RESEARCH COMMUNICATION

Maté Consumption and Risk of Cancer: a Multi-site Case-Control Study in Uruguay

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Abstract

In the time period 1990-2004 we conducted a multisite case-control study in order to examine the relationship of maté consumption and risk of 13 cancer sites in Montevideo, Uruguay. The study included 13,201 participants (8,875 cases and 4,326 controls) drawn from the four major public hospitals in the city of Montevideo. Newly diagnosed and microscopically confirmed cases of cancers of the mouth, pharynx, esophagus, stomach, colon, rectum, larynx, lung, female breast, cervix uteri, prostate, bladder and kidney were included in the study. Controls were drawn from the same hospitals and in the same time period and were afflicted by non-neoplastic conditions not related with tobacco smoking or alcohol drinking and without recent changes in their diets. Odds ratios for maté consumption was directly associated with cancers of the upper aerodigestive tract (UADT), esophagus, stomach, larynx, lung, cervix uteri, prostate, bladder, and kidney. In conclusion these results suggest that chemicals, like benzo[a]pyrene, could be responsible of the carcinogenic effect of maté in the above mentioned cancer sites.

Keywords: Maté drinking - cancer risk - contaminants - multi-sites

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Introduction

Maté is the folk name of the herb extracted fron the tree named as Ilex paraguariensis. The prevalence of consumption of maté in very high in temperate South America, that is Argentine, Paraguay, Uruguay, and southern Brazil (Heck et al., 2007). According to a monograph published by the International Agency for Research on Cancer (IARC), hot maté drinking has been considered as a 2A agent, that is, probably carcinogenic for humans (IARC, 1991).

Since then numerous studies, both experimental and epidemiologic, has been conducted. The main sources of these studies were Uruguay and southern Brazil (Vassallo et al., 1985; Victora et al., 1987; De Stefani et al., 1990; 1996; 1998; 2007; Castelletto et al., 1994; Pintos et al., 1994; Rolón et al., 1995; Castellsagué et al., 2002; Goldenberg et al., 2003; Sewram et al., 2003; Gomes Zuin et al., 2005; Fagundes et al., 2006; Abnet et al., 2007; Bates et al., 2007; Kamangar et al., 2008). Most studies in humans strongly suggested that maté acts as carcinogen due to the high temperature of the ingested liquid. In short, it was suggested a mechanism trough directed contact with the mucosa of the digestive tract, mainly the esophageal mucosa. The consequence of maté drinking is the production of esophagitis, the first step of esophageal carcinogenesis (Kinner, 2007).

The main purpose of the present study is to explore the effect of maté consumption in different sites.

Materials and Methods

Selection of cases

In the time period 1990-2004, all the newly diagnosed and microscopically confirmed cases of cancer of the mouth, pharynx, esophagus, stomach, colon, rectum, larynx, lung, female breast, cervix uteri, prostate, bladder, and kidney (only renal-cell carcinoma) were collected. The initial number was 9,093 patients; only two-hundred and eighteen (218) refused the interview (response rate 97.6 %), leaving a final number of 8,875 cases. The number of cases per cancer site, and the percentages are shown in Table 1.

Selection of controls

In the same time period and in the same hospitals, 4,451 patients afflicted with non-neoplastic diseases not related with tobacco smoking or alcohol drinking and without recent changes in their diets were considered as eligible for the study. One hundred and five (125) refused

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the interview, leaving a final total of 4,326 controls (response rate 97.2 %). These controls presented the following conditions: diseases of the skin (634 patients, 14.7 %), eye disorders (628, 14.5 %), ear disorders (530, 12.3 %), abdominal hernia (426, 9.9 %), fractures (321, 7.4 %), hydatid cysts (277, 6.4 %), lipoma (180, 4.2 %), osteoarticular diseases (166, 3.8 %), varicose veins (162, 3.7 %), injuries (160, 3.7 %), blood disorders (136, 3.1 %), acute appendicitis (121, 2.8 %), urinary stones (115, 2.7 %), prostate hypertrophy (92, 2.1 %), diseases of the nose (74, 1.7 %), goiter (71, 1.6 %), peritonitis (68, 1.6 %), diseases of the mouth (67, 1.6 %), diseases of the female genital tract (66, 1.5 %), and ill-defined symptoms (32, 0.7 %).

