Published in final edited form as:

Tob Regul Sci. 2020 November ; 6(6): 416–422. doi:10.18001/trs.6.6.5.

Variable Voltage, Tank-Style ENDS Do Not Always Deliver Nicotine

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Abstract

Objective: This study's objective was to characterize the nicotine delivery profile of a variable voltage, tank-style electronic nicotine delivery system (ENDS).

Methods: Ten cigarette smokers (8 men, 2 women) completed this within-subject study assessing effects of 2 device power settings (15 W, 45 W) and 3 liquid nicotine concentrations (0, 3, and 6 mg/ml) using a tank-style ENDS. Participants completed one directed (10 puffs) and one *ad libitum* use period for each condition, with blood sampled throughout.

Results: Plasma nicotine concentration did not increase significantly at 15 W regardless of liquid nicotine concentration. At 45 W, mean plasma nicotine increased (not significantly compared to 0 mg/ml) from 2.24 ng/ml (SD=0.2) at baseline to 3.4 ng/ml (SD=0.6) in the 3 mg/ml condition. In the 6 mg/ml, 45 W condition, mean plasma nicotine increased significantly (compared to 0 mg/ml) from 2.0 ng/ml (SD=0) at baseline to 5.96 ng/ml (SD=1.3) after 10 puffs. In general, puff duration and volume decreased as device power and nicotine concentration increased.

Conclusions: Despite using a variable wattage, tank-style device, nicotine delivery was minimal. These results, when combined with results from other studies using tank-style devices,

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Human Subjects Statement

This study was approved by Virginia Commonwealth University's (VCU's) institutional review board (IRB).

Conflict of Interest Statement

Dr. Eissenberg is a paid consultant in litigation against the tobacco industry and also the electronic cigarette industry and is named on one patent for a device that measures the puffing behavior of electronic cigarette users and on another patent for a smartphone app that determines electronic cigarette device and liquid characteristics.

highlight ENDS performance heterogeneity. Regulation may play a role in standardizing ENDS nicotine delivery.

Keywords

ENDS; nicotine delivery

INTRODUCTION

Electronic cigarettes, or electronic nicotine delivery systems (ENDS) produce an aerosol by heating a liquid that typically contains nicotine. As ENDS use has become increasingly popular worldwide,^{1,2} devices have diversified.³ For example, while early ENDS models looked like a combustible cigarette and operated at 5–10 watts (W), more recent models are varied in shape and size and electrical power may range from 8–200 W.⁴ Power is important, as doubling wattage can triple nicotine emissions⁵ and aerosols generated from a low nicotine concentration liquid (eg, 4 mg/ml) at higher wattages (ie, 70 W) can deliver nicotine as effectively as a combustible cigarette.⁶ However, ENDS nicotine delivery profiles can vary considerably,⁷ and users of high powered devices may not know if the power/liquid combination they are using will provide them with no nicotine, little nicotine, or more nicotine than a combustible cigarette. This study's purpose is to investigate further the heterogeneity in ENDS nicotine delivery by varying device power and liquid nicotine concentration systematically and measuring nicotine delivery as well as users' puffing behavior (puff topography), which can also affect nicotine delivery.⁸

METHODS

Participants

This study was approved by Virginia Commonwealth University's institutional review board. Eligible participants were healthy (based on self-reported medical history), between 18–55 years, weighed >110 pounds, smoked 10 cigarettes/day, and had an expired air carbon monoxide (CO) concentration 15 ppm at screening. Participants were excluded if they reported >20 ENDS uses lifetime, alcohol use >25 days/month, cannabis use >15 days/month, any other illicit drug use in the past month, chronic disease and/or psychiatric condition history, and current pregnancy or breastfeeding.

Materials

Participants used a Kangertech "Cupti" ENDS with a 3.7 volt battery and 0.5 ohm coil (one participant received a 1.5 ohm coil for one session, but the device adjusted voltage to assure the same power). When this study was initiated (2017), little data were available regarding variable-voltage devices. This device was recommended by local vape shop staff, who characterized it as popular and one of few ENDS devices with the power capabilities required for this study. The tank was filled with ~3 ml ENDS liquid (50%/50% PG/VG, AVAIL Vapor, Richmond VA), with menthol or tobacco flavor based on participants' preferred cigarette. For all liquids, labeled nicotine concentration was consistent with analysis results from an independent laboratory (+/-0.2 mg/ml). Sessions differed by power (15 or 45 W) and liquid nicotine concentration (0, 3, or 6 mg/ml, free base).

