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Acute effects of waterpipe tobacco smoking: A double-blind, placebo-control study☆

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ABSTRACT

Background: Waterpipe tobacco smoking usually involves heating flavored tobacco with charcoal and inhaling the resulting smoke after it has passed through water. Waterpipe tobacco smoking increases heart rate and produces subjective effects similar to those reported by cigarette smokers. These responses are thought to be nicotine-mediated, though no placebo-control studies exist. Accordingly, this double-blind, placebo-control study compared the acute physiological and subjective effects of waterpipe tobacco smoking to those produced when participants used a waterpipe to smoke a flavor-matched, tobacco-free preparation.

Methods: Occasional waterpipe tobacco smokers ($n = 37$; 2–5 monthly smoking episodes for ≥6 months) completed two double-blind, counterbalanced sessions that differed by product: preferred brand/flavor of waterpipe tobacco or flavor-matched, tobacco-free preparation. For each 45-min, *ad lib* smoking episode blood and expired air CO were sampled, cardiovascular and respiratory response were measured, and subjective response was assessed.

Results: Waterpipe tobacco smoking significantly increased mean (±SEM) plasma nicotine concentration (3.6 ± 0.7 ng/ml) and heart rate (8.6 ± 1.4 bpm) while placebo did not (0.1 ± 0.0 ng/ml; 1.3 ± 0.9 bpm). For carboxyhemoglobin (COHb) and expired air CO, significant increases were observed for tobacco ($3.8 \pm 0.4\%$; 27.9 ± 2.6 ppm) and for placebo ($3.9 \pm 0.4\%$; 27.7 ± 3.3 ppm) with no differences across condition. Independent of condition, symptoms of nicotine/tobacco abstinence (e.g., "urges to smoke", "anxious") were reduced and direct effects (e.g., "dizzy", "satisfy") increased.

Discussion: These results from the first placebo-control study of waterpipe tobacco smoking demonstrate that waterpipe-induced heart rate increases are almost certainly mediated by nicotine though the subjective effects observed in these occasional smokers were not.

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1. Introduction

For centuries, millions of people have smoked tobacco using a waterpipe (a.k.a. hookah, narghile, shisha): inhalation of charcoal-heated air passes through tobacco, travels down the body, and bubbles through water in the bowl before reaching smokers' lungs (World Health Organization, 2005). While often associated with southwest Asia, waterpipe tobacco smoking is now seen worldwide (e.g., Pärna et al., 2008; Jensen et al., 2010). In the U.S., for example, past 30-day waterpipe tobacco smoking has been reported by 9–20% of some college samples (Cobb et al., 2010). A survey of 8745 students from 8 universities revealed that 7.2% reported past 30-day use and 29.5% reported "ever use" (Primack et al., 2010). Past 30-day use among 14–18 year old Arab-Americans may be as high as 16% and non-Arab-Americans as high as 11% (Weglicki et al., 2007).

One reason for the global spread of waterpipe tobacco smoking may involve the oft-reported belief that waterpipes are less risky than cigarettes (Aljarrah et al., 2009; Smith-Simone et al., 2008). This belief seemingly is contradicted by demonstrations that various constituents of waterpipe smoke are known to cause cancer (e.g., polycyclic aromatic hydrocarbons [PAH]; Sepetdjian et al., 2008), lung disease (e.g., volatile aldehydes; Al Rashidi et al., 2008),

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cardiovascular disease (e.g., carbon monoxide [CO]; Shihadeh and Saleh, 2005), and dependence (i.e., nicotine; Shihadeh, 2003). At least some of these smoke toxicants have been found in waterpipe tobacco smokers during smoking, including CO and nicotine (El-Nachef and Hammond, 2008; Shafagoj and Mohammed, 2002).

