Marijuana and Tobacco Coexposure in Hospitalized Children

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abstract

BACKGROUND: The impact of secondhand marijuana smoke exposure on children is unknown. New methods allow for the detection of marijuana smoke exposure in children.

METHODS: We studied children who were hospitalized in Colorado and had a parent participating in a smoking cessation study; all children had urine samples remaining from the original study as well as consent for future research. Parents completed a survey and urine samples were analyzed for cotinine and marijuana metabolites, including 11-hydroxy-Δ9-tetrahydrocannabinol (COOH-THC), by using liquid chromatography-tandem mass spectrometry.

RESULTS: The median age of the children was 6.0 years (range 0–17 years); 57% were boys. Half (55%) were white, 12% were African American, and 33% were of another race; 39% identified as Hispanic. Approximately 46% had detectable COOH-THC, and 11% had detectable THC. Of those with detectable THC, 3 were teenagers, and 6 were <8 years of age. There were no significant differences in urinary COOH-THC concentrations by age, sex, race and/or ethnicity, or socioeconomic status. Children with positive results for COOH-THC were more likely to have parents who use marijuana daily, smoke marijuana versus other forms of use, use daily in the home, and smoke marijuana in another room if the children are around compared with smoking outside.

CONCLUSIONS: Approximately half of the children who qualified for our study had biological evidence of exposure to marijuana. Researchers in studies such as this provide valuable data on secondhand exposure to children from parents using tobacco and marijuana and can inform public health policies to reduce harm.

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Dr Wilson conceptualized the study, supervised the data collection and analyses, and drafted and finalized the manuscript; Dr Torok developed the study methods, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content; Dr Wei contributed substantially to the conception and design of the study, completed laboratory analysis, and critically revised the manuscript for important intellectual content; Ms Lowary contributed substantially to the conception and design of the study, oversaw the collection of the data, and critically revised the manuscript for important intellectual content; Dr Blount contributed substantially to the conception and design of the study, oversaw laboratory analysis, and critically revised the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Maternal exposure to marijuana smoke during pregnancy can cause lingering harm to children. Additionally, legalization increases the likelihood that children will be directly exposed to secondhand marijuana smoke, but the extent and consequences of exposure are still unclear.

WHAT THIS STUDY ADDS: We found that 46% of children who were hospitalized in Colorado with parents participating in a smoking cessation study had detectable metabolites of marijuana in their urine.

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The use of marijuana has been increasing in both acceptability and legality in the past 15 years. In 2013, according to the National Survey on Drug Use and Health, 5.7 million persons aged ≥12 years used marijuana on a daily or almost-daily basis in the past 12 months, which was an increase from the 3.1 million daily or almost-daily users in 2006.[1] As of January 8, 2018, 22 states plus Guam allow the legal use of marijuana for medical reasons, and 8 states plus Washington, District of Columbia, allow legal adult use.[2]

Although marijuana can be combusted, aerosolized, or ingested as hash oil or leaves, smoked marijuana is still the most common form.[3] A recent analysis of data from the US NHANES revealed that exclusive daily marijuana users who do not use tobacco have higher levels of smoke biomarkers (eg, volatile organic compounds and polycyclic aromatic hydrocarbons) than nonusers.[4] Exposure to marijuana smoke chemicals extends to adjacent nonusers,[5] as has been shown for tobacco smoke.[6] Although most states with legal marijuana use restrict its use in public indoor and outdoor spaces, they do not have any restrictions on combustible marijuana use in the presence of children. Although the prevalence of secondhand marijuana smoke exposure has not been widely studied, we recently found that 16% of young children who were hospitalized for bronchiolitis in Colorado had exposure to marijuana smoke.[7]

Although there is research on the dangers of secondhand tobacco smoke[6] and of prenatal marijuana exposure,[8–10] the impact of secondhand marijuana smoke on children has not yet been studied. There are several studies that indicate that marijuana smoke contains potentially harmful chemicals, including toxic and carcinogenic chemicals, such as volatile organic compounds, polycyclic aromatic hydrocarbons, and aromatic amines.[11,12] Studies in adults have revealed that it is possible to have similar drug effects as smoking marijuana from intense secondhand marijuana smoke exposure,[13] although this has not been demonstrated in children with secondhand exposure. Even brief exposure to levels of marijuana secondhand smoke that are similar to known tobacco secondhand smoke levels impaired vascular endothelial function in an animal model.[14] Children can be exposed to secondhand and thirdhand marijuana smoke when parents or other household members smoke indoors, similar to how children who live with tobacco smokers have higher tobacco smoke exposure than those living in smoke-free homes.[15]

