Research Article

Smokeless and Dual Tobacco Use Among Males Surviving Childhood Cancer: A Report From the Childhood Cancer Survivor Study

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Abstract

Cancer survivors experience treatment-related complications that can be exacerbated by tobacco use. This study reports the prevalence of smokeless and dual tobacco use, compares these rates to the U.S. population, and examines tobacco risk factors among males surviving childhood cancer. Data from the Childhood Cancer Survivor Study (CCSS) 2007 survey were used ($N = 3378$). Standardized incidence ratios (SIR) were obtained by comparing CCSS data with the National Survey on Drug Use and Health. Logistic regression was used to evaluate associations between risk factors and tobacco use. Among male survivors, 8.3% and 2.3% were current smokeless tobacco and dual tobacco users, respectively. Survivors were less likely than population males to report smokeless tobacco [SIR = 0.64; 95% confidence interval (CI), 0.57–0.72) or dual tobacco (SIR = 0.37; CI, 0.29–0.46) use; however, non-White survivors aged 35 to 49 years were more likely to use smokeless tobacco (SIR = 2.32; CI, 1.27–3.90). Smokeless tobacco use was associated ($P < 0.05$) with younger age at diagnosis, lower education, being married or divorced/separated, and not living in the Northeastern United State, whereas history of cardiovascular- and/or pulmonary-toxic treatment was protective. Dual tobacco use was associated with younger age at diagnosis, lower education, divorce/separation, and high psychologic distress. Having active heart or circulatory conditions was protective. Although smokeless tobacco/dual tobacco use is generally low among childhood cancer survivors, these findings suggest that tobacco use screening should be expanded to include smokeless tobacco use, and that smokeless tobacco-specific education and cessation interventions should be provided to users. Screening and intervening for smokeless tobacco/dual tobacco use in childhood cancer survivors will reduce tobacco-related morbidity and mortality. *Cancer Epidemiol Biomarkers Prev; 22(6); 1–5. ©2013 AACR.*

Introduction

Over the past 50 years, survival rates for childhood cancer have dramatically improved with 1 in 640 U.S. young adults now estimated to be survivors (1, 2). Survivorship is commonly affected by complications resulting from cancer treatment. Specifically, 42% of pediatric cancer survivors experience serious, disabling, or life-threatening illnesses by 30 years after diagnosis (3). These include cardiovascular disease, stroke, kidney failure, pulmonary fibrosis, and second malignancies, conditions that may be the result of, or exacerbated by, tobacco use. Antineoplastic therapies used in cancer treatments result in cardiopulmonary toxicities and organ compromise, which may be further potentiated by tobacco use. Patients who continue tobacco use after diagnosis are at increased risk for both acute (e.g., treatment complications) and long-term health risks (e.g., disease recurrence, secondary primary cancer, and reduced survival) relative to those who quit (4, 5). As such, survivors of childhood cancer should avoid tobacco to decrease their risk for long-term health problems.

Although smoking has been examined among pediatric cancer survivors, smokeless tobacco and dual tobacco use (e.g., usage of both combustible and smokeless tobacco) has not (4, 6). The 2 most commonly used smokeless tobacco products in the United States are snuff and chewing tobacco, and both are absorbed through tissue in the mouth (7). Smokeless tobacco includes up to 28 carcinogens and is associated with malignancies of the mouth, tongue, throat, esophagus, stomach, and pancreas and increased risk of cardiovascular disease, myocardial infarctions, and stroke (7, 8). As survivors are already susceptible to these late effects, tobacco use would be

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expected to not only add to this risk but also potentiate synergistic effects, thus increasing risk for chronic health conditions (3, 9).

The current study was conducted to determine the prevalence of smokeless tobacco and dual tobacco use among adult survivors of childhood cancer, and to identify risk factors associated with tobacco behaviors.

Materials and Methods

The Childhood Cancer Survivor Study (CCSS) is a multi-institutional study of individuals who have survived 5 years or more after diagnosis of childhood cancer. Diagnoses represented in this cohort include leukemia, brain tumor, Hodgkin lymphoma, non-Hodgkin lymphoma, Wilm's tumor, neuroblastoma, soft-tissue sarcoma, and bone tumors. Participants were diagnosed before 21 years of age and treated at one of the 26 collaborating institutions between January 1, 1970 and December 31, 1986. A detailed description of the CCSS study is reported elsewhere (10, 11). The study was approved by the Institutional review board at each institution, and informed consent was obtained from participants.

