

A Case-Control Study of Tobacco-Related Cancers in Colombia¹

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The work reported here examined the effects of smoking cigarettes made predominantly of dark tobacco, alcohol consumption, and coffee drinking upon the risk of developing cancers of the bladder, larynx, lung, and oral cavity/hypopharynx in Medellín, Colombia. For this purpose 439 subjects with newly diagnosed cancers at the indicated sites were selected. Each subject was then matched by age, sex, and socioeconomic status with at least one control. Data from interviews with the selected subjects, upon analysis, showed both the intensity and duration of cigarette smoking to be statistically significant predictors of cancer at all four sites. In addition, heavy alcohol consumption and coffee drinking in excess of seven cups daily were associated with some elevation of cancer risk at most of the sites studied.

Multivariate analyses of cigarette smoking, alcohol consumption, and coffee drinking showed that adjustment for coffee and alcohol consumption did not change the observed associations between elevated cancer risks and cigarette smoking. However, adjustment of the coffee and alcohol consumption data for cigarette smoking reduced most of the observed relative risks of coffee and alcohol consumption and eliminated the statistical significance of certain associations.

It is widely recognized that the figures for lung cancer incidence and mortality in developed nations are higher than

those recorded in most Latin American and Caribbean countries (1, 2). This contrasts with the higher incidences and mortality rates of bladder, larynx, and oral cavity cancers that have been documented in Latin American populations (1-3). For example, previous reports from Antioquia, one of Colombia's northwestern states, have indicated a high frequency of cancer of the larynx there, especially among women (4, 5).

Traditionally, Colombians typically smoked dark nonfilter cigarettes. This dark or "black" tobacco is similar to the type used for cigar manufacturing, and it has more nicotine, as well as a higher phenol concentration, than most other varieties. A shift from dark tobacco ciga-

¹This article has also been published in Spanish in the *Boletín de la Oficina Sanitaria Panamericana*, Vol. 105, No. 3, pp. 221-330, 1988. The project reported here was partially supported by U.S. Public Health Service Contract (Cali) No. I-CP33286 and No. I-CO53521 and by PAHO contract APO-24797 (WU) for final analysis of the data.

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rettes to light or "blond" tobacco United States-style cigarettes occurred as national tobacco industries gradually achieved the expertise to produce filter cigarettes made with refined light tobacco. Economic factors related to competition between nationally produced cigarettes and illegally marketed imports were the main reason for this trend, which began in the 1960s and 1970s.

We were interested in investigating associations between tobacco use and cancers at different sites in a population whose tobacco use patterns were changing with regard to the type of tobacco smoked. Among other things, it had been suggested that the carcinogenic effect of dark tobacco on exposed epithelium in experimental animals (6) might account for geographic differences in smoking-related cancers among smokers of dark and light tobacco (1, 2). Therefore, this matter was considered in a broader case-control study of bladder, larynx, lung, and oral/hypopharynx cancers that analyzed the effects of alcohol and coffee drinking as well as smoking upon the study population.

MATERIALS AND METHODS

Study subjects with newly diagnosed cancers of the larynx (N=137), oral cavity/hypopharynx (N=130), lung (N=102), and bladder (N=70) were selected from among residents of Medellín, the principal city in the state of Antioquia, Colombia. The subjects, enrolled in 1978-1980, were identified through the Social Security Cancer Registry, two general hospitals (the Hospital Universitario and the Hospital Pablo Tobón Uribe), and several private physicians. A trained study nurse made daily visits to the hospitals and clinics involved to ensure prompt identification of potential subjects.

Two control subjects were matched to each case by sex, age (within 2-3 years),

and socioeconomic status. Socioeconomic status was assessed according to criteria and standards developed by the Government Office of Planning of the City of Medellín, based on the subject's place of residence (neighborhood) and family head's occupation. Basic matching data on the selected cases and their controls are shown in Table 1.

