RESEARCH COMMUNICATION

Salted Meat Consumption and the Risk of Cancer: a Multisite Case-Control Study in Uruguay

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Abstract

Background: Previous studies have suggested that a high intake of salted meat may increase the risk of esophageal and stomach cancers, but the results are not conclusive. Methods: We used polytomous logistic regression to estimate odds ratios (ORs) and 95 % confidence intervals (CIs) for the association between salted meat intake and the risk of several cancers in a case-control study from Uruguay that was conducted between 1988 and 2005. The study included 13,050 participants (9,252 cases and 3,798 controls) which were drawn from the four major public health hospitals in Montevideo, Uruguay. Results: Salted meat intake was significantly associated with increased odds of cancers of the oesophagus (OR=2.28, 95% CI: 1.75-2.97), colon and rectum (OR=1.53, 95% CI: 1.16-2.03), lung (OR=1.57, 95% CI: 1.26-1.97), cervix uteri (OR=1.76, 95% CI: 1.05-2.25), prostate (OR=1.60, 95% CI: 1.18-2.17), urinary bladder (OR=2.23, 95% CI: 1.63-3.04), kidney (OR=1.62, 95% CI: 1.03-2.54) and non-Hodgkin's lymphoma (OR=1.81, 95% CI: 1.12-2.95). Conclusion: Our results confirm previous reports of an elevated risk of oesophageal cancer with higher intake of salted meat, but also suggest that salted meat intake may increase the risk of several other cancers.

Key Words: Salted meat - cancer - epidemiology

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Introduction

Evidence is emerging that red and processed meat intake is associated with increased risk of colorectal cancer and other cancers (Tavani et al., 2000; Cross et al., 2007; World Cancer Research Fund/American Insitute for Cancer Research, 2007; Hu et al., 2008; Aune et al., 2009a; 2009b). Among the different types of processed meat, salted meat is a less frequently consumed food item. Salting of meat and other foods has been used as a method of preservation to inhibit the growth of bacteria to slow down spoilage. In brief, the preparation of salted meat includes heavy salting of muscles of lamb and then air-drying the meat. Salted meat from lamb used to be a staple food among Uruguayan population until the late fifties. With the emergence of refrigeration, the need for salting of foods for preservation have decreased both in Uruguay and in other countries, thus resulting in a decline in the consumption of salt-preserved foods including salted meat. It is suspected that the decrease in salt intake may be part of the explanation for the decrease in stomach cancer rates in many populations around the world (World Cancer Research Fund/American Institute for Cancer Research, 2007).

Previous publications have suggested that salted meat may be associated with increased risk of cancers of the oesophagus (Gimeno et al., 1995; De Stefani et al., 1999; 2003; Zhou et al., 1999), mouth and pharynx (Zheng et al., 1992a; De Stefani et al., 1994), larynx (Zheng et al., 1992b; De Stefani et al., 1995) and stomach (De Stefani et al., 1990; 1998a; 2001; Strumylaite et al., 2006). However, not all studies found any association (Ward and Lopez-Carrillo, 1999; Takezaki et al., 2001) and there is a paucity of studies of salted meat intake in relation to the risk of other cancers. For this reason we decided to explore the relationship between salted meat consumption and several cancers in the framework of two case-control studies that were combined in a common database.

Materials and Methods

Data from two case-control studies, whose design has been described previously (Aune et al., 2009a; De Stefani et al., 2009), were combined in a common database for this analysis of salted meat intake and cancer risk. The studies were conducted between 1988 and 2005 and this analysis included 9,252 cases and 3,798 hospital controls aged 30-89 years. The cases and controls were

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administered a questionnaire in the hospitals by trained social workers shortly after admittance (no proxy interviews were accepted) and included questions on socio-demographic factors, occupational history, a history of cancer among 1st degree relatives, self-reported height and weight 5 years before admission, smoking history, alcohol intake (history and usual intake), mate intake (a local herbal tea), and, reproductive history (women). Dietary intake was assessed using a short food frequency questionnaire (FFQ). The FFQs used in the studies differed in the number of dietary items assessed, but the questions relating to salted meat intake were identical and we therefore combined the databases for the present analysis.

In total, 11,096 patients with diverse malignancies were identified. Four hundred and ninety-nine (499) patients either refused the interview or were too ill to be interviewed, leaving 10,597 cases (response rate 95.5 %). This analysis was restricted to the fourteen cancer sites listed in Table 1 and included 9,252 cases and 3,798 controls.