Of the 10,143 survivors eligible for the 2007 follow-up survey, 374 (3.7%) were lost to follow-up. Among participants successfully contacted, 82.0% ($n = 8,013$) completed the study questionnaire. Participants and those lost to follow-up were similar in regard to diagnosis and geographic region; however, study participants were more likely to be White and of older age at diagnosis ($P < 0.05$). Women were excluded because of low engagement in smokeless tobacco ($n = 6$) and dual tobacco ($n = 1$) use. The remaining sample of 4,000 males was further restricted to those living in the United States ($n = 3,717$) and those with complete tobacco data ($n = 3,378$). Canadian participants were excluded because the reference population used to calculate standardized incidence was U.S. based. Study outcomes were based on participants' self-report of smokeless and combustible tobacco use. Participants who did/did not complete the tobacco items were similar in regard to cancer type, race, age at diagnosis, income, geographic region, educational status, and marital status ($P > 0.05$).

Primary outcomes

Smokeless tobacco use. Participants who endorsed response options of "occasionally use" or "regularly use" for chewing and/or snuff tobacco over the last year were classified as smokeless tobacco users.

Dual tobacco use. Participants were classified as "dual users" if engaged in smokeless tobacco use as defined above, and responded "yes" to current cigarette use or "occasionally use" or "regularly use" of cigars or pipes.

Independent variables

Demographic/personal variables considered included age at and years since diagnosis, race, educational attainment, household income, marital status, geographic region of residence, and current age. Health condition variables included cancer diagnosis, history of relapse/second malignant neoplasms (SMN), and respiratory and heart/circulatory health status. Respiratory health status was based on 8 items querying history of breathing/lung problems (asthma, emphysema, lung fibrosis, etc.,). Heart/circulatory health was based on 13 items querying history of cardiovascular problems (myocardial infarction, arrhythmia, hypertension, etc.). For each system-specific condition, participants reported condition history based on the following response options: (i) "yes, condition still present," (ii) "yes, condition not present," (iii) "no history of condition," and (iv) "not sure." Participants were grouped into disease acuity categories based on endorsement of the condition at the highest level. Psychologic distress was based upon the Brief Symptom Inventory-18[12] (depression, somatization, anxiety, and Global Severity Index; GSI) applying a clinical cut-off score ≥ 63 (90th percentile; ref. 12) and antidepressant use. Participants' level of physical activity was based upon reported participation over the previous month.

Cancer treatments known to be associated with cardiovascular and/or pulmonary complications including chemotherapy (bleomycin, BCNU/CCNU, anthracyclines) and radiation therapy (cranial irradiation associated with increased risk of metabolic syndrome, chest irradiation involving the heart and/or lungs, and/or neck irradiation involving the carotid arteries) were also examined. Dichotomous (yes/no) variables were created to characterize exposure to any of the 3 chemotherapies (at-risk chemotherapy) or 3 exposure areas of radiation therapy (at-risk radiation therapy), as well as an overall dichotomous variable for exposure to any of the 6 treatment variables (at-risk cancer treatment).

Statistical analysis

Current rates of smokeless tobacco and dual tobacco use for the CCSS cohort were compared with data from the 2007 National Survey on Drug Use and Health (13). Using expected values standardized by age, sex, and White/non-White race, prevalence ratios (PR; PR = observed/expected) were computed along with corresponding 95% confidence intervals (CI). Probability values were estimated using Byar approximation. The associations between risk factors and tobacco outcomes were evaluated in generalized linear models using PROC LOGISTIC in SAS version 9.2. Univariate models were first conducted to test associations between single-risk factors and tobacco outcomes. Independent variables with initial P values < 0.15 were included in multivariable models. Final multivariate models were determined using a backward selection process based on minimum Akaike's information criterion (AIC). If there were variables that were not significant at the 5% level of significance, but were included in the model chosen by AIC, then the model was rerun without those variables. If the AIC for the new model didn't increase significantly, then the reduced model was

retained; otherwise, the model chosen by AIC was taken as the final model.