The couse of marijuana and tobacco is common. The National Survey on Drug Use and Health revealed that 36% of 18- to 25-year-olds and 11% of ≥26-year-olds who were current cigarette smokers were also current marijuana users.[16] In Colorado, we studied children who were hospitalized for bronchiolitis at Children's Hospital Colorado between 2013 and 2015 and found that the proportion of marijuana exposure among children who were also exposed to tobacco smoke was 56%.[7] Thus, is it likely that children who are exposed to marijuana smoke are also exposed to tobacco smoke, which is known to be harmful. In this study, we examine the prevalence and correlates of marijuana smoke exposure in a population of children who are hospitalized and have a parent who smokes tobacco and was enrolled in a tobacco smoking cessation program.

METHODS

Study Population

This is a secondary analysis of data and samples collected as part of a larger study to test the efficacy of a tobacco smoking cessation program for parents of children who are hospitalized. Families were referred to the study by using a standard screening tool ("Does anyone who lives in your home or who cares for your child use tobacco?") or by provider recommendation for participation; all families were recruited after the legalization of recreational marijuana in Colorado (January 1, 2014). We recruited parents of children up through the age of 17 years. To be eligible to participate, the parent had to be a current tobacco cigarette smoker (daily or less than daily but interested in quitting or reducing exposure), and the child had to have been admitted to the hospital within the previous 5 days. Informed consent was obtained; parents could elect to have their samples and research data available for future research. Both the initial study and the secondary analysis were approved by the Colorado Multiple Institutional Review Board.

The parent survey included questions about demographics, secondhand smoke exposure, tobacco use, and marijuana use and policies. Parent marijuana use was assessed with the question, "Do you currently smoke marijuana every day, some days, or not at all?" and household marijuana use was assessed with the question, "How often does anyone smoke marijuana in your home?" We collected urine samples from each child. For infants, young children, and older children who were developmentally disabled, we used cotton balls or a bag to collect in a diaper; older children provided a sample in a cup. Samples were mixed, separated into 10 mL aliquots, and frozen at −80°F. Samples were batched and sent on dry ice to the laboratory at the University of California, San Francisco for cotinine testing. Samples that were designated for future research were

sent on dry ice to the Centers for Disease Control and Prevention for testing of Δ9-tetrahydrocannabinol (THC), 11-hydroxy-Δ9-tetrahydrocannabinol (COOH-THC), and cannabidiol.

Analysis of Urinary Tobacco Biomarkers

Urinary cotinine was analyzed by using liquid chromatography–tandem mass spectrometry, as previously described.[17] The limit of detection (LOD) for cotinine was 0.030 ng/mL. Laboratory blank and quality-control samples were simultaneously processed and analyzed to ensure the quality of the analytical results.[15]

Analysis of Urinary Marijuana Biomarkers

Analysis for marijuana biomarkers was performed by using the method by Wei et al.[12] Urine samples were equilibrated with isotopically labeled internal standards, deconjugated by using enzymatic and alkaline hydrolysis, and extracted by using C18 sorbent. The final extracts were concentrated, and 10 μL of each sample was injected into an ultra-high–performance liquid chromatograph and analyzed by using tandem mass spectrometry under electrospray ionization mode. This method has LODs of 0.005, 0.015, and 0.009 ng/mL for the 3 urinary biomarkers (total THC, COOH-THC, and cannabidiol, respectively). THC is the primary psychoactive constituent in marijuana, and cannabidiol is the second most abundant cannabinoid after THC. Both THC and cannabidiol have short elimination half-lives in urine; therefore, their detection often indicates recent and active exposure. COOH-THC is the primary metabolite of THC, and its half-life is 3 to 4 days; its presence in urine provides a wider detection window and a more sensitive measure of both active and passive marijuana smoke exposure.

