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Menthol Cigarette Smoking and Obesity in Young Adult Daily Smokers in Hawaii

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Menthol cigarette smoking and obesity in young adult daily smokers in Hawaii

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A B S T R A C T

This study investigates 1) the relationship between menthol cigarette smoking and obesity and 2) the association of body mass index with the nicotine metabolite ratio among menthol and non-menthol daily smokers aged 18–35 (n = 175). A brief survey on smoking and measures of height and weight, carbon monoxide, and saliva samples were collected from participants from May to December 2013 in Honolulu, Hawaii. Multiple regression analysis was used to estimate differences in body mass index among menthol and non-menthol smokers and the association of menthol smoking with obesity. We calculated the log of the nicotine metabolite ratio to examine differences in the nicotine metabolite ratio among normal, overweight, and obese smokers. Sixty-eight percent of smokers used menthol cigarettes. Results showed that 62% of normal, 54% of overweight, and 91% of obese smokers used menthol cigarettes (p = .000). The mean body mass index was significantly higher among menthol compared with non-menthol smokers (29.4 versus 24.5, p = .000). After controlling for gender, marital status, educational attainment, employment status, and race/ethnicity, menthol smokers were more than 3 times as likely as non-menthol smokers to be obese (p = .04). The nicotine metabolite ratio was significantly lower for overweight menthol smokers compared with non-menthol smokers (16 versus .26, p = .02) in the unadjusted model, but was not significant after adjusting for the covariates. Consistent with prior studies, our data show that menthol smokers are more likely to be obese compared with non-menthol smokers. Future studies are needed to determine how flavored tobacco products influence obesity among smokers.

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Introduction

Cigarette smoking and obesity are leading causes of chronic disease and premature deaths worldwide (World Health Organization, 2010) and in the United States (USDHHS, 2014; NIH, 1998). Each year, smoking kills approximately 6 million people (Eriksen et al., 2012) and overweight/obesity an estimated 2.8 million people worldwide (WHO, 2010). In the United States alone, over 480,000 people die prematurely from smoking (USDHHS, 2014). Death rates due to overweight and obesity in the U.S. vary depending on how rates are calculated (Flegal et al., 2010), but their contributions to premature deaths are not debatable. Morbidity and mortality from smoking and obesity can be prevented, particularly among young adults. However, declines in cigarette smoking have been slow among young adults (USDHHS, 2012) and obesity remains relatively high in the U.S. (Ogden et al., 2014).

Approximately 18.7% of 18–24 year olds and 21.4% of 25–44 year olds reported current cigarette smoking in 2013 (Jamal et al., 2014). Local or national U.S. data on smoking are rarely reported by race/ethnicity-age for some groups, but data show that 47.9% of American Indians and Alaska Natives, 40.1% of whites, 37.7% of Native Hawaiians

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and Pacific Islanders, 29% of Hispanics, 26.5% of Black/African Americans, 20.2% of Asians, and 24.7% of Filipinos aged 18–24 reported current smoking (USDHHS, 2012). Smoking rates among racial/ethnic-age groups exceed the U.S. average of 17.8% reported 2013 (Jamal et al., 2014).

In addition, menthol cigarette use is higher among younger compared with older adult smokers (Giovino et al., 2015). Menthol is the most commonly used flavored tobacco product among 17–34 year olds (Villanti et al., 2013). The cooling, soothing, anesthetic, and analgesic effects appeal to many young people and make menthol cigarettes less harsh to smoke (Kreslakke et al., 2008). Menthol cigarette smoking rates range from 24% among white to 94% among African American smokers aged 18–34 in the U.S. (Giovino et al., 2015). U.S. national data on menthol smoking are not reported for young adult Filipino or Native Hawaiian/Pacific Islander smokers, but among all adults, 26.2% Asians/Pacific Islanders report menthol smoking (Lawrence et al., 2010). Non-menthol smoking significantly decreased from 2004–2010, while menthol smoking significantly increased among young adults in the U.S. (Giovino et al., 2015).

