Nicotine & Tobacco Research, 2016, 982–987
doi:10.1093/ntr/ntv158
Brief report
Advance Access publication July 17, 2015

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Passive and Active Tobacco Exposure and Children's Lipid Profiles

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Abstract

Introduction: Despite reductions in smoking rates, exposure to cigarette smoke remains common among US children and adolescents. In adults, active smoking and secondhand smoke (SHS) exposure have been linked to adverse changes in lipid profiles and increases in inflammatory markers. Evidence that such changes are present before adulthood remains limited, and the extent to which active smoking and SHS exposure affect these cardiovascular measures in children has not been thoroughly assessed.
Methods: We employed data from 2008 individuals aged 12–19 years from the 2005–2010 National Health and Nutrition Examination Survey. Comparisons of the lipid and inflammatory marker levels among active smokers, those exposed to SHS (as determined by serum cotinine levels), and those unexposed to tobacco smoke were made using linear regression with multiple propensity score adjustment.
Results: Compared to unexposed children, lipid and inflammatory marker profiles did not differ among those exposed to SHS exposure. Among active smokers, differences compared to unexposed children were observed in triglyceride levels ($\hat{\beta} = 8.5\,\text{mg/dL}$, $P = .01$), the ratio of triglycerides to high-density lipoprotein ($\hat{\beta} = 0.2$, $P = .045$), and low-density lipoprotein cholesterol ($\hat{\beta} = -4.1\,\text{mg/dL}$, $P = .03$), though these did not reach levels of confirmatory statistical significance.
Conclusions: After accounting for sociodemographic characteristics and medical comorbidities, serum lipids and markers of systemic inflammation were not associated with SHS exposure. Tobacco smoke exposure in children may require longer durations of compounded effect before serum lipid abnormalities are detected.
Implications: This paper adds detail to the study of secondhand smoke's effects on lipid profiles of children and adolescents. Prior research on this topic for these age groups has been limited, and this study provides national, cross-sectional data to show that both secondhand smoke and active smoking in childhood and adolescence is not associated with changes in lipid profiles or markers of inflammation. Tobacco smoke exposure may require longer durations of compounded effect before abnormalities are detected.

Introduction

Despite inroads in reducing smoking rates,[1] exposure to tobacco smoke remains common.[2] Over 12% of US adolescents remain active smokers[3] and nearly half of US children are exposed to secondhand smoke (SHS).[2] Even brief exposures to tobacco smoke may confer the majority of adverse health effects associated with active smoking.[4] How exposure to tobacco smoke increases the risk of cardiovascular mortality remains under study but links to increased platelet reactivity and endothelial dysfunction,[5–7] arterial stiffness

and atherogenesis,[5] inflammation,[8–10] and oxidative stress[4,11,12] are suspected.

Ties between SHS exposure and adverse lipid profiles have also been suggested. In adults, increases in low-density lipoprotein cholesterol (LDL-C)[13,14] and the ratio of total cholesterol to high-density lipoprotein cholesterol (HDL-C)[4,15,16] as well as decreases in HDL-C[17] have been reported. Other proinflammatory markers, including homocysteine,[4,9,10] fibrinogen,[4,9,18] and C-reactive protein,[4,9,10,18] also appear to be adversely affected by SHS.

Research in pediatrics has corroborated some, but not all, of these findings. Adolescents who actively smoke appear to have decreases in HDL-C similar in magnitude to that of adults,[19–21] though data have been equivocal regarding LDL[19,20] and total cholesterol.[19,21] The potential untoward effects of SHS on cardiometabolic risk in children remain even more debated.[22] In children, as with adults, SHS exposure has been linked by some to lower HDL-C[23–25] levels, as well as increases in levels of apolipoprotein B,[26] C-reactive protein,[27,28] and the ratio of total cholesterol to HDL-C.[24,25] Yet others have shown no difference in HDL-C[26,29] and total cholesterol[23,26] levels among those exposed to SHS. Many of these studies have been hampered by small sample sizes,[23,25,30] narrow age-ranges,[24,27] limited racial and ethnic diversity,[24,25] and a reliance on self-reported SHS exposure.[27] Alternative measures of cardiovascular risk (eg, non-HDL-C) that may be better predictors of adverse cardiovascular events in adulthood[31,32] have often not been assessed.