Interviews and questionnaire

All participants were administered a structured questionnaire by four trained social workers, shortly after admittance to the hospitals. The questionnaire included the following sections: 1) sociodemographics (age, sex, residence, education, income), 2) a complete occupational history based on the last four jobs and their duration in years, 3) self-reported weight and height five years before the date of the interview, 4) a complete smoking history (age of start, age of quit, number of cigarettes smoked per day, type of tobacco, type of cigarette, inhalation practices), 5) a complete history of alcohol drinking (age of start, age of quit, number of glasses drunked per day, type of alcoholic beverages), 6) non-alcoholic beverages (maté, coffee, tea, soft drinks), 7) a food frequency questionnaire (FFQ) on 64 food items. The FFQ allowed the calculation of total energy intake and was representative of the Uruguayan diet. Furthermore the FFQ was tested for reproducibility with good results (Ronco et al., 2006).

Maté variables included into the study

The following maté variables were included in the study: mate status, mate consumption, years of drinking maté, cumulative exposure (maté years), and temperature.

Statistical analysis

Relative risks, approximated by the odds ratios, for each cancer site were calculated using polytomous multiple regression (Rothman et al., 2008). The basic model included the following terms: age (continuous), sex (ordinal), residence (categorical), education (categorical), smoking status (categorical), smoking cessation (categorical), smoking intensity among current smokers (categorical), alcohol drinking, and each maté variable (categorical). Total energy intake and foods did not confound the relationship maté-disease. For this reason they were not included into the basic model. Moreover, there was no heterogeneity by sex (see Table 1). For this reason, all models were fitted for both sexes together, after including a term for gender. All the calculations were performed with the software Stata (StatCopr, 2007).

Results

Cases were younger than the controls and there were significant differences in the sex ratios. Residence, education and income were roughly similar between cases and controls. On the other hand, cases smoked much more heavily than controls. The same was the case for alcohol drinking. Finally cases consumed much more maté than controls (global p-value <0.0001).

The highest risks for ever drinkers of maté was observed for cancers of the esophagus (OR 2.66, 95 % CI 1.74-4.05), lung (OR 1.69, 95 % CI 1.34-2.14), and bladder (OR 2.12, 95 % CI 1.40-3.22). Also cancers of the cervix, prostate, and kidney were significantly associated with risk (OR for ever drinkers with prostate cancer 1.54, 95 % CI 1.15-2.05, p-value=0.004). Cancers of the upper aerodigestive tract (UADT) were marginally associated with an increased risk (OR 1.25, 95 % CI 0.99-1.57, p-value=0.051). Ever drinking of maté were not associated cancers of the mouth, pharynx, larynx, colon, rectum, and female breast.

Regarding odds ratios of sites for amounts of maté consumption (see Table 2), cancers of the esophagus (OR 3.09, 95 % CI 1.95-4.91), stomach (OR 1.52, 95 % CI 1.01-2.29), lung (OR 1.99, 95 % CI 1.55-2.58), cervix uteri (OR 2.10, 95 % CI 11.19-3.72), prostate (OR 1.73, 95 % CI 1.22-2.45), bladder (OR 3.88, 95 % CI 2.47-6.08), kidney (OR 2.27, 95 % CI 1.39-3.72), and UADT (OR 1.37, 95 % CI 1.06-1.77) were positively associated with high consumption of maté. Also laryngeal cancer was marginally associated. Cancers of the mouth, pharynx, colon, rectum, and female breast were not associated with maté drinking.

Regarding the effects of years of drinking maté, cancers of upper aerodigestive tract (UADT) (OR 1.41, 95 % CI 1.12-1.79), esophagus (OR 2.88, 95 & CI 1.88-4.41), larynx (OR 1.57, 95 % CI 1.07-2.31), lung (OR 1.95, 95 % CI 1.53-2.49), prostate (OR 1.58, 95 % CI 1.18-2.13), bladder (OR 2.42, 95 % CI 1.58-3.69), and kidney (OR 1.96, 95 % 1.22-3.14) were positively associated with more than 50 years of drinking maté. All these sites displayed significant dose-response trends. On the other hand, cancers of the mouth, pharynx, colon, rectum, breast, and cervix uteri were not associated with maté duration.

Cancers of the upper aerodigestive tract (UADT) (OR 1.28, 95 % CI 1.01-1.63), esophagus (OR 3.06, 95 % CI

Table 1. Distribution of Cases by Site and Controls

Cancer site	No of cases	%	Heterogeneity by sex
Mouth	360	2.7	0.13
Pharynx	424	3.2	0.39
Esophagus	605	4.6	0.66
Stomach	408	3.1	0.99
Colon	334	2.5	0.61
Rectum	428	3.2	0.39
Larynx	554	4.2	0.33
Lung	2,045	15.5	0.74
Female breast	2,061	15.6	-
Cervix uteri	233	1.8	-
Prostate	720	5.4	-
Bladder	429	3.3	0.89
Kidney[1]	274	2.1	0.80
Controls	4,326	32.8	-
Total participants	13,201	100.0	