Obesity rates have dramatically increased in the past 50 years (Burkhauser et al., 2009; Komlos and Brabec, 2010) and are projected to exceed 50% by 2030 (Finkelstein et al., 2012). U.S. guidelines for ages 20 and over indicate that persons with a body mass index (BMI) below 18.5 are underweight, 18.5 to 24.9 of normal weight, 25.0 to 29.9 over weight, and 30 and above obese (National Cancer Institute). U.S. data show that 60% of young adults aged 20–39 are overweight or obese and over weight; obesity is higher among Black (71.7%) and Hispanic than white (57.5%) and Asian American (30.3%) racial/ethnic aggregate groups aged 20–39 (Ogden et al., 2014). Other studies show that 39.6–40.8% of Native Hawaiians and Pacific Islanders and 16.5–20.6% of Filipinos are obese (Singh and Lin, 2013; Robert Wood Johnson Foundation, 2013), but national data are not reported by race/ethnicity-age. Prior studies suggest that cigarette smoking has been used to control weight (Pomerleau et al., 2001) and that non-smokers have a higher BMI than current smokers (Albanes et al., 1987; Molarius et al., 1997; Kaufman et al., 2012; Prospective Studies Collaboration, 2009).

To our knowledge, only two studies have examined whether or not the type of cigarette smoked is differentially associated with BMI. Miguez-Burbano et al. (2014) found that current menthol smokers have a 40% increased risk of abdominal obesity and are twice as likely to have hypertension and moderate to high cardiovascular disease risk. This study was conducted among a sample of adults enrolled in a cohort study in South Florida, which included Blacks, whites, and Hispanics who were non-HIV and HIV positive (n = 393). Using data from the U.S. National Health Interview Survey (n = 12,004), Mendiondo et al. (2010) found that current menthol smokers had a marginally higher, but not significantly higher BMI than non-menthol smokers (1.01, 95% CI = 1.001,1.01). Among former smokers, menthol smokers had a marginally, but significantly higher BMI than non-menthol smokers (1.01, 95% CI = 1.01,1.02).

These two studies provide some evidence of the potential relationship of menthol cigarette smoking and obesity using national and local data, but are not sufficient to draw definitive conclusions. The prior two studies either did not include or report on data for Native Hawaiians and Filipinos. Compared with whites, Native Hawaiians and Filipinos suffer disproportionately from smoking related morbidity and mortality (American Cancer Society, 2010), and in Hawaii, menthol smoking is unusually high with 40% of whites and 76% of Native Hawaiian adult smokers reporting menthol smoking (Hawaii Department of Health, 2010). Prior studies did not specifically focus on young adults or daily smokers. Daily smoking is more prevalent among young adults than non-daily smoking (23.3 vs. 16.7%), and approximately 47.3% of 18–25 year olds smoked on 30 days in the past month and 13.2% on 20–29 days (USDHHS, 2012). Daily smoking increases the risk for tobacco caused morbidity and mortality (USDHHS, 2014) and understanding how to intervene during young adulthood could substantially reduce the burden.

Furthermore, prior studies did not examine the relationship between BMI and nicotine metabolism. Menthol inhibits nicotine metabolism in the liver (Benowitz et al., 2004; MacDougal et al., 2003) and menthol smokers have slower metabolism than non-menthol smokers as indicated by the nicotine metabolite ratio (NMR = ratio of trans 3'-hydroxycotinine to cotinine) (Chenoweth et al., 2014; Mwenifumbo et al., 2007; Wang et al., 2010). Nicotine metabolism is primarily mediated by the enzyme cytochrome P450 2A6 (CYP2A6), and studies suggest that the NMR is a valid phenotypic marker of CYP2A6 activity (Dempsey et al., 2004; Nakajima et al., 1996; Zhu et al., 2013). Studies generally show that the higher the NMR, the greater the nicotine clearance (Benowitz et al., 2003). Like menthol, BMI independently influences the NMR (Ho et al., 2009), but studies have not determined the relationship between BMI and the NMR by cigarette type. If overweight or obese menthol smokers have a lower NMR compared with obese non-menthol smokers, then the data would be suggestive of slower nicotine metabolism. Slower metabolism may result in greater harm since smoking would have a greater exposure to nicotine and may even have greater difficulty quitting. Such data could inform the design of future smoking cessation intervention studies for obese menthol smokers in the clinical setting.