Procedure

Prior to each laboratory session, participants abstained from nicotine/tobacco for 12 hours (verified with expired air CO 10 ppm). Participants attended a total of 6 sessions separated by 48 hours. Each session consisted of one 10-puff directed ENDS use bout (~30 sec interpuff interval)^{8,9} followed by a 30-minute waiting period, after which participants completed a 90-minute *ad libitum* bout.

Outcome measures

Physiological measures.—Blood was sampled (7 ml) immediately before and twice after the directed bout (0, 10, and 20 min), immediately before and twice during the *ad libitum* bout (35, 65, and 95 min), and twice after the *ad libitum* bout (125 and 140 min). Blood samples were processed and analyzed as reported previously (LOQ=2 ng/ml).¹⁰

Puff topography.—Puff topography was measured by a mouthpiece-based topography recording device (eTop, American University of Beirut, Lebanon). Puff number, duration and volume were recorded.

Measures collected but not reported.—Subjective effects (ie, nicotine/tobacco abstinence, direct effects of nicotine)¹⁰ and heart rate and blood pressure were assessed but are not reported here due to space constraints.

Data Preparation and Statistical Analyses

Baseline plasma samples were examined for nicotine/tobacco abstinence; values greater than 5.0 ng/ml nicotine indicated failure to abstain.¹⁰ Fourteen participants completed this study, and 10 were included in final analyses. Among the 4 participants not included, 2 were excluded due to baseline plasma nicotine >5 mg/ml, and 2 due to experimenter error.

Repeated measures ANOVAs with liquid nicotine concentration (0, 3, and 6 mg/ml), device power (15 and 45 W), and time (8 levels for plasma nicotine; 2 for topography) were performed using IBM SPSS (Version 26). Paired samples t-tests (with Bonferroni corrections for non-orthogonal comparisons) were used to analyze plasma nicotine concentration and topography measures across liquid nicotine concentration and device power.¹¹

Exploratory analyses of the device itself were also conducted (pressure drop and the mass of aerosol exiting the device).

RESULTS

Participant Characteristics

Data from 10 cigarette smokers (8 men and 2 women; 5 African American, 4 Caucasian, one “other”) were included in the analyses. One participant identified as Hispanic. Participants’ mean age was 35.3 years (SD=10.2), and they reported smoking 16.4 cigarettes/day (SD=4.9) for an average of 11.7 years (SD=8.3); mean screening CO was 21.8 ppm

(SD=6.3). Participants were moderately nicotine dependent, as indicated by a mean score of 4.7 (SD=1.9) on the Fagerström Test for Nicotine Dependence.¹²

Plasma Nicotine Concentration

A significant liquid nicotine concentration by time interaction was observed for plasma nicotine concentration [$F(1,9)=4.9$, $p < .05$]. Significant main effects of nicotine concentration, power, and time also were observed [$F(1,9)>7.0$, $ps < .05$]. Figure 1 depicts the plasma nicotine means for each condition and time point.

Paired samples t-tests revealed no significant differences at any time point within the 15 W conditions. For the 3 mg, 45 W condition, mean plasma nicotine concentration was 2.2 ng/ml (SD=0.2) at baseline and 3.4 ng/ml (SD=0.6) after 10 puffs, with no significant differences compared to 0 mg, but significant differences were observed between 0 and 3 mg/ml at all time points during and following the *ad libitum* bout [$t(9)<-3.4$; $ps < .025$] (see Figure 1).

