spread of WPS, especially among youth.

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Trial registry
ClinicalTrials.gov; No.: NCT01157832; URL: www.clinicaltrials.gov

Abbreviations
COHb 5 carboxyhemoglobin; EBC = exhaled breath condensate; $FEF_{25\%–75\%}$ = forced expiratory flow between 25% and 75% of FVC; Feno = fractional exhaled nitric oxide; PEFR = peak expiratory flow rate; WP = water pipe; WPS = water-pipe smoking

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Author contributions
Drs Hakim and L. Bentur both had full access to the data and both will vouch for the integrity of the data analysis.
Dr Hakim: contributed to the recruitment of patients, performance of all tests, and writing of the study.
Mr Hellou: submitted the institutional review board application and contributed to the recruitment of patients, performance of all tests, data analysis, and literature survey.
Dr Goldbart: analyzed the nitrotyrosine data and contributed to the discussion of the exhaled breath condensate parameters.
Ms Katz: analyzed the 8-isoprostane data.
Dr Y. Bentur: contributed to the study design, data analysis, and writing of the study.
Dr L. Bentur: contributed to the study design, institutional review board application, data analysis, and writing of the study.

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