Our exploratory study examines 1) the relationship between menthol cigarette smoking and obesity and 2) the association of BMI with the nicotine metabolite ratio among menthol and non-menthol daily cigarette smokers aged 18–35. Based on prior studies, we expect that menthol smokers will have higher rates of obesity than non-menthol smokers. Since both BMI and menthol influence nicotine metabolism, we expect that the NMR will be lower among obese menthol smokers compared with obese non-menthol smokers. Menthol is the only characterizing flavor that was not banned by the 2009 U.S. Family Smoking Prevention and Tobacco Control Act. Further investigation of the relationship between menthol cigarette smoking and obesity may increase our understanding on how to reduce the burden of these risk factors among vulnerable groups.

Materials and methods

Study sample

We used www.craigslist.com, newspaper advertisements, and peer-to-peer referral to recruit young adult daily cigarette smokers aged 18–35 into our study on smoking in our lab. All interested persons were screened by telephone by trained research staff from May 2013 to December 2013. Participants were eligible if they were aged 18–35; self-identified as Native Hawaiian, Filipino, or white race/ethnicity; could read and speak English well; had a working phone, email, and home address; were willing to provide consent; stated that they smoked menthol or non-menthol; and smoked at least five cigarettes per day on average. Smokers using other tobacco products, nicotine delivery devices, pharmacotherapy, or who indicated that they smoked no usual brand type were ineligible. Pregnant women were excluded from the study. Our study aimed to recruit 200 participants. Ninety-eight percent (n = 336) of eligible participants agreed to voluntarily participate in the survey and were invited to come to the University of Hawaii Cancer Center in central Honolulu to complete the survey in the translational research laboratory. Of the eligible participants, 59.5% completed the study, a consent rate higher than (Ramos et al., 2010; Ramo and Prochaska, 2012) and comparable with other studies that recruited young adult smokers (Ramo et al., 2014).

Procedures

All participants were forwarded the consent form prior to their visit to the University of Hawaii Cancer Center. Participants completed the consent form during the one-hour visit and prior to survey administration. Participants brought in the cigarettes they regularly smoked to verify
whether it was menthol or non-menthol. A saliva sample was collected using standard passive drool procedures, aliquoted, and stored at −80 °C. Height and weight were measured in the lab for all participants. Trained research staff provided instructions to participants to complete the online survey in the research lab. All participants received a $40 gift card and a one-page fact sheet on quitting smoking at the end of the one-hour study. The study was approved by the Western Institutional Review Board and we secured a Certificate of Confidentiality from the National Institutes of Health.

**Measures**

We assessed age, gender, race/ethnicity, sexual orientation, educational attainment, marital status, employment status, financial dependence on parents/guardians, personal financial situation, household income, and BMI (lbs/in²). Age groups were categorized as 18–24 and 25–35. Race/ethnicity categories included Native Hawaiian, Filipino, and white. Participants were asked if they were heterosexual/straight, homosexual/gay/lesbian, bisexual, transgender, other, or not sure. Due to the sample size, we collapsed categories into heterosexual/straight or homosexual/bisexual/other. To measure educational attainment, we asked participants to indicate their highest level of school/degree completed. Educational attainment was categorized as persons with no diploma, with a high school diploma, and college education or higher. Marital status included the categories now married, widowed, divorced, separated, never married and living with a partner. Categories were collapsed into single, married and other. Employment status was categorized as full-time, part-time 15–34 h/week, part-time <15 h/week, or do not work for pay. Financial dependence on parents/guardian response categories included completely/ almost completely dependent, partially dependent, and not dependent. Personal financial situation response categories included live comfortably, meet needs with a little left, just meet basic expenses, and do not meet basic needs. Total household income included the categories <$20,000, $20,000–49,999, or ≥$50,000. Measured height and weight were taken in the lab and used to calculate the BMI. BMI was categorized into normal weight (18.5–24.9), overweight (25.0–29.9), and obese (30 and over). Underweight (less than 18.5) was dropped due to small sample size.

To measure smoking status we examined usual type of cigarette smoked (menthol or non-menthol), frequency of smoking, days smoked in past 30 days, number of cigarettes smoked per day (cpd) (National Cancer Institute, 2010–2011). Usual type of cigarette was assessed and response categories included menthol, non-menthol, and no usual type. Only persons who smoked daily were included in the analysis.