Significant differences were observed in the 45 W condition between 0 and 6 mg/ml at the 10 minute, 20 minute, and 35 minute time points [$t(9)<-2.8$, $ps < .025$]. For the 6 mg, 45 W condition, following the directed bout, mean plasma nicotine concentration was 6.0 ng/ml (SD=1.3), significantly higher than the 0 mg, 45 W condition at this time point. Last, as Figure 1 also shows, relative to the 15 W condition, plasma nicotine concentration was significantly greater ($ps < .05$) in the 45 W condition for the 3 mg/ml condition at the 35-minute [$t(9) = -2.5$] and 140-minute [$t(9) = -2.6$] timepoints, and for the 6 mg/ml concentration at the 10 minute [$t(9)=-2.9$], 20 minute [$t(9)=-3.2$], and 35 minute [$t(9)=-2.5$] time points.

Puff Topography

A main effect of concentration was observed for puff duration, and a main effect of power was observed for puff duration and puff volume [$F(1,9)>6.0$, $ps < .05$]. Significant differences in puff duration were revealed between 15 W and 45 W for all liquid nicotine concentrations [$t>3.1$, $ps < .05$] during both ENDS use bouts. Generally, puff duration was shorter in the higher-powered conditions. For example, within the 6 mg/ml condition, mean puff duration in the 15 W condition was 3.25 seconds (SD=0.25) compared to the 45 W condition mean of 1.89 seconds (SD=0.23). Comparing the 15 W to the 45 W conditions, puff volume decreased significantly in the higher-powered conditions for the 0 and 6 mg/ml conditions during the directed bout [$t>3.3$, $ps < .025$], and in all liquid nicotine concentrations during the *ad libitum* bout [$t>3.5$, $ps < .025$]. Mean puff volume in the 3 mg/ml condition was 185.0 ml (SD=24.6) in the 15 W condition compared to 98.4 ml (SD=31.7) in the 45 W condition. Means are presented in Table 1.

Device Testing

The specific device used (Kangertech “Cupti”) may be relevant. From a design perspective, compared to other sub-Ohm ENDS, this device has smaller airflow passages, making user inhalation more difficult (higher pressure drop). This feature may influence puffing behavior; in combustible cigarettes, pressure drop and flow rate are correlated inversely.¹⁶

To test this theory, we measured the pressure drop of the Cupti and found it to be relatively high compared to other sub-Ohm devices operating at similar conditions. Interestingly, when participants puffed on a Cupti in this study, the average flow rate was relatively low, 38.3 (SD=2.4) vs. 160.2 (SD=55.4) ml/sec reported with a different device.¹³ A lower flow rate indicates less air dilution and, therefore, a higher concentration aerosol inside the ENDS which can result in greater aerosol losses. As the aerosol exits through the ENDS' air tube, a fraction of the aerosol will condense on its surfaces: a higher concentration will generally result in higher aerosol amounts condensing on the surface of the wall and less aerosol (and nicotine) exiting the mouthpiece. To test this hypothesis, we compared the mass of aerosol exiting the 45 W Cupti after 15, 4-sec puffs at 1, 2, and 8 L/min and observed a mean of 364 (SD=39), 564 (SD=103), and 744 (SD=117) mg.⁵ This outcome suggests a correlation between air flow rate and the aerosol mass exiting the ENDS, mostly likely due to deposition parameters. In addition, the Cupti tank is located near the bottom of the battery, which features a vertical cavity. Thus, the aerosol needs to travel a longer distance to reach the device's mouthpiece and user, which may increase aerosol losses.

CONCLUSIONS

This study examined the interaction between 2 factors (device power and liquid nicotine concentration) previously shown to influence nicotine delivery for some ENDS.^{6,8} Following 10 puffs, reliable nicotine delivery was observed in the 6 mg/ml, 45 W condition only.

One other study has been conducted with a device set to a similar wattage and using similar liquid nicotine conditions.¹³ In that study, which used 40.5 W and 3 and 8 mg/ml nicotine, reliable nicotine delivery was observed, along with slightly longer puff durations. Thus, for higher wattage devices (ie, 40.5–45 W), paired with 3–8 mg/ml nicotine, puff duration may affect nicotine delivery, as others have noted.^{14,15} However, the puff duration observed in this study was similar to other studies on ENDS-naïve cigarette smokers.⁸ Differences in puff duration do not fully explain all differences in nicotine delivery.