To assess more comprehensively the association between children's cardiovascular risk profiles and tobacco smoke exposure, we examined recent data from the National Health and Nutrition Examination Survey. Using serum cotinine levels as an objective measure with which to measure individuals exposure to tobacco smoke, we employed a multiple propensity score-adjusted approach to adjust for nonequivalence between exposure groups.

Methods

Study Population

Data from 2008 subjects aged 12–19 years with available laboratory data from the 2005–2010 waves of continuous National Health and Nutrition Examination Survey were examined.[33,34] Described elsewhere,[35] National Health and Nutrition Examination Survey is a repeated cross-sectional, multistage, survey designed to assess the health status of the civilian, non-institutionalized US population. The study combined interview, laboratory, and physical examination components.[35] Interviews were conducted in subjects' homes; a parent, guardian, or other household adult answered demographic and household questions. Physical examinations were conducted in mobile examination centers and included anthropomorphic measurements and a blood sample collection. Study protocols were approved by the National Center for Health Statistics institutional review board.[35]

Measures

Smoking Exposure

Serum cotinine, a measurable metabolite of nicotine and validated biomarker of both SHS exposure and active smoking, was employed.[36] Consistent with prior studies,[22,37,38] we defined individuals as active smokers if they had serum cotinine levels ≥15.0 ng/ml or if participants reported using any product containing nicotine including cigarettes, pipes, cigars, chewing tobacco, snuff, nicotine patches, nicotine gum, or any other product containing nicotine within the past 5 days. We classified those with a detectable serum cotinine (ie, ≥0.05 ng/ml) but <15 ng/ml but who did not report nicotine use within the last 5 days as exposed to SHS. Those with undetectable serum cotinine levels were classified as unexposed.

Laboratory Measures

Data from a subset of children asked to fast prior to the laboratory exam was employed. Measures of total cholesterol, HDL-C, LDL-C, triglycerides, apolipoprotein B, and fasting glucose were obtained. LDL-C was calculated using the Friedenwald equation for those with triglyceride levels ≤400 mg/dL.[39] Non-HDL-C cholesterol was calculated as the difference between total cholesterol and HDL-C. High-sensitivity C-reactive protein (hsCRP) was measured in all participants using latex-enhanced nephelometry; the lower limit of detection was 0.02 mg/dL.

Other Covariates

Demographic variables used to adjust for differences between groups included subjects' age and ethnicity. In addition, body mass index, assessed by age- and sex-specific percentiles,[40,41] was included. Blood pressure was also included, characterized by age- and sex-specific percentiles.[42] Subjects were classified as having diabetes mellitus if the respondent reported being been told by a doctor that the child had diabetes mellitus, if the child used oral hypoglycemic agents or insulin, or if the child had a fasting serum glucose ≥126 mg/dL or HgbA1c ≥ 6.5%.[43] Following prior work on diet's effects on lipids,[23] dietary recall data was used to calculate the ratio of ingested saturated fat and cholesterol to ingested calories.

Statistical Methodology

Since characteristics differed between smoking exposure groups, we pursued multiple propensity scores to adjust for such differences.[44] This approach expands on widely used methods for dichotomous treatment variables.[45] Here, multiple propensity scores were estimated from a multinomial logistic regression model in which tobacco smoke exposure status served as the dependent variable while the variables listed in Table 1 served as independent variables. Each propensity scores reflects the estimated probability of assignment to each tobacco smoke exposure status. To adjust for nonequivalence between groups, linear regression models were used to assess differences in means in cardiovascular risk factors by including two of the three estimated propensity scores. All analyses were conducted using Stata 11.2. Given the exploratory nature of the analysis, two-sided *P* values are reported without adjustment for multiple testing. To ascertain whether threshold levels of cotinine exposure employed in our analysis influenced the results presented here, a sensitivity analysis examining low and high cotinine levels was conducted. Individuals classified as exposed to SHS were divided into low or high cotinine levels if they had levels below or above, respectively, the median cotinine value for that group.

Results

Significant differences in characteristics between exposure groups were noted. Shown in Table 1, subjects exposed to SHS were more likely than their unexposed peers to be male and overweight, and were more likely to have elevated blood pressure and diabetes. Active smokers were more likely than their nonsmoking peers to be older, white, and male, and to have elevated blood pressure. After adjustment with propensity scores, balance in these covariates among the exposure groups improved.