One of these control subjects was selected from the same hospital or clinic as the case. This group of controls was selected exclusively from patients admitted with conditions unrelated to smoking who had no history of cancer, cardiovascular disorders, chronic respiratory diseases, gastric ulcers, or duodenal ulcers. A second control subject was chosen from the same neighborhood or workplace as the case. The first choice was a neighborhood person selected by relatives of the initial (ill) study subject from a list of possibly similar persons of appropriate age and sex. The second choice was a subject selected at a workplace visited by an interviewer. Overall, most (67%) of those in this second group of controls consisted of residents in the initial subject's neighborhood, the remaining 33% coming from an appropriate workplace. In some instances only one control subject (usually the hospital one) was enrolled in the study.

Personal interviews with the study subjects and controls were conducted by trained nurses using a study questionnaire requesting personal and sociodemographic information as well as data on smoking and other possible risk factors. Data on alcohol consumption were not collected during the initial phase of the study but were collected later. For this reason, alcohol consumption data are lacking for 11.3% of the cases and 12.7% of the controls. Measures of smoking exposure such as length of time smoking, number of cigarettes smoked per day, fractional length of cigarette smoked,

Table 1. Percentage distribution of study subjects with cancer cases and control subjects with regard to age group, sex, socioeconomic level, and urban versus rural residence.

	Sites of study subject cancers							
	Bladder		Larynx		Lung		Oral cavity/ hypopharynx	
	Cases (N=70)	Controls (N=124)	Cases (N=137)	Controls (N=249)	Cases (N=102)	Controls (N=181)	Cases (N=130)	Controls (N=205)
<i>Age group (in years):</i>								
<45	7.1	9.7	10.2	11.2	10.9	10.5	12.4	13.2
45-64	42.9	46.8	57.7	58.6	53.5	55.8	48.7	52.2
≥65	50.9	43.6	32.1	30.1	35.6	33.7	38.9	34.6
<i>Sex:</i>								
Male	81.4	79.8	72.3	69.5	74.3	72.4	62.8	59.0
Female	18.6	20.2	27.7	30.5	25.7	27.6	37.2	41.0
<i>Socioeconomic level:</i>								
Low	74.3	80.7	75.9	79.9	66.3	70.2	80.5	84.9
Medium	10.0	6.5	18.3	14.9	18.8	17.1	15.9	11.2
High	15.7	12.9	5.8	5.2	16.8	12.7	3.5	3.9
<i>Residence:</i>								
Urban	67.1	68.6	87.6	88.3	76.2	81.2	73.6	82.4
Rural	32.9	31.4	12.4	11.7	23.8	18.8	26.5	17.6

type of tobacco used (dark or light), degree of inhalation, and modality⁷ were based on information from the time smoking began.

Cases at each selection site and their matched controls were analyzed separately. Since the hospital and neighborhood controls did not differ substantially with respect to sociodemographic factors, and since risk estimates for smoking variables were similar for each control group compared to the study cases, the two control groups were pooled.

The data analysis was performed using both stratified and multivariate approaches. The measure of association used was the relative risk (RR), approximated by the odds ratio (7). Stratified techniques were utilized to adjust for the effects of confounding variables (8), de-

veloping adjusted maximum likelihood RR estimates (9). Approximate 95% confidence intervals were calculated for the adjusted RR (10). For exposure patterns, Mantel's test for linear trend was used to assess significance (11). To control for several potentially confounding factors, logistic regression was performed (9). Matched and unmatched analyses were completed for smoking and alcohol exposures. Since the results were similar, only unmatched results are presented.

RESULTS

Because relatively few smokers of "light" tobacco (only 11 of the study subjects with cancer cases and 42 of the controls) were encountered, the results presented in Tables 2, 3, and 4 can be considered mainly to reflect the effects of dark tobacco smoking.

Table 2 shows the apparent relative risks of various activities and types of smoking. Cigarette smoking was found

⁷"Modality" refers to the nature of the smoking habit (i.e., chain-smoking or smoking with the lit end inside the mouth—the latter being a frequent practice in some sociocultural groups in Colombia).

Table 2. Relative risk (RR)^a of developing cancer of the bladder, larynx, lung, or oral cavity/hypopharynx among subjects with different patterns of smoking, alcohol consumption, and coffee drinking.

