Research Article

Cancer Epidemiology, Biomarkers & Prevention

Significance of Smoking Machine Toxicant Yields to Blood-Level Exposure in Water Pipe Tobacco Smokers

Alan L. Shihadeh[1] and Thomas E. Eissenberg[2]

Abstract

Background: The global increase in tobacco smoking with a water pipe (hookah, narghile, or shisha) has made understanding its health consequences imperative. One key to developing this understanding is identifying and quantifying carcinogens and other toxicants present in water pipe smoke. To do so, the toxicant yield of machine-generated water pipe smoke has been measured. However, the relevance of toxicant yields of machine-generated smoke to actual human exposure has not been established.

Methods: In this study, we examined whether carbon monoxide (CO) and nicotine yields measured with a smoking machine programmed to replicate the puffing behavior of 31 human participants who smoked a water pipe could reliably predict these participants' blood-level exposure. In addition to CO and nicotine, yields of polyaromatic hydrocarbons, volatile aldehydes, nitric oxide (NO), and "tar" were measured.

Results: We found that when used in this puff-replicating manner, smoking machine yields are highly correlated with blood-level exposure (nicotine: $r > 0.76$, $P < 0.001$; CO: $r > 0.78$, $P < 0.001$). Total drawn smoke volume was the best predictor of toxicant yield and exposure, accounting for approximately 75% to 100% of the variability across participants in yields of NO, CO, volatile aldehydes, and tar, as well as blood-level CO and normalized nicotine.

Conclusions: Machine-based methods can be devised in which smoke toxicant yields reliably track human exposure.

Impact: This finding indicates the basic feasibility of valid analytic laboratory evaluation of tobacco products for regulatory purposes. *Cancer Epidemiol Biomarkers Prev; 20(11); 2457–60. ©2011 AACR.*

Introduction

As elsewhere in the world, tobacco smoking with a water pipe (hookah, narghile, or shisha) is rapidly becoming an epidemic in the United States, particularly among adolescents and young adults: 17% of a nationwide sample of 12th graders reported water pipe use in the past year (1), whereas water pipe tobacco smoking is the second most popular form of tobacco use among U.S. university students (Primack and colleagues, unpublished data). With a tobacco water pipe, burning charcoal is used to heat sweetened and flavored tobacco that is placed in the "head." When users inhale through the mouthpiece of the water pipe, hot charcoal combustion products are drawn through the tobacco, producing the mainstream smoke. The smoke is drawn through a water bubbler and then travels through the hose to the user (2).

To assess potential hazards posed by this burgeoning tobacco use method, we conducted studies on water pipe smoke toxicant content using laboratory smoking machines (e.g., see refs. 2, 3). These studies have shown that machine-generated water pipe smoke contains numerous toxicants implicated in smoking-related cardiovascular disease, cancer, lung disease, and addiction (3–5). However, the relevance of smoking machine yields to toxicant exposure of the water pipe user has not been established. Indeed, there is uncertainty about this relationship with cigarettes as well, despite decades of effort (e.g., see refs. 6–8). This uncertainty has become particularly salient in the United States following passage of the Tobacco Control Act. The act charged the U.S. Food and Drug Administration with regulating tobacco products and publishing product-specific test data on harmful smoke constituents. Importantly, the act defines as a tobacco product "any product made or derived from tobacco that is intended for human consumption" and thus includes in its purview water pipe tobacco. To inform this effort, in this study, we examined whether the toxicant yield of machine-generated water pipe smoke can predict human exposure to 2 important tobacco smoke toxicants: carbon monoxide (CO) and nicotine.

Authors' Affiliations: [1]Department of Mechanical Engineering, Faculty of Engineering and Architecture, American University of Beirut, Beirut, Lebanon; and [2]Department of Psychology, Virginia Commonwealth University, Richmond, Virginia

Corresponding Author: Thomas E. Eissenberg, Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Box 980205, Richmond, VA 23298. Phone: 804-827-4617; Fax: 804-828-7862; E-mail: teissenb@vcu.edu

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Materials and Methods

The Institutional Review Board–approved study involved recording digitally the puff topography of individual participants who smoked a water pipe under controlled conditions in a clinical laboratory while their blood was sampled to assess CO and nicotine exposure using carboxyhemoglobin (COHb) and blood nicotine concentration, respectively. Recruitment by printed media and word of mouth for the study resulted in 63 qualified individuals (who used 2–5 self-reported water pipe sessions per month, were between 18 and 50 years of age, healthy, and smoked <5 cigarettes per month) who consented to participate in the protocol. Of these, 22 did not pass initial screening and did not begin the study and 4 were discontinued during the study. The resulting pool of 37 participants (3 African American, 7 Asian, 20 Caucasian, 1 Hawaiian/Pacific Islander, and 6 mixed/other ethnicity) included 8 women and 29 men aged 20.5 ± 2.1 years (mean ± SEM), self-reported smoking water pipe tobacco 2 to 5 times per month (3.8 ± 1.0) for 6 months or longer (20.2 ± 12.9). Individuals were free to schedule the smoking session for any time of day and were required to abstain from smoking from the previous night onward (verified by exhaled breath CO <10 ppm). Participants were given a minimum of 45 minutes to puff freely from a water pipe loaded with 10 g of their preferred flavor of tobacco while watching a video of their choice. Tobacco was sourced from www.hookahcompany.com. Additional details of the clinical laboratory work can be found elsewhere (9).