Table 2 displays results from the unadjusted and adjusted comparisons of tobacco smoke exposure status and cardiovascular measures. After adjustment, no differences in lipid profiles among SHS-exposed

Table 1. Demographic Characteristics (*N* = 2008)

	Exposure status				
	Unexposed	Secondhand smoke exposed	Smokers	*P*	Adjusted *P* value[a]
Age (mean ± *SD*)	14.9 ± 2.2	15.5 ± 2.3	17.5 ± 1.5	<.001	.49
Male, %	48.9	52.7	65.4	<.001	.99
Non-Hispanic white, %	25.7	26.2	44.0	<.001	.76
BMI, percentile[b]				<.001	.32
85th–94th	17.4	16.9	17.3		
≥95th	16.3	25.2	19.8		
Elevated BP, %[c]				<.001	.97
Pre-hypertensive	11.8	15.7	22.9		
Hypertensive	1.9	2.7	2.0		
Diabetes, %	1.36	1.24	3.46	.02	.77
RISCC score[d]	18.6 ± 6.9	18.8 ± 7.1	18.2 ± 7.0	.55	.35
Cotinine, ng/ml (median, IQR)	0.02 (0.01–0.03)	0.26 (0.09–0.94)	82.3 (19.9–174)	<.001	—[e]

BMI = body mass index; BP = blood pressure; IQR = interquartile range; RISCC = ratio of ingested saturated fat and cholesterol to calories.

[a]Adjusted with the use of multiple propensity scores.

[b]BMI percentiles shown are calculated as BMI-for-age percentiles from the 2000 CDC growth charts.

[c]Elevated blood pressure follows definitions from the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents.

[d]The RISCC is a single score that conveys the potential effect of diet on lipoproteins; it is calculated as: {(1.01 × saturated fat [in grams]) + (0.05 × cholesterol [in milligrams])} / (kcal/1000).

[e]Cotinine is not included in the propensity score estimation since it is used to define exposure status.

Table 2. Differences in Mean Lipid and Inflammatory Markers, Unadjusted and With Adjustment by Multiple Propensity Scores (*N* = 2008)

	Unadjusted estimates (mean ± *SD*)			Adjusted differences in means			
				SHS		Smokers	
Biomarker[a]	Unexposed	SHS	Smokers	Diff.	*P*	Diff.	*P*
Total cholesterol	158.9 ± 28.4	159.4 ± 31.9	160.3 ± 32.7	−0.5	.75	−2.7	.22
HDL-C	54.4 ± 12.8	53.4 ± 12.4	51.5 ± 13.9	0.3	.58	−0.3	.71
Non-HDL	104.5 ± 28.0	106.0 ± 31.3	108.8 ± 31.8*	−0.8	.57	−2.4	.27
LDL-C	88.3 ± 24.4	89.7 ± 27.7	89.1 ± 26.5	−0.2	.85	−4.1	.03
Triglycerides	81.0 ± 44.2	81.4 ± 45.0	98.2 ± 56.6**	−3.0	.19	8.5	.01
Triglyceride-HDL ratio	1.67 ± 1.26	1.70 ± 1.28	2.12 ± 1.52**	−0.1	.18	0.2	.045
Apolipoprotein B	71.9 ± 18.4	73.2 ± 0.6	75.1 ± 20.6*	−0.1	.91	−0.7	.61
C-reactive protein	0.17 ± 0.65	0.19 ± 0.49	0.18 ± 0.33	−0.1	.59	0.0	.36

HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; SHS = secondhand smoke.

[a]Biomarker values are in mg/dL, except triglyceride-HDL ratio, which is unitless.

*$P < .05$; **$P < .001$. Statistically significant differences from those unexposed are indicated.

adolescents were observed. Adjusted results showed active smokers to have increased levels of triglycerides, the triglyceride-to-HDL-C ratio as well as mildly decreased LDL-C. It merits noting that, of these estimated relationships, only the association between smoking and triglyceride levels approached near confirmatory statistical significance, which would incorporate the multiple comparisons made in our analysis (ie, a *P* value of .006 to preserve a Type I error rate of 0.05). Results of the sensitivity analysis corroborated the presented results (Supplementary Table 1).

Discussion

Despite consensus that tobacco smoke, including SHS, is associated with adverse cardiovascular consequences,[5,11,17,46,47] conflicting evidence exists as to whether the lipid profiles of children are adversely affected. Using a multiple propensity score approach, we report that tobacco smoke exposure was not materially associated with lipid profiles in a national sample of US children.