While there is a growing literature investigating waterpipe smoke toxicant content and exposure, relatively few studies have examined the acute effects of waterpipe tobacco smoking. In terms of cardiovascular response, two laboratory studies demonstrate that waterpipe tobacco smoking produces clear cardiovascular effects. A single 45-min waterpipe smoking episode has been shown to increase average heart rate (HR) by 6 (Eissenberg and Shihadeh, 2009) or 16 bpm (Shafagoj and Mohammed, 2002), as well as to increase systolic blood pressure (SBP) by 6.7 mmHg, diastolic blood pressure (DBP) by 4.4 mmHg and mean arterial pressure (MAP) by 5.2 mmHg (Shafagoj and Mohammed, 2002). In both studies these cardiovascular effects were attributed to waterpipe-induced increases in plasma nicotine (see also Shafagoj et al., 2002). Subjective effects of waterpipe tobacco smoking have also been observed; the suppression of tobacco abstinence symptoms commonly reported in cigarette smokers (e.g., urges to smoke, craving) were suppressed following a single waterpipe use episode (Maziak et al., 2009). These subjective effects are also thought to be mediated by waterpipe-delivered nicotine.

Importantly, the role of nicotine as a causal factor in the acute effects of waterpipe smoking is speculative, as no study has included a nicotine-free placebo condition using double-blind administration procedures. Without such a study, several non-nicotine factors might explain some effects observed during waterpipe tobacco smoking, including CO intoxication (e.g., Lim et al., 2009), expectancy, or activity associated with the use episode. Therefore, the purpose of this double-blind, placebo-control, within-subject study of waterpipe use was to determine the extent to which the acute effects of waterpipe tobacco smoking were due to nicotine exposure. We hypothesized that cardiovascular and subjective effects reported elsewhere would also be observed when participants used a waterpipe to smoke tobacco that delivered nicotine, but not when participants smoked a tobacco-free herbal waterpipe preparation that did not deliver nicotine.

2. Materials and methods

2.1. Participants

Eight women and 29 men were recruited for this university IRB-approved study. These individuals (three African-American, seven Asian, 20 Caucasian, one Hawaiian/Pacific Islander and six mixed/other ethnicity) were healthy, between the ages of 18–50 (mean ± standard error of the mean [SEM] = 20.5 ± 2.1 years) and reported smoking waterpipe tobacco 2–5 times/month (3.8 ± 1.0) for ≥six months (20.2 ± 12.9). Participants' average expired air CO level at screening was 2.5 ± 1.6 ppm. Exclusion criteria included self-reported history of chronic health problems or psychiatric conditions, regular use of prescription medications (other than vitamins or birth control), and current pregnancy (verified by urinalysis) or breastfeeding, as well as self-reported current use of >5 cigarettes/month, other tobacco products, marijuana (>5 days in past month) or other illicit drugs (past 30-day use of cocaine, benzodiazepines, opioids, or methamphetamine; confirmed by urinalysis).

2.2. Materials

The waterpipe consisted of a chrome body (43 cm) screwed into an acrylic base (24 cm; volume 1230 ml; www.myasaray.com). Approximately 2.5 cm of the body's conduit was submerged by 870 ml water poured into the base. The glazed ceramic head (7.6 cm; five, 6 mm holes in bottom) was covered with a circular sheet of aluminum foil, perforated by a screen pincher (www.smoking-hookah.com). A 33 mm, quicklighting charcoal briquette (Three Kings, Holland) was placed on top of the foil. The leather hose was fitted with topography measurement hardware and included a wooden mouthpiece capped with a sterile plastic tip (www.hookahcompany.com).

During the active waterpipe condition, participants smoked their preferred brand and flavor of product. The most popular tobacco brand was Starbuzz (U.S.; $n = 18$), followed by Nakhla (Egypt; $n = 2$) and Al Fakher (United Arab Emirates; $n = 2$); Nakhla was used as the default brand for participants who did not report a preference ($n = 15$). The most popular flavors were fruit-based: apple/double apple ($n = 8$), strawberry ($n = 6$), mango ($n = 4$), peach ($n = 3$), cherry ($n = 2$), watermelon ($n = 2$), as well as grape, mixed fruit, orange, and guava (each $n = 1$). Other preferred flavors were mint ($n = 6$), rose ($n = 1$), and vanilla ($n = 1$). During the placebo waterpipe condition, participants smoked a flavor-matched, tobacco-free herbal product (Soex; Soex India Pvt. Ltd., Mumbai, India). According to the manufacturer, Soex is "100% tobacco-free and nicotine-free", primarily composed of chopped "sugar cane, molasses, and flavor".