Variable	Cancer site:			
	Bladder	Larynx	Lung	Oral cavity/hypopharynx
<i>Cigarette smoking:</i>				
Nonsmokers	1.00	1.00	1.00	1.00
Former smokers	3.62 ^c	4.69	4.72 ^c	3.23
Current smokers ^b	3.73 ^c	37.86 ^c	10.28 ^c	11.16 ^c
<i>Inhalation:</i>				
Nonsmokers	1.00	1.00	1.00	1.00
Deep inhalation	4.59 ^c	49.45 ^c	13.90 ^c	9.22 ^c
Partial chest inhalation	3.42	33.59 ^c	7.68 ^c	13.17 ^c
Throat inhalation	4.04 ^c	11.83 ^c	3.31	7.35
Mouth inhalation	5.04 ^c	16.85 ^c	2.45	6.32
<i>Fractional length of cigarette smoked:</i>				
Nonsmokers	1.00	1.00	1.00	1.00
1/4–1/2 of length	1.19	19.29 ^c	5.90 ^c	3.08
3/4 of length	2.79	23.14 ^c	7.77 ^c	7.45 ^c
All	5.30 ^c	39.19 ^c	10.41 ^c	11.82 ^c
<i>Alcohol consumption:</i>				
Nondrinkers	1.00	1.00	1.00	1.00
Former drinkers	3.28	1.53	1.22	1.68
Occasional drinkers	1.90	0.69	1.03	2.75 ^c
Habitual drinkers	6.03 ^c	3.39 ^c	1.66	9.85 ^c
<i>Coffee drinking, cups per day:</i>				
0	1.00	1.00	1.00	1.00
1–3	3.84	0.90	1.24	1.91
4–6	1.66	1.17	0.92	2.71 ^c
≥7	7.47 ^c	6.35 ^c	2.39 ^c	8.17 ^c

^a RR adjusted for age and sex.

^b Current smokers include a small number of occasional smokers.

^c 95% confidence interval excludes 1.0.

to be a significant risk factor for cancer at all four sites. Former smokers evidenced moderately elevated risks of developing cancer at all four sites. However, current smokers showed substantial elevations in the risk of developing cancers of the larynx (38:1), lung (10:1), and oral cavity/hypopharynx (11:1).

Also, data on the degree of inhalation showed that any degree of inhalation was related to an increase in the cancer risk at each site studied, as compared to the risk experienced by nonsmokers. The highest risks, associated with the greatest degree of cigarette smoke inhalation, were found for cancer of the larynx

(RR=49.5) and lung (RR=13.9). Important risk differences were associated with the degree of inhalation. Deep inhalation and partial chest inhalation entailed higher risks than mouth and throat inhalation for cancers of the larynx, lung, and oral cavity/hypopharynx. Another variable, the average fractional length of cigarette smoked, showed a direct relationship to increased risk, the greatest risk (especially risk of laryngeal cancer) being experienced by those who smoked a relatively greater length.

Histories of alcohol consumption and coffee drinking were related to some elevation of cancer risk. Compared to non-

Table 3. Relative risk (RR)^a of developing cancer of the bladder, larynx, lung, or oral cavity/hypopharynx among smokers, according to the number of years smoking and the average number of cigarettes smoked per day.

Variable	Cancer site:			
	Bladder	Larynx	Lung	Oral cavity/hypopharynx
<i>Number of years smoking:</i> ^b				
<21	1.00	1.00	1.00	1.00
21–30	1.98	1.07	2.73	1.65
31–40	3.19	2.57	10.67	2.58
41–50	2.39	5.82	11.55	1.95
≥51	5.46	5.83	24.01	6.83
Test for trend	P=0.13	P=0.002	P=0.006	P=0.059
<i>Number of cigarettes smoked per day:</i> ^c				
1–10	1.00	1.00	1.00	1.00
11–20	3.95	4.71	9.60	1.51
21–40	7.89	17.38	35.24	5.46
≥41	14.51	38.15	162.70	6.12
Test for trend	P<0.001	P<0.0001	P<0.001	P<0.002

^a Analysis limited to smokers.

^b Adjusted for age, sex, and number of cigarettes smoked per day.

^c Adjusted for age, sex, and number of years smoking.

Table 4. Results of multivariate analyses of cigarette smoking, alcohol consumption, and coffee drinking indicating the relative risks (RR) of developing cancer of the bladder, larynx, lung, or oral cavity/hypopharynx derived from logistic regression analyses.