Notably, participants in this study were able to obtain nicotine during the *ad libitum* use period, particularly in the 6 mg/ml, 45 W condition, but this was after an average of 40.1 (SD=4.8) puffs. Even after 40 puffs, nicotine delivery was much less than typically seen after 10 puffs of a combustible cigarette (~16–20 ng/ml).⁹ Additionally, only 2 participants' plasma nicotine concentration increased to over 10 ng/ml during the *ad libitum* use period. These results suggest that this device can deliver nicotine in some instances, but nicotine delivery is atypical. As described in the results section, our findings may be influenced by the design of this particular device.

The results presented here suggest caution when making assumptions about ENDS type/style and nicotine delivery. While early "cig-alike" devices generally failed to deliver nicotine after 10 puffs,^{9,17} and some studies have shown that later "pen-like" styles and tank systems can deliver nicotine,^{6,8,13,17–19} device type alone does not predict nicotine delivery reliably (even when operating at ~45 W). This observation is not unique: other work demonstrates that some devices categorized as "advanced" or "third generation"

deliver less nicotine while others deliver more.^{6,19} Comparing devices head-to-head across studies is difficult as puffing regimens, power settings, and liquid concentrations often differ. Several studies have used a 10-puff use period along with a tank-style system, and these methodological similarities make cross-study comparisons more meaningful. In one study, with an EVIC device paired with 18 mg liquid, plasma nicotine increased after 10 puffs from 2.46 ng/ml (SEM=0.33) to 6.59 ng/ml (SEM=0.62).¹⁷ In another study, after 10 puffs from a Subox Mini C (varying liquid and power settings) no nicotine delivery was observed in one condition (3 mg/ml nicotine; 13.5 W), in another (3 mg/ml nicotine; 40.5 W) nicotine increased from 2.5 ng/ml (SD=1.5) to 7.0 ng/ml (SD=5.0), and in another (8 mg/ml nicotine; 40.5 W) nicotine increased from 2.7 ng/ml (2.6) to 10.2 ng/ml (8.2).¹³ In a third study, after 10 puffs, plasma nicotine with participants' own brand of "third generation" device increased to 17.5 ng/ml (SD=12.9; note that this large standard deviation suggests substantial variability within the group).⁶ Taken together, these data from several studies using tank systems to investigate ECIG nicotine delivery profile demonstrate the tremendous heterogeneity in nicotine delivery profile across this one class of ECIGs. Importantly, terms such as "tank-style" (or "advanced" or "third generation") often are used to categorize ENDS in survey studies in the US and other countries.^{20, 21} Such categorizations are unreliable with respect to device nicotine delivery profile and should not be used for that purpose.

This study had several limitations. First, the sample size was small. However, observed effect sizes for plasma nicotine and puff duration were large, particularly for the main effects of nicotine concentration and power setting (for plasma nicotine partial eta squared=0.44 and 0.45; for puff duration, partial eta squared=0.41 and 0.87). Second, the range of liquid nicotine concentrations was narrow. Third, this study investigated a single device and did not compare across different devices.

IMPLICATIONS FOR TOBACCO REGULATION

There is much concern about how to regulate ENDS effectively in the United States. Many international regulations already implemented do not address the heterogeneity of ENDS device and liquid components.^{22,23} Some have suggested nicotine delivery as a target for regulation;²³ another potential regulatory target is nicotine flux, or the amount of nicotine emitted from ENDS mouth-end per unit time.²⁴ Regulations addressing this target, rather than individual device/liquid characteristics that influence it, would be a step toward reducing the heterogeneity of nicotine delivery across ENDS devices. While this heterogeneity remains, device "generation" or appearance will continue to be unreliable proxies for ENDS nicotine delivery.

Acknowledgements

This study was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number P50DA036105 and U54DA036105 and the Center for Tobacco Products of the U.S. Food and Drug Administration. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Food and Drug Administration.

The authors would like to thank and recognize the contributions of Barbara Kilgalen, Janet Austin, Melanie Crabtree, and Lauren Ratliff, who assisted with data collection and management.