**Biomarkers and analytical methods**

We measured saliva cotinine as a nicotine exposure biomarker using isotope dilution liquid chromatography/tandem mass spectrometry (LC/MS) in a modification of a previous protocol (Shakleya and Huestis, 2009). Our methods have been previously described and thus, we briefly describe the method here. A description of general MS condition can be found elsewhere (Fagan et al., 2015). The assay included unconjugated (free) nicotine, cotinine and 3HC. Defrosted saliva was centrifuged and a 120 μL clear aliquot was combined with a 12 μL internal standard solution (1000 ng/mL each of (±)-nicotine-d₄ and (±)-cotinine-d₃ in MeOH; Cerilliant Corporation Round Rock, Texas) followed by the addition of 100 μL MeCN to precipitate proteins. This mixture was vortexed, then extracted with 1 mL dichloromethan:2-propanol: NH₄OH (78:20:2, v/v/v) using a mechanical shaker in pulse mode (1550 rpm) for 2 min followed by centrifugation. The organic layer was mixed with 100 μL 1% HCL solution in MeOH then dried under a nitrogen flow. The dried residue was redissolved in 120 μL 0.1% formic acid in H₂O. 20 μL was injected into the LC/MS system, which consisted of a model Accela ultra-HPLC system coupled to a model TSQ Ultra tandem mass spectrometer (Thermo Electron, Waltham, MA). Separation was performed using a Kinetic C18 column (150 × 30 mm, 2.6 μm; Phenomenex, Torrance, CA) by elution with a linear gradient consisting of (A) 0.05% NH₄OH in H₂O and (B) 0.05% NH₄OH in MeOH at 0.150 mL/min as follows: 0–5 min 55% B, 5–19 min linear gradient to 80% B and keep at 80% B for 1 min, then equilibrate at 35% B for 5 min.

Cotinine was calculated in nanograms per milliliter. The limit detection level used for this procedure was 2.5 ng/mL. Persons who were determined not to be daily smokers were excluded from the analysis (n = 14). The salivary nicotine metabolite ratio (NMR) was defined as the ratio of trans 3′ hydroxycotinine over cotinine (non-glucuronidated).

**Statistical analysis**

The SAS 9.4 statistical software was used for all data management and analyses (SAS, 2011). We calculated descriptive statistics for the sociodemographic and smoking behavior. Chi-square independence tests (for categorical variables) and t-tests (for continuous variables) examined differences between menthol and non-menthol smokers and BMI categories, normal weight, overweight, and obese. We used multivariate logistic regression to examine the association between menthol cigarette smoking and obesity versus not obese (BMI ≥30 versus BMI <30) while controlling for covariates, gender, marital status, education, employment status, and race/ethnicity. Analysis of covariance (ANCOVA) models tested biomarker differences among menthol and non-menthol smokers who were of normal weight, overweight, and obese. In each model the dependent variable was the logged biomarker value. Logging the values improved the normality of the distributions and made them more closely related to the metabolic clearance of nicotine (Levi et al., 2007). We report the geometric means and standard errors of the NMR. We excluded 14 people from the analyses who were not daily smokers. 7 underweight people due to small sample sizes, and 4 additional were excluded for whom there were missing data. A total of 175 daily smokers were included in the analysis.

**Results**

**Sociodemographic characteristics of daily smokers**

Table 1 shows the sociodemographic characteristics of the sample by menthol and non-menthol smoking status. The sample was evenly distributed by gender. There was a greater proportion of Native Hawaiians and whites than Filipinos who enrolled in the study. The sample also included a greater proportion of 18–24 year olds, high school graduates, single persons, full-time workers, financially non-dependent, person who just meet their basic needs, and person with household incomes below $40,000/year. Chi-square independence tests and t-tests showed significant differences between menthol and non-menthol smokers by gender, race/ethnicity BMI categories, education, marital status, and employment status. Sixty-eight percent of the sample smoked menthol cigarettes (data not shown).