Results

At the time of data collection, the mean population age was 36.4 years (SD 7.5; range, 21.0–58.0). The majority of participants (86.5%) were self-identified as White, 55.9% were married, 65.5% had Bachelor degrees or more, and 48.1% reported annual household income $60,000 or more. Distribution of diagnoses is as follows: leukemia (33.1%), central nervous system tumor (11.9%), Hodgkin lymphoma (13.7%), non-Hodgkin lymphoma (10.8%), Wilm's tumor (7.9%), neuroblastoma (5.6%), soft-tissue sarcoma (9.2%), and bone tumors (8.1%). Almost 61% were diagnosed between ages 0 to 9 and 25.3% experienced relapse. Participants received the following cardiovascular- and/or pulmonary-toxic therapies: bleomycin (6.0%), BCNU/CCNU (7.0%), anthracyclines (37.2%), chest irradiation (17.5%), neck irradiation (16.4%). Overall, 40.4% of the sample received at-risk chemotherapy, 46.5% received at-risk radiation therapy, and 65.8% received at-risk cancer treatment. More than 32% of participants reported a current heart/circulatory condition (6.4% reported past history), and 11.9% reported a current respiratory condition (8.5% reported past history). Approximately 5% experienced clinically significant global psychologic distress, or disordered somatization (5.5%), depression (8.0%), or anxiety (5.1%). Nearly 12% were taking antidepressants, and 77.7% reported engaging in physical activity.

Of the 3,378 participants, 279 (8.3%) reported current use of smokeless tobacco and 79 (2.3%) reported dual tobacco use. Comparisons of age- and race-standardized prevalence rates of tobacco use between survivors and the general population revealed that smokeless tobacco use (PR, 0.64; 95% CI, 0.57–0.72) was significantly lower among survivors (Table 1). Dual tobacco use (PR, 0.37; 95% CI, 0.29–0.46) was also significantly lower in survi-

vors. Significant PRs 1.0 or more were found only for smokeless tobacco use in non-White survivors aged 35 to 49 years ($P = 0.008$).

Univariate analyses identified associations between smokeless tobacco use and age at diagnosis, race, education, household income, marital status, U.S. region of residence, cancer diagnosis, psychologic distress (anxiety, somatization, and GSI), antidepressant use, and exposure to various cancer treatments. In multivariable models, at-risk cancer treatment and GSI were used to represent treatment and psychologic distress to reduce potential collinearity between constructs. In the final multivariable logistic model, factors that remained independently associated with smokeless tobacco use included early age at cancer diagnosis, not being a college graduate, being married or divorced/separated, and not residing in the Northeast (Table 2). Decreased risk of smokeless tobacco use was associated with having received at-risk cancer treatment.

Univariate analyses assessing dual tobacco use identified associations between age at diagnosis, current age, education, household income, marital status, U.S. region of residence, heart/circulatory problem, physical activity, psychologic distress (anxiety, somatization, and GSI), antidepressant use, bleomycin exposure, anthracycline exposure, at-risk chemotherapy, and at-risk cancer treatment. The final multivariable logistic model identified dual tobacco use to be independently associated with younger age at cancer diagnosis, not being a college graduate, being separated/divorced, and being psychologically distressed (Table 3). Existing heart and/or circulatory problems were associated with a decreased likelihood of dual tobacco use.

Discussion

Males surviving childhood cancer engage in smokeless tobacco and dual tobacco use, but their rates are lower than the U.S. population. Sex, education, U.S. region of

Table 1. Comparison of smokeless tobacco use among males in the U.S. population and CCSS cohort

Age, y	Race	Prevalence		PR	95% CI	P
		U.S. population	Cancer survivors			
21–25	White	19.85%	7.10%	0.36	(0.19–0.61)	<0.0001
	Others	5.35%	4.35%	0.81	(0.01–4.52)	0.69
26–29	White	18.67%	7.67%	0.41	(0.28–0.58)	<0.0001
	Others	3.46%	7.59%	2.20	(0.80–4.78)	0.12
30–34	White	15.12%	9.98%	0.66	(0.50–0.85)	0.0008
	Others	3.65%	2.17%	0.60	(0.07–2.15)	0.69
35–49	White	13.14%	9.24%	0.70	(0.59–0.83)	<0.0001
	Others	2.63%	6.11%	2.32	(1.27–3.90)	0.008
50+	White	3.86%	3.36%	0.87	(0.28–2.03)	0.97
	Others	1.35%	0.00%	0.00		
Total			8.27%	0.64	(0.57–0.72)	<0.0001

Table 2. Multivariable model for risk of current smokeless tobacco use among adult male survivors of childhood cancer

	Risk ratio	95% CI	P
Age at cancer diagnosis			
0–9 years	1.46	(1.05, 2.01)	0.02
10–20 years (referent)	1.00		
Education status			
1–12 years	1.18	(0.49–2.84)	0.04
HS grad/post HS	1.58	(1.11–2.24)	
College grad/post college (referent)	1.00		
Marital status			
Divorced/separated	3.81	(2.35–6.17)	<0.0001
Married/live as married	1.79	(1.23–2.60)	
Single (referent)	1.00		
U.S. region of residence			
Midwest	2.10	(1.22–3.60)	0.001
South	2.78	(1.66–4.66)	
West	1.82	(1.04–3.21)	
Northeast (referent)	1.00		
At-risk cancer treatment[a]			
Yes	0.71	(0.53–0.96)	0.02
No (referent)	1.00		

[a]At-risk cancer, treatment is assigned if patient has a history of receiving one or more of the 6 listed cancer treatments. Abbreviations: HS, high school; Grad, graduate.