[1]Only cases of renal-cell carcinoma

Table 2. Odds Ratios of Cancer Sites for Amount of Maté Consumption (liters /day) [1,2]

	0.1-0.9		1.0-1.9		2.0+		p-value
Cancer site	OR	95 % CI	OR	95 % CI	OR	95 % CI	trend
UADT[3]	1.18	0.72-1.51	1.28	1.01-1.63	1.37	1.06-1.77	0.01
Mouth	0.94	0.62-1.43	1.03	0.69-1.52	0.95	0.61-1.46	0.98
Pharynx	1.19	0.78-1.82	1.12	0.75-1.67	1.15	0.75-1.77	0.75
Esophagus	2.23	1.43-3.47	2.90	1.88-4.47	3.09	1.95-4.91	<0.0001
Stomach	1.18	0.81-1.71	1.41	0.99-2.02	1.52	1.01-2.29	0.02
Colon	1.13	0.78-1.64	1.03	0.71-1.49	1.33	0.87-2.03	0.39
Rectum	0.87	0.68-1.23	1.01	0.73-1.38	1.15	0.80-1.67	0.24
Colorectum	0.99	0.76-1.28	1.02	0.79-1.31	1.22	0.92-1.63	0.17
Larynx	1.32	0.88-1.99	1.25	0.85-1.84	1.54	1.03-2.32	0.055
Lung	1.59	1.23-2.05	1.69	1.30-2.11	1.99	1.55-2.58	<0.0001
Female breast	1.14	0.95-1.37	1.13	0.94-1.37	0.85	0.67-1.09	0.31
Cervix uteri	1.33	0.77-2.29	2.42	1.45-4.04	2.10	1.19-3.72	<0.0001
Prostate	1.41	1.02-1.95	1.52	1.12-2.07	1.73	1.22-2.45	0.003
Bladder	1.22	0.76-1.95	2.21	1.43-3.41	3.88	2.47-6.08	<0.0001
Kidney	1.32	0.82-2.13	1.74	1.10-2.75	2.27	1.39-3.72	<0.0001
Total sites	1.30	1.14-1.47	1.38	1.22-1.56	1.50	1.30-1.72	<0.0001

[1]Adjusted for age, sex, residence, education, income, smoking status, smoking cessation, smoking intensity, and alcohol drinking; [2]Reference category: never drinkers; [3]Cancer of the upper aerodigestive tract, including mouth, pharynx, and larynx

Table 3. Odds Ratios of Cancer Sites for Maté Temperature[1,2]

	Warm		Hot		
Cancer site	OR	95% CI	OR	95% CI	p-value
UADT[3]	1.01	0.77-1.31	1.41	1.12-1.79	0.0001
Mouth	0.74	0.47-1.16	1.13	0.76-1.67	0.21
Pharynx	0.95	0.61-1.46	1.25	0.84-1.86	0.13
Esophagus	2.32	1.44-3.75	2.88	1.88-4.41	<0.0001
Stomach	1.29	0.86-1.95	1.39	0.98-1.96	0.07
Colon	1.12	0.73-1.71	1.14	0.80-1.62	0.49
Rectum	0.96	0.66-1.38	1.01	0.74-1.38	0.91
Colorectum	1.03	0.77-1.37	1.07	0.88-1.36	0.60
Larynx	0.91	0.59-1.40	1.57	1.07-2.31	0.001
Lung	1.29	0.99-1.67	1.95	1.53-2.49	<0.0001
Female breast	1.04	0.86-1.27	1.16	0.96-1.40	0.11
Cervix uteri	2.04	1.23-3.40	1.56	0.88-2.76	0.13
Prostate	1.30	0.88-1.92	1.58	1.18-2.13	0.002
Bladder	1.37	0.82-2.28	2.42	1.58-3.69	<0.0001
Kidney	1.35	0.83-2.19	1.96	1.22-3.14	0.004
Total sites	1.22	1.07-1.39	1.46	1.29-1.66	<0.0001

[1]Adjusted for age, sex, residence, education, income, smoking status, smoking cessation, smoking intensity, and alcohol drinking; [2]Reference category: never drinkers; [3]Cancer of the upper aerodigestive tract, including mouth, pharynx, and larynx.