**Daily cigarette smoking and BMI**

Overall, the BMI for all young adult daily smokers was 27.8 (see Table 1). Chi-square independence tests and t-tests showed significant differences in BMI categories among menthol and non-menthol smokers. Menthol cigarette smokers had a significantly higher BMI than non-menthol smokers. Over one-third of all smokers, 9.1% of non-menthol smokers, and 40.8% of menthol smokers were obese. Table 2 shows the characteristics of smokers by BMI category. Chi-square independence tests and t-tests showed significant differences in BMI categories by age, race/ethnicity, and menthol smoking status. We found that 90.7% of obese smokers used menthol and 93.3% smoked...
All data were collected from May to December 2013 in Honolulu, Hawaii. Bold face indicates statistical significance p < 0.05.

Numbers may not add up to 100 due to missing values. Bold face indicates statistical significance p < 0.05. All data were collected from May to December 2013 in Honolulu, Hawaii. a SD = standard deviation. b $\chi^2$ and t-tests were applied for categorical and continuous variables. c Other: includes separated or widowed.

Non-menthol cigarettes. Nearly 62% of normal weight and 54.2% of overweight smokers were non-menthol smokers and 38.4% and 45.8% respectively were menthol smokers.

Unadjusted and adjusted models of the relationship between daily menthol cigarette smoking and obesity

Table 3 shows the association of menthol smoking status with obesity. The unadjusted model shows that daily menthol cigarette smokers had nearly 7 times the odds of being obese compared with non-menthol smokers. After adjusting for gender, marital status, education, employment, and race/ethnicity, menthol smokers had more than 3 times the odds of being obese compared with non-menthol smokers.

BMI categories and the NMR

We examined the relationship between BMI and the NMR among menthol and non-menthol smokers. Normal weight and obese menthol smokers had a lower NMR than non-menthol smokers, but the differences were not statistically significant (normal weight unadjusted = .19 [SE = .02] versus .25 [SE = .04], p = .15; adjusted = .18 [SE = .02] versus .20 [SE = .04], p = .64) (obese unadjusted = .18 [SE .02] versus .25 [SE = .04], p = .22; obese adjusted = .18 [SE = .02] versus .23 [SE = .02]).
Multivariate regression of menthol smoking and obesity among daily smokers aged 18–35.

|            | Odds ratio | LCL | UCL | p-value |
|------------|------------|-----|-----|---------|
| Adjusted   |            |     |     |         |
| Non-menthol versus menthol | 3.19 | 1.04 | 9.78 | 0.04 |
| Female versus male | 0.94 | 0.42 | 2.11 | 0.89 |
| Never married versus now married | 0.80 | 0.24 | 2.66 | 0.71 |
| Other versus now married | 0.74 | 0.21 | 2.57 | 0.63 |
| High school versus no degree | 1.83 | 0.58 | 5.80 | 0.30 |
| College versus no degree | 1.87 | 0.46 | 7.53 | 0.38 |
| Work 15–34 h versus work full-time | 0.80 | 0.27 | 2.35 | 0.69 |
| Work less than 15 h versus work full-time | 4.60 | 0.48 | 44.49 | 0.19 |
| Don’t work versus work full-time | 0.87 | 0.34 | 2.23 | 0.77 |
| Filipino versus Hawaiian | 6.56 | 1.61 | 26.76 | 0.01 |
| White versus Hawaiian | 5.11 | 2.03 | 12.88 | 0.000 |

Bold face indicates statistical significance p < 0.05.
All data were collected from May to December 2013 in Honolulu, Hawaii.

Adjusted models were statistically significant for the overweight category with menthol smokers having a lower NMR than non-menthol smokers (.16 [SE .03] versus .26 [SE .05], p = .02) in the unadjusted model. However, after adjusting for gender, marital status, education, employment, and race/ethnicity, the differences were no longer statistically significant (.15 [SE .03] versus .18 [SE .05], p = .50) (Fig. 1).