Our results differ in part from prior research, which merits comment. Among adolescent smokers, no difference was observed in HDL-C levels, a focus of prior studies conducted in both adults[48,49] and adolescents.[19–21] Our results examining active smokers also differ from prior work in that we found no differences in total cholesterol levels.[21] Most notably, our results suggest an increase in triglycerides and the triglyceride-HDL ratio among active smokers. As noted above, the relationship between smoking and increased triglycerides approach confirmatory statistical significance levels that would account for multiple comparisons. Such a finding comes amidst recent studies[50,51] on children that suggest the ratio of triglycerides to HDL-C may prove a superior marker of both increased arterial stiffness and cardiometabolic risk.[49,50]

While past studies have suggested associations between SHS exposure and decreased HDL-C levels,[23–25,30] and SHS exposure and increased apolipoprotein B,[26] our analysis found no such differences. Existing evidence suggests tobacco smoke exposure may provoke lipid

changes through oxidative damage to HDL-C particles, altering their metabolism, antioxidant properties, and reducing their capacity for lipid transport and potential atheroprotective properties.[52] The timeline of such changes remains unclear, though some evidence suggests that these qualitative and functional changes to HDL-C may not only precede quantitative changes, but also result in paradoxically pro-atherogenic HDL-C particles.[53] Prior work that may provide insight into this timeline indicates that active adolescent smokers can show quantifiable changes in HDL-C within 1–2 years of smoking initiation,[20] and may only show significant decreases in HDL-C when smoking more than three packs per week.[54] In aggregate, these studies suggest that tobacco smoke exposure may not exert a quantifiable difference in serum lipids unless an individual is a long-term, active smoker. However, those exposed to tobacco smoke at lower levels may still be affected by a subclinical process of functional lipid alteration, which may be the primary mechanism underlying their increased cardiovascular risk.

Results regarding SHS and hsCRP also merit comment. Our results showed no association between hsCRP levels and SHS exposure. The association between SHS and hsCRP in children has previously been debated. Two prior studies demonstrated such an association[27,28] but another,[27] which adjusted for body mass index as we do here, found no association between SHS and hsCRP. Elevated CRP levels in active adolescent smokers have also been previously described,[55] though no such effect was observed in our study.

Given the well-described adverse cardiovascular outcomes caused by smoking and SHS exposure, our results suggest that the mechanism of those negative effects does not occur through substantive quantitative alterations in serum lipoproteins. Reviewed elsewhere, mounting evidence suggests that vascular endothelial dysfunction, and not serum lipids, may be the underlying etiology.[18,49] Evidence has increasingly linked SHS exposure to markers of endothelial stress and decreased endothelial repair.[56] Parental smoking, for example, has been linked to impaired brachial artery flow-mediated vasodilation in children decades later.[57] It remains tenable then that exposure to tobacco smoke has a cumulative effect on lipoprotein metabolism still undetectable in the pediatric population.

This study is also not, however, without its limitations. Cross-sectional in nature, inferences are not causal. Random serum cotinine measurements have a limited ability to identify SHS exposure beyond a few days[37] and may not wholly reflect the extent or frequency of smoking exposure. Residual confounding, by variables unaccounted for in our propensity score estimation, may exist and unexpectedly bias results. We were unable to incorporate physical activity levels, for example, given inconsistencies across survey waves. Total cholesterol[58] and HDL-C[59] may change during puberty and correlate with androgen levels, which were unavailable in our current sample.

Yet our study has important strengths. It employed a large, racially diverse sample to assess smoke exposure and lipid profiles across a wide age range. In doing so, we used serum cotinine levels as a biochemical marker for nicotine exposure. In contrast to some prior studies that rely on self-report alone,[23,25] this method is advantageous by including those exposed to SHS but unaware of that exposure. Statistically, we employed a multiple propensity scores approach to balance likely confounders among the exposure groups.

In sum, we assessed the association between tobacco smoke, and lipid and inflammatory measures in a national sample of US children. We report that children exposed to tobacco smoke did not differ substantively in their profiles of lipoproteins or inflammatory markers. Future studies investigating alternative mechanisms of cardiovascular risk including vascular endothelial damage and reactivity may provide insight into the pathogenesis of the increased cardiovascular morbidity associated with passive smoke exposure.

Supplementary Material

Supplementary Table 1 can be found online at http://www.ntr.oxfordjournals.org

Funding

This work was supported by NIH/NCI 3 P30 CA016087-33S1 and by NIH/NIEHS 5 P30 ES000260-49. The authors have no financial relationships relevant to this article to disclose.

Declaration of Interests

None declared.

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