2.3. Study design and procedures

Participants completed two counterbalanced, 2-h sessions that differed by product used: active waterpipe tobacco or flavor-matched tobacco-free placebo. Participants were notified during the informed consent process that they would be a smoking a product that "may or may not contain tobacco" during each session. Once overnight tobacco abstinence was verified (CO levels ≤10 ppm), a catheter was inserted into a forearm vein and physiological recording commenced. Thirty minutes later, breath, blood, and subjective response were measured and session-specific product was administered: a waterpipe containing 10 g of product in the foil-covered head with a lit charcoal briquette placed on top (additional half briquettes available upon request). The waterpipe head was always packed and emptied by a researcher who had no participant contact. A foil covering obscured head contents, and neither participant nor study staff was informed of the product to be used on a particular day. Participants were given a minimum of 45 min to smoke the waterpipe *ad lib* while watching a video of their choice. Blood, breath, and subjective response were measured periodically during and/or after the smoking episode. The laboratory was ventilated and during session mean peak ambient CO level was 4.0 ± 1.0 ppm (collapsed across condition, $n = 64$ samples). Payment for completing both sessions was $175.

2.4. Physiological measures

Expired- and ambient-air CO were assessed with a BreathCO monitor (Vitalograph, Lenexa, KS). Carboxyhemoglobin (COHb) concentration was analyzed within 2 min after venous blood sampling (NPT7 blood gas analyzer, Radiometer America); 10 ml of the blood sample was centrifuged, plasma stored at −70 °C, and analyzed for nicotine level (limit of quantitation [LOQ] 2.0 ng/ml; modified LC–MS/MS version of that reported by Naidong et al. (2001); see Breland et al., 2006). HR was measured every 20 s and BP every 5 min (Model 507E, Criticare Systems).

Cigarette smoking has been shown to alter expired air nitric oxide (NO) acutely (Kharitonov et al., 1995; Chambers et al., 1998), and NO is related to pulmonary disease (Louhelainen et al., 2008); changes in NO due to waterpipe tobacco smoking are unclear. Thus, expired NO was analyzed using a Nitric Oxide Analyzer (280i, Ionics Inst); the average of three satisfactory measurements for each time point was used in analyses. Previous work suggests that waterpipe smoking may impair lung function (Aydin et al., 2004; Kiter et al., 2000); thus, pulmonary function testing (PFT) was performed with a spirometer (Vitalograph, Lenaxa, KS) to measure forced expiratory volume in 1 s (FEV_1), forced expiratory vital capacity (FVC), and FEV_1/FVC ratio (National Collaborating Centre for Chronic Conditions, 2003). The better of two satisfactory PFT maneuvers (based on FEV_1 results) was used in analyses.

2.5. Subjective measures

All subjective measures were computerized (as in Breland et al., 2006). Individual items for each measure are outlined in Table 1.

The Hughes and Hatsukami (1986) questionnaire consists of 11 Visual Analog Scale (VAS) items. Items are presented as a word or phrase centered above a horizontal line that ranges from 0 ("Not at all") to 100 ("Extremely"). Participants used a computer mouse to place a vertical mark anywhere along the horizontal line, and the score is the distance of the vertical mark from the left anchor, expressed as a percentage of total line length.

The Tiffany-Drobes Questionnaire of Smoking Urges (QSU): Brief Form (Cox et al., 2001) consists of 10 smoking-related items (e.g., "I crave a cigarette right now") that participants rate on a 7-point scale ("Strongly disagree" to "Strongly agree"). The items were collapsed into two previously-defined factors: 'intention to smoke' (Factor 1) and 'anticipation of relief from withdrawal' (Factor 2).

The Direct Effects of Nicotine Scale (DENS) consists of 15 VAS items developed to assess the incidence of nicotine-related side effects (Evans et al., 2006), and the Direct Effects of Tobacco Scale (DETS) consists of 13 VAS items developed to asses commonly reported cigarette smoking effects (Foulds et al., 1992; items modified so that the word "cigarette" was replaced by "waterpipe").

2.6. Smoking topography measures

Topography was measured via a pressure transducer integrated into the waterpipe hose (Shihadeh et al., 2005), whereby inhalation-induced pressure changes are amplified, digitized, and sampled. Software converts signals to air flow (ml/s) and