Statistical Analysis

We used frequencies and proportions to describe categorical data and measures of median (interquartile ranges) or geometric means (95% confidence limits) to describe continuous data. For categorical variables, bivariate analyses were performed by using χ^2 tests and Fisher's exact tests when indicated. For continuous data, we used *t* tests or Wilcoxon rank tests for bivariate analyses. We used Spearman's correlation coefficient to evaluate the correlation between COOH-THC and cotinine. For bivariate analyses, the outcome variable (COOH-THC level) was dichotomized into below or above the LOD. The level of statistical significance was set at .05. Analyses were performed by using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

Of the 146 subjects recruited into the original study at the time of these analyses, 120 (82%) had given consent for future research; 83 (69%) of these had a sufficient sample remaining for the analysis and were included in the study. The median length of time between admission and urine sample collection was 36 hours. At the time of hospitalization, the median age of the children was 6 years (range 1–17 years), and 56.6% were boys. Most (54.9%) were white, 12.2% were black and/or African American, and 32.9% were of another race; 38.6% identified as being of Hispanic or Latino ethnicity. The median age of the parents was 33 years; most (54.2%) were married, 56.3% had at least some college, 22.7% had annual incomes of at least $50 000, and 61.4% lived in detached homes (Table 1). Parents smoked a mean of 11 tobacco cigarettes per day; most (83.1%) had also used electronic cigarettes at least 1 or 2 times, but <4% reported using them daily. Most parents (85.4%) reported ever using marijuana; 11.0% of parents reported smoking marijuana every day, and 23.2% reported smoking on some days. Smoking was the most common form of marijuana use (30.1%), followed by edibles (14.5%) and vaporizers (9.6%). Although most parents reported that no one ever smokes marijuana inside their homes (84.0%), 7.4% reported marijuana smoking in the home daily. When asked what happens if someone wants to smoke marijuana in the home while children are present, 51.8% reported that there is no smoking when children are home, 21.7% step outside, and 9.6% smoke in another room or on another floor.

Overall, 45.8% of the children had detectable levels of COOH-THC; 8% also had detectable cannabidiol, and 10.8% had detectable THC, which would be suggestive of active exposure. For those with detectable metabolites, the geometric means were THC 0.02 (95% confidence interval [CI] 0.01–0.07), COOH-THC 0.016 (95% CI 0.08–0.36), and cannabidiol 0.39 (95% CI 0.02–9.83). Of those with detectable THC, 3 were adolescents (14–16 years old); the remaining 6 children were ≤7 years old. Of those with detectable THC who were ≤7 years old, 83% of their parents reported household marijuana use on some days or every day. The geometric mean cotinine level was 1.0 ng/mL; there was no statistically significant correlation between COOH-THC and cotinine levels ($P = .18$); these results were not significantly different when analyzed without 3 adolescent presumed marijuana users (based on THC levels) and a possible tobacco user (based on urine cotinine level).

Marriage status was significantly associated with detectable COOH-THC ($P = .02$); otherwise, there were no statistically significant demographic differences between patients with COOH-THC above and below the LOD (Table 1). Daily parent and/or caregiver smoking of marijuana was

TABLE 1 Child and Parent Demographics and COOH-THC Levels

Variables	Total (n = 83)	≥LOD COOH-THC (n = 38)	<LOD COOH-THC (n = 45)	P
Child sex, %				
Male	56.6	46.8	53.2	.83
Female	43.4	44.4	55.6	—
Child age, y, median (IQR)	6.0 (2.0–11.0)	7 (4–12)	5 (2–9)	.09
Is your child Hispanic or Latino? %				
No	61.4	47.1	52.9	.77
Yes	38.6	43.8	56.3	—
Race, %				
White	54.9	44.4	55.6	.49
Black and/or African American	12.2	30.0	70.0	—
Other and/or multiracial	32.9	51.9	48.1	—
Parent age, y, median (IQR)	33.0 (27.0–38.0)	34 (29–39)	33 (27–36)	.60
Marriage status, %				
Married or member of a couple	54.2	33.3	66.7	.02
Single (never married)	30.1	52.0	48.0	—
Divorced, widowed, or separated	15.7	76.9	23.1	—
Highest educational level, %				
Some college or college graduate	56.3	40.0	60.0	.42
High school graduate	20.0	43.8	56.3	—
Less than high school graduate	23.8	57.9	42.1	—
Household income from all sources before taxes last y, $, %				
≥50 001	22.7	29.4	70.6	.14
25 001–50 000	36.0	40.7	59.3	—
≤25 000	41.3	58.1	41.9	—
Housing type, %				
Standalone home	61.4	41.2	58.8	.29
Multiunit housing	38.6	53.1	46.9	—