1.99-4.73), stomach (OR 1.48, 95 % CI 1.03-2.12), larynx (OR 1.37, 95 % CI 0.93-2.02), lung (OR 1.88, 95 % CI 1.47-2.39), cervix uteri (OR 2.18, 95 % CI 1.23-3.85), prostate (OR 1.58, 95 % CI 1.17-2.15), bladder (OR 2.78, 95 % CI 1.81-4.26), and kidney (OR 1.93, 95 % CI 1.21-3.07) were positively associated high cumulative exposure of maté. On the other hand, cancers of the mouth, pharynx, colon, rectum, and breast were not associated with this maté variable.

Regarding effects of maté temperature for cancer sites is shown in Table 3. Cancers of the stomach and colon were not associated with hot maté drinking. On the other hand, the remaining cancer sites displayed a high risk for hot maté drinking, with significant dose-response trends. In particular cancers of the lung (OR 1.95, 95 % CI 1.53-2.41), esophagus (OR 2.88, 95 % CI 1.88-4.41) and bladder (OR 2.12, 95 % CI 1.58-3.69) were strongly positively associated with hot maté dinking.

Regarding confounding effects of smoking, although the risk estimates were attenuated in the model which included pack years, there was no significant heterogeneity between never smokers and ever smokers.

Discussion

The present study displayed high risk with hot maté consumption for cancers of the esophagus, stomach, upper aerodigestive tract (UADT), larynx, lung, cervix uteri, prostate, bladder, and kidney. On the other hand cancers of the mouth, pharynx, colon, rectum, and female breast were not associated with maté drinking.

Yerba maté has been extensively studied regarding to its chemical properties (Heck et al., 2007; Loria et al., 2009). In brief, maté infusions contain xanthines, caffeoyl derivatives, chlorogenic acid, saponins, minerals, and antioxidants. These compounds could suggest a protective effect of maté tea. Nevertheless, previous studies failed to report a decreased risk associated with this beverage (Heck et al., 2007; World Cancer Research Fund/American Institute for Cancer Research, 2007; Loria et al., 2009) .

On the other hand, recent studies strongly suggest that maté contains high levels of carcinogenic polycyclic aromatic hydrocarbons (Gomes Zuin et al., 2005; Fagundes et al., 2006; Abnet et al., 2007). Among them phenanthrene and benzo[a]pyrene are present among hot and cold maté (Abnet et al., 2007). Both are considered as carcinogens to humans (IARC, 2007). Therefore, these compounds could be responsible of the effect of maté in organs not in direct contact with the beverage. In fact, it has been suggested that the association of maté drinking and cancers like lung, bladder, and kidney could be due to the presence of benzo[a]pyrene in maté drinks (Abnet et al., 2007). Previous studies on lung cancer, bladder cancer, and kidney cancer strongly suggested an increased risk associated with maté consumption (Rolón et al., 1995; De Stefani et al., 1998; 2007).

According to Kamangar et al (2008), previous studies have attributed the carcinogenicity of maté to thermal injury, chemical components, or both. Thus, mechanisms of maté in carcinogenicity of human cancers are open to discussion.Tobacco smoking could be a powerful confounder of maté consumption. This is particularly important in tobacco-related cancer sites like lung, bladder, kidney, and esophagus. We tried to control the effect of tobacco, using an smoking index. This included smoking status, years after quitting, and intensity of smoking among current smokers. Other studies used a data-driven model which included the following variables: current smoker, former smoker, number of cigarettes currently smoked, duration of smoking, a quadratic term for duration, inhalation, interaction term between genders and number of cigarettes currently smoked. We fitted a model with never smokers and a model with ever smokers and the likelihood-ratio test for heterogeneity was of 0.77, strongly suggesting that there was not heterogeneity between the model without smoking and the model with smoking.

As other case-control studies, the present one has limitations. Perhaps selection bias and recall bias are the major limitations. Since both groups of participants were drawn from the low socioeconomic strata which is treated in the public health hospitals of Montevideo, selection bias appears to be unlikely. On the other hand, recall bias is more difficult to rule out. This is a problem which affects retrospective studies like our study. Since controls were very similar to cases concerning diet and sociodemographic variables it is possible that misclassification were non-differential. Therefore, the worse consequence could lead to effects attenuated and closer to the null. The present study showed important strengths. In first place the cases were microscopically confirmed by expert pathologists. Secondly the high sample size increased the power of the study. Finally both groups of participants showed elevated response rates. This is probably to the fact that this population is very cooperative.

In summary, the present study displayed that maté drinks were positively associated with cancers of upper aerodigestive tract, esophagus, stomach, larynx, lung, cervix uteri, bladder, and kidney. On the other hand, cancers of the mouth, pharynx, colon, rectum, and female breast were not associated with maté consumption. Further studies, focused on mechanisms of maté influence on carcinogenesis are needed.

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