Each puff topography record was then used to generate smoke with a smoking machine programmed to mimic human behavior to reproduce the puffing behavior of each participant in detail resolved to 0.1 seconds (10). The entire smoking session was replicated for each individual in the study whose puff topography record was valid (6 records could not be used because of technical errors with the topography instrument), and the resulting nitric oxide (NO), CO, nicotine, "tar", volatile aldehydes (VA), and polyaromatic hydrocarbons (PAH) were quantified. Except for NO, all analytes were determined as previously reported (3–5, 10), using gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography–mass spectrometry, Karl–Fisher titration, and electrochemical analyzers. NO was determined with a rapid-response EcoChem CLD 70S chemiluminescence analyzer. After passing through the filter assembly, a small fraction of the smoke drawn during each puff was diverted into the NO analyzer, and the resulting instantaneous NO volume concentration signal was logged. NO yield was then computed as the average of the instantaneous NO concentration times the total drawn volume. Nicotine content of the raw products was also analyzed by GC-MS (3) and used to calculate normalized nicotine dose (NND) as follows:

$$\mathrm{NND} = \frac{\text{Blood nicotine concentration} \times \text{blood volume}}{\text{Nicotine mass in raw product}}$$

NND is a nondimensional measure of blood level nicotine exposure relative to the total amount of nicotine available in the product. For each participant, blood volume was calculated on the basis of height, weight, and sex according to the formula of Nadler (11).

Pearson correlation coefficients (r) and probability values (P) were computed by the VassarStat CORRWIN macro (12) running in MS Excel 2007.

Results and Discussion

As shown in Fig. 1, we found that CO and nicotine yields were highly correlated with COHb ($r = 0.789$, $P < 0.0001$) and plasma nicotine concentration ($r = 0.762$, $P < 0.0001$). Similar relationships were found when plasma concentrations were adjusted for participant blood volume. Thus, at least for CO and nicotine, water pipe smoke yield closely tracks user exposure when a machine is programmed to reproduce the individual smoking behavior of water pipe tobacco smokers.

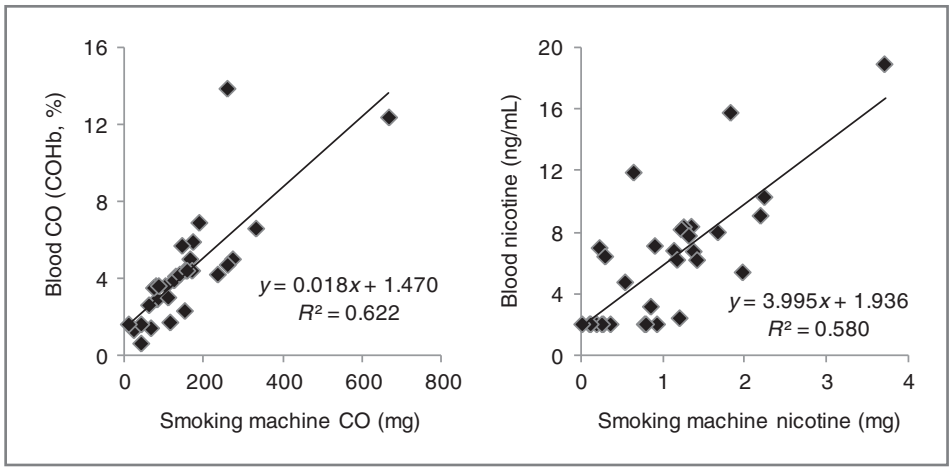

Figure 1. COHb and blood nicotine concentration post-smoking versus smoking machine yields for 31 participants. Smoking machine yields obtained by replicating recorded puffing sequences.

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We also found that toxicant yields and exposure were strongly correlated with CO yield, CO exposure, and drawn smoke volume (Table 1). These significant correlations suggest that any of these variables may have a value as a convenient proxy measure for other smoke toxicants such as NO, PAH, and VA. Except for PAH yield, smoke volume was the best predictor (i.e., largest Pearson *r*) of toxicant yield and exposure, accounting for approximately 75% to 100% of the variability across participants in yields of NO, CO, VA, and tar and exposure to CO and NND.