Table 3. Multivariable model for risk of current dual tobacco use among adult male survivors of childhood cancer

	Risk ratio	95% CI	P
Age at cancer diagnosis			
0–9 years	3.07	(1.51–6.25)	0.002
10–20 years (referent)	1.00		
Education status			
1–12 years	1.74	(0.40–7.61)	0.03
HS grad/post HS	2.22	(1.23–4.01)	
College grad/post college (referent)	1.00		
Marital status			
Divorced/separated	6.39	(2.92–13.97)	<0.0001
Married/live as married	1.89	(0.95–3.76)	
Single (referent)	1.00		
Heart/circulatory condition(s)			
Yes, condition still present	0.35	(0.15–0.79)	0.009
Yes, condition not present	1.80	(0.78–4.16)	
None (referent)	1.00		
Psychologically distressed			
Yes	2.50	(1.01–6.21)	0.048
No (referent)	1.00		

Abbreviations: HS, high school; Grad, graduate.

residence, psychologic functioning, age at diagnosis, and marital status were identified as risk factors for tobacco use, whereas active heart/circulatory conditions and at-risk cancer treatment were protective. Despite their vulnerable health status, these results suggest that surviving childhood cancer does not make one immune to tobacco use. As such, careful screening and the provision of risk-based care should be prioritized among all adults as recommended by the Public Health Service clinical guidelines (14). This is particularly important for survivors of childhood cancer, as suboptimal application of the guidelines has been reported in this group (15). As 90% of survivors experience medical encounters at least biannually (16), screening may be conducted more often by health professionals, thus maximizing the opportunity for tobacco surveillance and intervention.

Although White survivors reported lower rates of smokeless tobacco when compared with the general population, non-White survivors had comparable or increased rates. Specifically, 6.1% of middle-aged non-White survivors (and 2.6% of their population peers) reported smokeless tobacco use. These findings are concerning as survivors are at increased health risk secondary to treatment, and are less likely to quit tobacco use in general (17). Furthermore, ethnic minorities are at disproportionally high risk of cerebral vascular disease and mortality sec-

ondary to diseases such as cancer and cardiovascular disease (14). Therefore, ethnic minority status compounds the risk of smokeless tobacco use for this group of non-White survivors (14, 18). However, this finding should be interpreted within the confines of limited cell sizes among subgroups, which limit the generalizability of this finding.

Several risk factors were identified for both smokeless tobacco and dual tobacco use including younger age at diagnosis, lower education, and being divorced/separated. Unique predictors of smokeless tobacco included being married and not living in the Northeast, whereas a history of at-risk cancer treatment was protective against smokeless tobacco. Dual tobacco was independently associated with high psychologic distress, a factor, which associates with both smoking and difficulty quitting (19, 20). Finally, having an active heart/circulatory condition was protective against dual tobacco, which is notable considering the cardiovascular risk associated with both smokeless tobacco and combustible tobacco use (21). Similar risk (lower education, psychologic distress) and protective factors (at-risk treatment) have been previously shown for smoking in childhood cancer survivors (6, 22, 23).

These results may be limited by potential under-reporting of tobacco use given this population's susceptibility

to tobacco-related complication, and stigma associated with tobacco use (24). Future designs should consider strategies that will increase the validity of tobacco use outcomes such as biochemical verification or bogus pipeline (25). Also, this study did not consider contemporary forms of tobacco use (hookah, narghile, bidis, kreteks, e-cigarettes).

Over the past 50 years, survival rates for childhood cancer have increased exponentially (1, 2). As such, a longer continuum of care has been necessitated, which focuses on the reduction of risk for second cancers and adverse late effects. Interventions to eliminate or reduce cancer-linked behaviors (including smokeless tobacco and dual tobacco use) are now fundamental components of survivorship care. The promotion of healthy behaviors will not only reduce morbidity/mortality in this population, but also translate to better quality of life outcomes.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

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