Discussion

Only two prior studies to our knowledge documented the relationship between obesity and menthol cigarette smoking. Our study found that over 40% of menthol smokers were obese compared with 9% of non-menthol smokers. After controlling for gender, marital status, education, employment status, and race/ethnicity, menthol smokers were more than 3 times more likely to be obese compared with non-menthol smokers. Furthermore, menthol smokers were over-represented among persons who were obese with 90% of obese persons being menthol smokers. We found that among persons who were overweight, menthol smokers had a lower NMR than non-menthol smokers, but after adjusting for the covariates, the differences were no longer statistically significant. Like prior studies, our study is cross-sectional in nature, but suggests a need to further investigate how menthol smoking increases the risk for obesity and vice versa.

Our study is unique in that it explores an understudied area of research among young adults. Menthol cigarette smoking and obesity are both growing epidemics among young people and understanding the relationship between these two leading chronic disease risk factors may better inform interventions for populations who would greatly benefit. Overall, nearly 60% of all young adults were overweight or obese, which is consistent with U.S. data that show that 60.3% of adults 20–39 are overweight or obese (Ogden et al., 2014). However, this is surprising since these young adults are smokers. Studies have shown that some people have used smoking to control their weight (Cavall et al., 2006; French et al., 1994; Potter et al., 2004). Combined with smoking, obesity early in life may contribute to an increase in overall excess morbidity and mortality.

The study enrolled established daily smokers from multiple ethnic groups in Hawaii with a high lung cancer risk (American Cancer Society, 2010). Most young adults are daily smokers (USDHHS, 2012) which increases the risk for chronic diseases and nicotine dependence (USDHHS, 2014). It is unclear why we observe higher rates of obesity among menthol smokers who have slower nicotine clearance. Nicotine is a known appetite suppressant (Kroemer et al., 2014; McFadden et al., 2014) and studies show that nicotine decreases food intake in mice (Mineur et al., 2011). Thus, one would expect that smokers with slower nicotine metabolism may potentially have lower BMI, but our hypothesis was not supported. This may be due to small sample sizes. It is possible that persons who like flavored cigarettes may also like foods that are rich and high in fat or sugar. Smokers of flavored cigarettes could potentially crave foods that are rich and sweet, which counteracts any appetite suppressant characteristics of nicotine. Studies need to investigate the relationship between menthol smoking and food consumption behaviors.

Limitations

This cross-sectional study limits our ability to determine the causality of the relationships between menthol smoking and obesity. Samples were recruited from Craigslist and newspaper advertisements and may lack generalizability to other smokers. The data collected were limited to adults aged 18–35; Native Hawaiians, Filipinos, and whites; and daily smokers in Hawaii only. Because our study was lab based, smokers originated from the island of Oahu, where most residents in Hawaii and approximately 60% of Native Hawaiians live (U.S. Census Bureau, 2010). Due to sample size, we are unable to examine the relationship between cigarette type smoked and all three BMI categories in racial/ethnic or gender groups. BMI is only one measure of health risk associated with obesity and we did not measure food consumption and cravings, high blood pressure, physical activity, family history, history of obesity related disease, or use of medications that are related to conditions associated with obesity. We did not measure waist circumference and studies have shown that nicotine increases insulin resistance and is associated with central fat accumulation (Chiolero et al., 2008).

Conclusions

This study suggests that the relationship between menthol smoking and obesity, the nation’s two leading causes of chronic disease, be further examined. By 2050, menthol smoking is estimated to result in

Fig. 1. Interaction plot for log NMR. The figure represents the log of the nicotine metabolite ratio (logNMR) for persons who are of normal weight (BMI = 18.5–24.9), overweight (BMI = 25.0–29.9), and obese (BMI = 30 and over). The blue line and dots represent menthol smokers and the red line and dots represent non-menthol smokers. The horizontal lines show that menthol smokers have a significantly lower nicotine metabolite ratio. After adjusting for gender, marital status, educational attainment, employment status, and race/ethnicity, for each BMI group, none of the differences were statistically significant for menthol and non-menthol smokers in Honolulu, Hawaii. Data were collected from May to December 2013.
over 300,000 cumulative excess deaths (Levy et al., 2011). Future cross-sectional, longitudinal and mechanistic studies are needed to determine how menthol smoking and obesity are related and whether or not these two leading chronic disease risk factors lead to excess disease risk in menthol compared with non-menthol smokers.

Conflict of interest statement
The authors declare that there are no conflicts of interests.

Transparency document
The Transparency document associated with this article can be found, in the online version.

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