This work has been presented previously at the 2018 NIH Tobacco Regulatory Science Meeting in Bethesda, MD.

References

1. King BA, Gammon DG, Marynak KL, et al. Electronic cigarette sales in the United States, 2013–2017. *JAMA*. 2018;320(13):1379. [PubMed: 30285167]
2. Yoong SL, Stockings E, Chai LK, et al. Prevalence of electronic nicotine delivery systems (ENDS) use among youth globally: a systematic review and meta-analysis of country level data. *Aust N Z J Public Health*. 2018;42(3):303–8. [PubMed: 29528527]
3. Breland A, Soule E, Lopez A, et al. Electronic cigarettes: what are they and what do they do? *Ann N Y Acad Sci*. 2016;1394(1):5–30. [PubMed: 26774031]
4. Rudy AK, Leventhal AM, Goldenson NI, et al. Assessing electronic cigarette effects and regulatory impact: challenges with user self-reported device power. *Drug Alcohol Depend*. 2017;179:337–340. [PubMed: 28843084]
5. Talih S, Balhas Z, Eissenberg T, et al. Effects of user puff topography, device voltage, and liquid nicotine concentration on electronic cigarette nicotine yield: measurements and model predictions. *Nicotine Tob Res*. 2014;17(2):150–157. [PubMed: 25187061]
6. Wagener TL, Floyd EL, Stepanov I, et al. Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. *Tob Control*. 2016;26(e1).
7. Voos N, Goniewicz ML, Eissenberg T. What is the nicotine delivery profile of electronic cigarettes? *Expert Opin Drug Deliv*. 2019;16(11):1193–1203. [PubMed: 31495244]
8. Hiler M, Breland A, Spindle T, et al. Electronic cigarette user plasma nicotine concentration, puff topography, heart rate, and subjective effects: influence of liquid nicotine concentration and user experience. *Experi Clin Psychopharmacol*. 2017;25(5):380–392.
9. Vansickel AR, Cobb CO, Weaver MF, et al. A clinical laboratory model for evaluating the acute effects of electronic “cigarettes”: nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiol Biomarkers Preven*. 2010;19(8):1945–1953.
10. Maloney SF, Breland A, Soule EK, et al. Abuse liability assessment of an electronic cigarette in combustible cigarette smokers. *Experi Clin Psychopharmacol*. 2019;27(5):443–454.
11. Ramôa CP, Hiler MM, Spindle TR, et al. Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: a preliminary report. *Tob Control*. 2015;25(e1).
12. Heatherton TF, Kozlowski LT, Frecker RC, et al. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict*. 1991;86(9):1119–1127. [PubMed: 1932883]
13. Hiler M, Karaoghlanian N, Talih S, et al. Effects of electronic cigarette heating coil resistance and liquid nicotine concentration on user nicotine delivery, heart rate, subjective effects, puff topography, and liquid consumption. *Experi Clin Psychopharmacol*. 2019.
14. Devito EE, Krishnan-Sarin S. E-cigarettes: Impact of e-liquid components and device characteristics on nicotine exposure. *Curr Neuropharmacol*. 2018;16(4):438–459. [PubMed: 29046158]
15. Blank MD, Pearson J, Cobb CO, et al. What factors reliably predict electronic cigarette nicotine delivery?. *Tob Control*. 2019.
16. Zacny JP, Stitzer ML, Yingling JE. Cigarette filter vent blocking: effects on smoking topography and carbon monoxide exposure. *Pharmacol Biochem Behav*. 1986;25(6):1245–1252. [PubMed: 3809227]
17. Farsalinos KE, Spyrou A, Tsimopoulou K, et al. Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices. *Sci Rep*. 2014;4(1).
18. Harvanko AM, Helen GS, Nardone N, et al. Twenty-four-hour subjective and pharmacological effects of ad-libitum electronic and combustible cigarette use among dual users. *Addiction*. 2020.
19. Yingst JM, Foulds J, Veldheer S, et al. Nicotine absorption during electronic cigarette use among regular users. *PloS One*. 2019;14(7).