—, not applicable.

significantly associated with positive results for COOH-THC (72.0% vs 28% negative for COOH-THC; P < .01), whereas the use of edibles was not significantly associated with detectable positive results for COOH-THC (58.3% positive results for COOH-THC vs 41.7% negative results for COOH-THC; P = .35). Regular vaporizer use was also not significant; 75.0% were positive for COOH-THC compared with 25.0% being negative for COOH-THC (P = .13). Removing the 3 adolescent presumed users from these analyses did not substantively change these results. All of the children with a parent reporting daily marijuana use had detectable COOH-THC along with 47.4% of those using some days and 37.0% of those using not at all (P < .01). Similarly, 100% of children for whom there was daily marijuana use inside the home had detectable COOH-THC compared with 66.7% of those reporting weekly use, 100% of those reporting monthly use, and 36.8% of those reporting never smoking marijuana in the home (P < .001; Table 2). Smoking marijuana in another room was also strongly associated with COOH-THC (100% vs 44.2% of those who reported never smoking when the children are home and 29.4% of those who reported stepping outside; P = .004).

DISCUSSION

Nearly half of the children who were hospitalized and had a parent enrolled in a tobacco smoking cessation program had a biological confirmation of marijuana smoke exposure. Secondhand exposure to tobacco smoke causes an increased risk of sudden infant death syndrome, acute respiratory infections, middle ear disease, and more severe and frequent asthma attacks in infants and children[6]; tobacco smoke and marijuana smoke contain similar harmful smoke chemicals.[11] In addition, our study comprises a significant population of parents who are cousing marijuana and tobacco. Interestingly, there was no correlation between COOH-THC and urine cotinine levels. Although all the parents in the study reported being current tobacco cigarette smokers, the results from this study reveal significant variability in how people may use marijuana and tobacco, with some people primarily using tobacco, with occasional marijuana use, and others using more marijuana and less tobacco.

Because the terminal elimination half-life of THC is short, THC is the cannabinoid that is most frequently tested to assess for active marijuana use, and it requires higher levels of exposure for a positive result.[18] In this study, 9 (10.8%) children were positive for detectable levels of THC. Although 3 of the 9 subjects were adolescents, and potentially marijuana users themselves, 6 of the THC-positive children were ages ≤7 years, and most had parents who reported marijuana use some days or every day. Not surprisingly, children whose parents reported smoking marijuana in another room while children were home had detectable COOH-THC. Research on secondhand and thirdhand tobacco smoke has clearly revealed that smoking in the home, even in a different room, results in significant exposure to children.[19] Parents and caregivers who avoid smoking tobacco, marijuana, or both in the home are thus likely to reduce exposure to infants and children residing there.

There are several limitations to this study. We studied children who were hospitalized and had a

TABLE 2 Comparison of Parent Report of Marijuana and Tobacco Use and Urine COOH-THC Level