Variables in model ^a	Cancer site:			
	Bladder	Larynx	Lung	Oral cavity/hypopharynx
<i>Number of cigarettes smoked per day:</i>				
Nonsmoker	1.00	1.00	1.00	1.00
1–10	1.18	7.74	1.29	5.79
11–20	5.17	41.21	12.40	9.22
21–40	8.08	107.70	42.49	33.73
≥41	8.39	305.60	169.90	35.85
Test for trend	P<0.0001	P<0.0001	P<0.0001	P<0.0001
<i>Alcohol consumption:</i>				
Nondrinker	1.00	1.00	1.00	1.00
Former drinker	2.38	1.05	0.63	0.77
Occasional drinker	2.01	0.58	0.87	2.21
Habitual drinker	4.76 ^b	2.22	1.11	7.36 ^b
<i>Coffee drinking, cups per day:</i>				
0	1.00	1.00	1.00	1.00
1–3	3.05	0.93	1.45	1.68
4–6	1.21	1.00	0.58	2.05
≥7	4.89	2.87	1.11	5.12
Test for trend	P=0.18	P=0.012	P=0.67	P=0.002

^a Also adjusted for age, sex, and socioeconomic level.

^b 95% confidence interval excludes 1.0.

drinkers, habitual alcohol drinkers experienced significantly increased risks of cancers of the bladder (RR=6.0), larynx (RR=3.4), and oral cavity/hypopharynx (RR=9.9). Alcohol consumption did not appear to be an important risk factor for lung cancer (RR=1.66), the slightly increased observed risk not being statistically significant.

Surprisingly, however, heavy coffee drinking (at least seven cups a day) was related to cancer at all four sites, the strongest effects involving cancers of the bladder (RR=7.5) and oral cavity/hypopharynx (RR=8.2). More generally, such heavy coffee drinking was associated with statistically significant risks at all four sites relative to the risks found for those who consumed no coffee. Adjustment of these data for cigarette smoking, as was done in this study, should also be done in future studies to avoid confounding associations.

Both the intensity and duration of smoking were significant predictors of cancer at all four sites. To determine the independence of effects, further analysis concentrated on smokers and adjustment of each variable tested for the other variable involved (Table 3).

The reference group used to assess the effects of duration of smoking were smokers who had been smoking less than 21 years, since observed differences in the risk of smoking one to 20 years appeared minimal. Subjects who reported smoking for 51 years or more experienced substantial elevations in the risks of developing bladder cancer (RR=5.5), laryngeal cancer (RR=5.8), lung cancer (RR=24.0), and oral/hypopharyngeal cancer (RR=6.8), after adjusting for the number of cigarettes smoked per day. Tests of linear trends were significant for both laryngeal and lung cancers.

The average number of cigarettes smoked per day, adjusted for the number

of years smoking, appeared to be a more important predictor of cancer risk than the total number of years smoked. Statistically significant dose-response relationships were noted with respect to all four cancer sites studied.

Table 4 summarizes results of the multivariate analyses of cigarette smoking, alcohol consumption, and coffee drinking. The number of cigarettes smoked per day was found to be a significant predictor of risk at each of the four cancer sites. Compared to nonconsumption of alcohol, habitual alcohol intake was significantly correlated with elevations in the risk of cancers of the bladder (RR=4.8) and oral cavity/hypopharynx (RR=7.4).

Similar analyses of smoking and coffee consumption showed significant dose-response patterns varying according to the amount smoked per day with respect to all four cancer sites. Adjustment for coffee and alcohol consumption did not change observed associations between elevated cancer risks and cigarette smoking. However, adjustment of the coffee and alcohol consumption data for cigarette smoking did produce noteworthy changes, reducing most of the observed relative risks of coffee and alcohol consumption and eliminating the statistical significance of certain associations—such as that between consuming seven or more cups of coffee daily and bladder cancer. Because the number of subjects smoking light tobacco was small, and also because the duration of smoking involved was relatively short, the hypothesis that risks at different cancer sites would vary in accordance with the type of tobacco smoked could not be tested in this study.