20. Coleman B, Chang JT, Rostron BL, et al. An examination of device types and features used by adult electronic nicotine delivery system (ENDS) users in the PATH study, 2015–2016. *Int J of Environ Res Public Health*. 2019;16(13):2329.
21. Hitchman SC, Brose LS, Brown J, et al. Associations between e-cigarette type, frequency of use, and quitting smoking: findings from a longitudinal online panel survey in Great Britain. *Nicotine Tob Res*. 2015;17(10):1187–1194. [PubMed: 25896067]
22. Kennedy RD, Awopegba A, De León E, et al. Global approaches to regulating electronic cigarettes. *Tob control*. 2017;26(4), 440–445. [PubMed: 27903958]
23. Mallock N, Trieu HL, Macziol M, et al. Trendy e-cigarettes enter Europe: chemical characterization of JUUL pods and its aerosols. *Arch Toxicol*. 2020;94(6):1985–1994. [PubMed: 32189038]
24. Eissenberg T, Shihadeh A. Nicotine flux: a potentially important tool for regulating electronic cigarettes. *Nicotine Tob Res*. 2014;17(2):165–167. [PubMed: 25332456]

Figure 1. Mean Plasma Nicotine Concentration by Device Power and Liquid Nicotine Concentration

Mean ($\pm$ SEM) plasma nicotine concentration ($n=10$). On the left is the 15 W condition, and the right is the 45 W condition. The square depicts 0 mg/ml, the triangle depicts 3 mg/ml, and the circle depicts 6 mg/ml. Asterisk (*) indicates significant ($p < .05$) difference from 15 W at same time point and liquid nicotine concentration condition. Pound sign (#) indicates significant ($p < .025$) difference from 0 mg/ml at same time point and power condition.

Table 1.

Mean (SD) Puff Topography by Device Power and Liquid Nicotine Concentration

	0 mg		3 mg		6 mg	
	15 W	45 W	15 W	45 W	15 W	45 W
Puff Number						
Directed bout	10.1 (0.1)	10.3 (0.2)	10.0 (0)	10.8 (0.7)	10.2 (0.2)	10.5 (0.3)
<i>Ad libitum</i> bout	63.5 (15.3)	41.7 (7.6)	46.3 (10.3)	46.9 (6.0)	49.4 (11.5)	40.1 (4.8)
Puff Duration (sec)						
Directed bout	3.9 (0.6)	1.9 (0.2) ^a	3.3 (0.3)	1.8 (0.2) ^a	2.9 (0.2)	1.7 (0.2) ^a
<i>Ad libitum</i> bout	3.8 (0.4)	2.1 (0.3) ^a	3.9 (0.4) ^b	2.0 (0.3) ^a	3.2 (0.3)	1.9 (0.2) ^a
Puff Volume (ml)						
Directed bout	183.5 (34.0)	66.8 (7.2) ^a	159.1 (16.9)	95.2 (35.7)	135.2 (11.4)	66.9 (9.6) ^a
<i>Ad libitum</i> bout	179.2 (26.6)	62.8 (8.9) ^a	185.0 (24.6)	98.4 (31.7) ^a	145.7 (15.5)	69.0 (9.4) ^a
Inter-puff Interval						
Directed bout	25.8 (0.7)	27.8 (0.4)	26.7 (0.3)	26.8 (1.5)	26.4 (0.4)	27.2 (0.7)
<i>Ad libitum</i> bout	135.7 (41.1)	113.5 (22.5)	181.9 (64.7)	124.5 (23.6)	161.8 (49.2)	127.0 (17.8)
Flow Rate (ml/sec)						
Directed bout	46.3 (3.2)	35.6 (3.2)	48.8 (2.4)	47.8 (12.5)	46.6 (2.3)	38.3 (2.4)
<i>Ad libitum</i> bout	46.0 (3.2)	33.0 (4.1)	47.4 (2.7)	51.9 (17.1)	45.1 (3.2)	33.4 (4.9)

^aIndicates a significant difference between the 15 W condition and the 45 W condition within the same liquid nicotine concentration condition and ENDS use bout.

^bIndicates a significant difference between the directed and the *ad libitum* bouts within in the same liquid nicotine concentration and power condition.