It is notable in Table 1 that nicotine yields and exposure are the least well-predicted parameters. However, when nicotine yield and exposure were normalized by the nicotine content of the raw tobacco product (NND = 15.2 ± 3.0 μg/mg), the strength of the correlations increased substantially and was similar in magnitude to that of other toxicant measures. Thus, nicotine yield and exposure are related to both the quantity of nicotine in the tobacco and the quantity of smoke inhaled: the more the user inhales, and the more nicotine that is available in the tobacco, the greater the amount of nicotine available to the user. That nicotine varied sufficiently across participants (and therefore tobacco products) to affect correlation with smoke volume, while other toxicants did not, is consistent with a physical model in which some smoke toxicants originate from the tobacco preparation (e.g., nicotine, tobacco-specific nitrosamines, and tar; ref. 2) whereas

Table 1. Pearson *r* correlations of toxicant exposure and smoking machine yield obtained for CO yield, CO dose, and smoke volume

	CO yield	CO dose	Smoke volume
Puff topography			
Smoke volume	0.92[a]	0.94[a]	1
Blood exposure			
COHb	0.79[a]	0.98[a]	0.90[a]
CO dose	0.82[a]	1	0.94[a]
Nicotine concentration	0.37[b]	0.44[b]	0.41[b]
Nicotine dose	0.36[b]	0.43[b]	0.41[b]
Normalized nicotine dose	0.49[b]	0.71[a]	0.79[a]
Machine yields			
Tar	0.82[a]	0.64[a]	0.76[a]
CO	1	0.82[a]	0.92[a]
NO	0.97[a]	0.93[a]	0.98[a]
Nicotine	0.41[b]	0.29 (n.s.)	0.36[b]
Nicotine (normalized)	0.57[b]	0.52[c]	0.65[a]
PAH			
Fluoranthene	0.65[a]	0.48[a]	0.59[a]
Pyrene	0.67[a]	0.51[a]	0.63[a]
Benzo[*a*]anthracene	0.72[a]	0.50[a]	0.60[a]
Chrysene	0.60[a]	0.48[a]	0.56[a]
Benzo[*b*+*k*]fluoranthenes	0.60[a]	0.43[a]	0.54[a]
Benzo[*a*]pyrene	0.56[a]	0.24[a]	0.33[a]
Benzo[*g*,*h*,*i*]perylene	0.58[a]	0.42[a]	0.42[a]
Indeno[1,2,3-*cd*]pyrene	0.57[a]	0.40[a]	0.42[a]
Aldehydes			
Formaldehyde	0.62[a]	0.92[a]	0.84[a]
Acetaldehyde	0.91[a]	0.87[a]	0.94[a]
Acetone	0.85[a]	0.77[a]	0.87[a]
Propionaldehyde	0.82[a]	0.82[a]	0.86[a]
Methacrolein	0.71[a]	0.57[a]	0.65[a]
Nicotine content in product			
Nicotine in product	–0.069 (n.s.)	0.25 (n.s.)	0.23 (n.s.)

NOTE: Dose = blood concentration × estimated blood volume. Normalized nicotine dose = nicotine dose/nicotine in tobacco product.
Abbreviation: n.s., not significant.
[a]$P < 0.001$.
[b]$P < 0.05$.
[c]$P < 0.01$.

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others are produced by the burning charcoal (e.g., CO and PAHs; ref. 13), or its interaction with tobacco humectants and flavorings (e.g., VA).

Taken together, the data show that water pipe smoke that is generated by a machine programmed to mimic human behavior can be used to predict CO and nicotine exposure and that smoke volume or CO exposure may also be valuable in predicting exposure to other toxicants, especially when the contents of the smoked products are taken into account.

Although this study used a machine that was programmed to reproduce multiple individuals' puffing sequences, averaged smoking profiles may be more cost-efficient and equally valuable. That is, we have previously found that CO, nicotine, and tar content of smoke sampled in real time from the water pipes of individual users can be estimated reliably by programming a machine to smoke using puff parameters that represent the averaged puff number, volume, duration, and interpuff interval for those individuals (14). Combined with the observation reported here that yield relates to exposure, it can be deduced that meaningful estimates of toxicant exposure can likely be obtained when a water pipe tobacco product is machine tested using an average puffing regimen that reflects the ordinary use of that product. Similar lessons may hold for other tobacco use methods, including cigarettes. However, the generalizability of the results may be limited to the population represented by the individuals whose topography records were averaged.

In conclusion, this study empirically shows that machine-based methods can be devised in which smoke toxicant yields reliably track human exposure. This finding suggests the basic feasibility of laboratory evaluation of smoked tobacco products for regulatory purposes.

Disclosure of Potential Conflicts of Interest

The study sponsor had no role in the study design, data collection, data analysis and interpretation, or in the preparation of this report.

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