DISCUSSION AND CONCLUSIONS

Few cancer case-control studies have been performed in Colombia and other Latin American countries. However, Co-

Colombia's Social Security System offers a compulsory government-sponsored health insurance program that provides a favorable setting for conducting this type of study in terms of access to patient material, availability of interviewers, coverage of a well-defined population, and provision of information on occupational factors. Many such systems are operating elsewhere in Latin America.

Information about smoking in Latin America is derived mainly from a few surveys. A prevalence survey of eight Latin American cities (12) made in 1971 showed that 59% of the male smokers in Bogotá, Colombia, preferred dark tobacco cigarettes, as did 42% of the female smokers.

Similarly, data from our investigation show that dark tobacco consumption predominated in the Colombian population studied, only 15.3% of the smokers (cases and controls) having predominantly smoked light tobacco.

The current Medellín study confirmed the association between dark tobacco smoking habits and cancer of the lung, an association that has been documented in Cuba (13). It also showed definite relationships between dark tobacco smoking and cancers of the bladder, larynx, and oral cavity/hypopharynx. Such associations have previously been suggested by other works—the association with cancer of the larynx by De Stefani in Uruguay (14), that with oral cancer by Simarak in Thailand (15), and that with bladder cancer by Viners in Italy (16). De Stefani (14) described the same sales and consumption trend from dark to light tobacco in Uruguay as has been observed in Colombia and correlated it with trends in mortality from cancer of the larynx.

In view of the pronounced risk gradients found and the high proportion of smokers existing in the Latin American population, it remains unclear why the male lung cancer rates there are lower

than those observed in North America. More research on this subject is needed.

Alcohol consumption, alone and synergistically with smoking, has been found by several studies to affect rates of cancers of the upper respiratory and gastrointestinal tracts (17-26). Findings of the study reported here tend to confirm the association between alcohol consumption and cancers of the larynx and oral cavity. Also, the increased risk of bladder cancer among habitual drinkers that was observed in this study supports the hypothesis of Hinds et al. (23) of a definite link between hard liquor drinking and bladder cancer. The liquor most commonly consumed by members of the Medellín study population was "aguardiente," a hard liquor made from sugar cane. This is quite different than the type of liquor associated with oral, laryngeal, and esophageal cancer by Tuyns in France (26), where wine consumption is high. (Wine was infrequently consumed by the Medellín study population.)

The effect of coffee drinking detected in this study appears to be a new finding deserving further investigation. The relationship between coffee and cancer has been hard to interpret, due to the direct and confounding relationship between cancer and smoking. There have been suggestions of an association between coffee drinking and bladder cancer (27, 28). The significant relationships found between coffee drinking and cancers of the larynx and oral cavity/hypopharynx after adjustment for cigarette smoking (see Table 4) need to be verified by future studies.

In 1983 the WHO Expert Committee on Smoking noted that "developing countries are increasingly becoming targets for highly sophisticated and ruthless campaigns promoting smoking" (29). Especially in view of such tendencies, dissemination of research results on the harmful effects of smoking to affected

populations is highly recommended. Evidence of the damaging effects of tobacco smoking such as that provided by our study supports strong action against tobacco use in our countries.

Acknowledgments. We extend our thanks to Dr. Janet Stanford for her collaboration in data processing and to Mrs. Edna Roberts for her support in the last phase of the study.

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Critical Situation in Nursing and Midwifery

A report submitted to the 42nd World Health Assembly in Geneva in May 1989 stated that almost all countries are experiencing shortages of qualified nurses. One reason is that nurses are leaving their profession at an alarming rate, chiefly due to poor working conditions and low wages. For example, in one country surveyed, staff nurses received a salary equivalent to US\$6.00 per month, while domestic servants of foreigners earned 10 times that amount. Migration of nurses to developed countries has also exacerbated shortages in the Third World, as has the concentration of resources on training physicians and dentists.

The World Health Assembly passed a resolution calling on countries to recruit more nurses and midwives, promote them to leadership positions, and reorient educational programs for nurses and midwives toward primary health care. It also requests WHO's increased support to Member States for strengthening the role of nursing and midwifery in national health programs.

Source: World Health Organization, Press Release WHA/10, Geneva, 18 May 1989.