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High exposure to nicotine among adolescents who use JUUL and other vape pod systems (“pods”)

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Introduction

Although e-cigarette use among US youth decreased in 2016 for the first time since 2011,^{1,2} with the introduction of the new generation of nicotine vaporizers, “pods,” this trend may not continue. Pods are compact, lightweight, ultra-portable, and easy to use inconspicuously. Popularity of these devices has increased in the past year, most notably, one brand, Juul. Use of Juul and similar products (*‘juuling’*) among youth has parents, teachers and the lay public

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Clinical Trial Registration: N/A

appropriately concerned. However, to date there are no data on nicotine exposure among youth who use pod systems.

Methods

Survey:

To characterize the use of pods among adolescents, we surveyed patients 12-21 seen at three Stony Brook Children's Hospital outpatient clinics (Long Island, NY) from April 2017 - April 2018. The study was approved by university IRB; all participants/parents provided written consent. Participants completed a 60-item anonymous questionnaire about personal use of e- cigarettes, including specific product types and brands, and provided a spot urine sample.

Product analysis:

Using previously described analytical methods,³ we measured total nicotine concentration in pod products, purchased online, that were popular among our participants. We also measured total nicotine yields in aerosols generated from these products using a smoking machine and standardized laboratory puffing protocol (70 ml puff volume; 2 sec puff duration; puff intervals of 10 seconds).³ We used gas chromatography-mass spectroscopy to identify type of nicotine salt used in pod products.⁴

Biomarker analysis:

We estimated nicotine exposure in our participants who reported exclusive use of pods (i.e., no combusted tobacco use) by measuring cotinine, a major metabolite of nicotine in collected urine samples.⁵ Non-smoking status reported by our participants was verified by measuring urinary levels of tobacco-specific biomarker (NNAL).⁵ Due to urinary cotinine's short elimination half-life, we restricted analysis to 22 subjects who used pods within 7 days prior to the clinic visit. Of the 22 participants included in the urine analysis, average age was 16.8 ± 1.8 (mean \pm SD; range 13-21 years).

Results

Survey results:

A total of 506 patients were consented for the study and all completed administered questionnaires. Based on product brand names reported by study participants, we estimated that among 506 surveyed, 7.7% (n=38) reported current daily or some day use of pods. The most popular brands of pod systems used by our patients in the past 30 days were Juul (79.7% of pod users), Bo (36.4%), Phix (18.2%), and Sourin (12.1%)(multiple answers allowed). Preferred flavors in our participants were menthol/mint (24.2%), fruit (21.2%), and candy, desserts or other sweets (18.2%).

Results of product testing:

All tested products contained high nicotine concentrations, from 21.8 to 56.2 mg/ml in a form of salt with benzoic acid (nicotine benzoate) or levulinic acid (nicotine levulinate) dissolved in a mixture of propylene glycol and vegetable glycerin (Table 1). We estimated

that users of prefilled pod systems (Juil, Bo, Phix) may inhale with 10 puffs from 0.77 to 0.85 mg of nicotine (Table 1), considerably higher than previously reported in older generations of e-cigarettes (0.02–0.51 mg/10 puffs).³

Biomarker data:

The median urinary cotinine concentration measured in our participants who used pods was 244.8 ng/mL (IQR 8.4-1,255.8), higher than 155.2 ng/mL (IQR: 68.8-579.2) reported by Benowitz et al. in 55 adolescents (ages 13-19) who regularly smoked conventional tobacco cigarettes.⁶ All analyzed samples had either undetectable or very low levels of the urinary tobacco-specific biomarker, NNAL, confirming lack of exposure to tobacco smoke.

Discussion

Product testing results and participants' high urinary cotinine levels provide physiologic evidence for significant nicotine exposure among pod users. Indeed, such high cotinine levels raise concerns about the potential for earlier and more significant nicotine addiction in teens. Although the exact physiological mechanisms of nicotine salts are not well studied, these compounds are believed to increase the amount and rate of nicotine uptake in e-cigarette users.⁷ Potential health risks of repeated inhalation of high doses of nicotine salts are unknown.

Study limitations include small sample size and a convenience sample of adolescents presenting to clinics in suburban Long Island, NY. These findings are not representative of the entire population of U.S. adolescents and may not be generalizable to other e-cigarette user groups. Additionally, survey response to self-reported pod use in the past 7 days may introduce recall bias.

Clinicians must be aware of and educate their patients about the potential for long-term sequelae of using e-cigarettes, especially pods. Public health advocates and regulatory agencies must act now to restrict youth access to e-cigarettes before decades of progress in tobacco control is undone. On April 24, 2018, FDA announced several enforcement actions as part of a new Youth Tobacco Prevention Plan to stop youth use of and access to Juul and other e-cigarettes. Additionally, raising the legal age to 21 ("Tobacco 21") to purchase tobacco products has gained traction as an evidenced-based measure to prevent teen access to all tobacco products, including e-cigarettes.

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Nicotine levels in the pod products and urine cotinine concentrations detected in 22 surveyed patients (aged 13-21) who reported pods use within 7 days prior to the clinic visit.

Table 1.

Brand name of pod system	Number of patients who reported using the pod product (single brand/in combination with other pod products)	Nicotine concentration in a pod (mg/ml)	Nicotine yields in 10 puffs (mg)	Type of nicotine salt	Median urinary cotinine concentration in exclusive users (ng/mL)
Juul	10/6	56.2	0.83	Benzoate	135.1
Bo	3/6	37.9	0.85	Levulinate	508.4
Phix	2/3	48.0	0.77	Benzoate	906.4
Sourin (refilled with Blow Sauce e-liquid)	0/2	21.8	0.26	Benzoate	N/A*

Note:

* all users of Sourin brand reported using multiple products