Variables	Total (n = 83)	≥LOD COOH-THC (n = 38)	<LOD COOH-THC (n = 45)	P
Have you ever used marijuana, even 1 or 2 times? n (%)				
No	12 (14.6)	33.3	66.7	.37
Yes	70 (85.4)	47.1	52.9	—
Do you have a medical marijuana license?[a] n (%)				
No	18 (66.7)	61.1	38.9	.78
Yes	9 (33.3)	55.6	44.4	—
What form(s) of marijuana do you regularly use (check all that apply)?[a] n (%)				
Smoked (pipes, joints, bongs)				
No	58 (69.9)	34.5	65.5	<.01
Yes	25 (30.1)	72.0	28.0	—
Edibles				
No	71 (85.5)	43.7	56.3	.35
Yes	12 (14.5)	58.3	41.7	—
Vaporizer				
No	75 (90.4)	42.7	57.3	.13
Yes	8 (9.6)	75.0	25.0	—
Flavored drops				
No	80 (96.4)	43.8	56.3	.09
Yes	3 (3.6)	100	0.0	—
Beverages				
No	81 (97.6)	44.4	55.6	.21
Yes	2 (2.4)	100	0.0	—
Other				
No	80 (96.4)	43.8	56.3	.09
Yes	3 (3.6)	100	0.0	—
Do you currently smoke marijuana every day, some days, or not at all?[a] n (%)				
Every day	9 (11.0)	100	0.0	<.01
Some days	19 (23.2)	47.4	52.6	—
Not at all	54 (65.9)	37.0	63.0	—
How often does anyone smoke marijuana inside your home? n (%)				
Daily	6 (7.4)	100	0 (0.0)	<.01
Weekly	3 (3.7)	2 (66.7)	1 (33.3)	—
Monthly	4 (4.9)	4 (100)	0 (0.0)	—
Less than monthly	0 (0.0)	0	0	—
Never	68 (84.0)	36.8	63.2	—
In general, what usually happens when you, friends, or other family want to smoke marijuana when children are at home? n (%)				
I (we) never smoke when the children are home.				
No	40 (48.2)	47.5	52.5	.76
Yes	43 (51.8)	44.2	55.8	—
I (we) smoke in another room or floor of my home away from the children.				
No	75 (90.4)	40.0	60.0	<.01
Yes	8 (9.6)	100	0.0	—
I (we) step outside (to smoke) when the children are home.				
No	65 (78.3)	49.2	50.8	.23
Yes	18 (21.7)	33.3	66.7	—
On an average day, about how many cigarettes do you currently smoke? median (IQR)	10.0 (5.0–15.0)	10 (6–15)	10 (5–15)	.83
Over the past 3 months, has anyone smoked tobacco anywhere inside your home?				
No	61 (75.3)	36.1	63.9	<.01
Yes	20 (24.7)	75.0	25.0	—
Please tell me which best describes how cigarette smoking is handled in your home. n (%)				
No one is allowed to smoke anywhere.	52 (65.0)	40.4	59.6	.38
Smoking is permitted in some places or at some times.	25 (31.3)	56.0	44.0	—
Smoking is permitted anywhere.	3 (3.8)	66.7	33.3	—
Urinary cotinine, ng/mL (geometric mean), median (IQR)	0.9 (0.4–2.3)	1.0 (0.6–3.9)	0.7 (0.2–2.1)	.17

—, not applicable.

[a] Questions were asked only of parents who said they had smoked marijuana.

parent who is a cigarette smoker in Colorado, and the results may not be generalizable to the outpatient setting and to children whose parents do not smoke cigarettes, especially because we know the couse of marijuana and tobacco is common.[16] We also cannot generalize to states where marijuana is not legal recreationally or for parents who are not willing to consider quitting smoking. Our sample is small, which limits our ability to do further analyses. Participation in this study was dependent on families in the parent study approving their data to be used for future research. However, we compared demographic characteristics, children's urinary cotinine, and parents' reported frequency of marijuana smoking between subjects who gave consent for future research with those who did not and found no statistically significant differences between the 2 groups. We assessed urine cotinine and marijuana metabolites from samples obtained while the children were in the hospital; although the median length of time from admission to urine sampling was 36 hours, it is possible that there were some who had been exposed before admission but no longer had detectable metabolites. Although we found that children of married couples were the least likely to have positive results for COOH-THC, the reasons for this association are unclear and likely confounded by other factors. Finally, we are unable to assess whether the exposure to marijuana had any impact on the health of the children.

CONCLUSIONS

Almost half of the children with parents who were enrolled in a tobacco cessation program had biological evidence of exposure to marijuana. Studies such as this provide valuable data on secondhand exposure in children whose parents use tobacco and marijuana; future research is needed to understand the potential for harm.

ABBREVIATIONS

CI: confidence interval
COOH-THC: 11-hydroxy-Δ9-tetrahydrocannabinol
LOD: limit of detection
THC: Δ9-tetrahydrocannabinol

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