One hundred and fifty-five (155) controls refused the interview, leaving 3,864 controls (response rate 96.6 %). From these, 3,798 were included in the present analysis. The controls were affected with the following conditions: eye and ear disorders (445, 11.7 %); appendicitis (110, 2.9%); abdominal hernia (423, 11.1 %); benign breast diseases (408, 10.7 %); fractures, accidents, injuries (394, 10.4 %); diseases of the skin (720, 19.0 %); infectious diseases (145, 3.8 %); vein and lymph diseases (115, 3 %); urinary system diseases (110, 2.9 %); and various other conditions (928, 24.4 %).

Statistical analysis

Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using polytomous (multinomial) regression. The basic model included the following terms: 1) age (continuous), 2) residence (ordinal), 3) urban/rural status (ordinal), 4) education (categorical, 3 strata), 5) smoking index (smoking status, years since stopping smoking, number of cigarettes among current smokers, categorical, 8 strata), 6) alcohol drinking (categorical, 5 strata), total food intake (continuous), total vegetables and fruits (categorical, 3 strata) and whole milk intake (categorical, 3 strata). Since there was no heterogeneity by sex for the individual cancer sites we decided to fit this model for both men and women combined, adding a term for gender. All the analyses were conducted with the STATA software program.

Results

The distribution of cases and controls by frequency of salted meat consumption is shown in Table 1. The largest number of cases was observed for breast cancer (2,159 patients), followed by lung cancer (2,104 patients), prostate cancer (741 patients) and oesophageal cancer (613 patients).

Socio-demographic characteristics of the cases and the controls, and use of tobacco and alcohol is shown in Table 2. The highest mean age was observed among prostate cancer cases (70.9 years), whereas the lowest mean age was observed among patients afflicted by cancer of the cervix uteri (49.3 years). Among the non-sex-specific cancers, the highest percentage of men was observed among patients with laryngeal cancer (95.7 %). Lung and laryngeal cancer patients showed the highest mean number of cigarettes smoked per day (30.7 and 31.3 cigarettes/day, respectively), whereas pharyngeal cancer patients had the highest alcohol intake per day (209.2 ml of ethanol per day).

Odds ratios (ORs) and 95% CIs of the various cancer sites for salted meat intake are shown in Table 3. The multivariate-adjusted ORs for the highest vs. the lowest intake showed a significant increase in the odds of oesophageal cancer (OR 2.28, 95 % CI 1.75-2.97), colorectal cancer (OR 1.53, 95 % CI, 95 % CI 1.16-2.03), lung cancer (OR 1.57, 95 % CI 1.26-1.97), cervical cancer (OR 1.76, 95 % CI 1.05-2.25), prostate cancer (OR 1.60,

Table 1. Relative Frequency of Cancer Sites by Consumption of Salted Meat (1)

Cancer site	Never eaters N (%)	1-52* N (%)	53+ N (%)	Total N
Oral cavity	253 (77.6)	45 (13.8)	28 (8.6)	326
Pharynx	329 (80.0)	41 (10.0)	41 (10.0)	411
Oesophagus	433 (70.6)	65 (10.6)	115 (18.8)	613
Stomach	341 (85.5)	33 (8.3)	25 (6.2)	399
Colon	291 (85.3)	19 (5.6)	31 (9.1)	341
Rectum	352 (82.0)	30 (7.0)	47 (11.0)	429
Larynx	457 (81.6)	44 (7.9)	59 (10.5)	560
Lung	1,585 (75.3)	292 (13.9)	227 (10.8)	2,104
Breast	1,876 (86.9)	143 (6.6)	140 (6.5)	2,159
Cervix uteri	214 (82.6)	24 (9.3)	21 (8.1)	259
Prostate	577 (77.9)	80 (11.8	84 (11.3)	741
Bladder	329 (74.6)	43 (9.8)	69 (15.6)	441
Kidney	224 (82.0)	24 (8.8)	25 (9.2)	273
Lymphoma	158 (80.6)	16 (8.2	22 (11.2)	196
All cases	7,419 (80.2)	899 (9.7	934 (10.1)	9,252
All controls	3,302 (86.9)	274 (7.2	222 (5.8)	3,798

*servings/year

Table 2. Sociodemographic Characteristics, Smoking and Alcohol Drinking by Cancer Site and Controls

Cancer site	Age	Males[1]	Education[2]	Smoking[3]	Alcohol[4]
Oral cavity	62.6	89.4	4.1	24.8	163.9
Pharynx	61.0	93.3	4.5	26.5	209.2
Oesophagus	66.5	75.9	3.4	20.4	124.1
Stomach	64.7	68.9	4.1	15.7	83.5
Colon	63.6	46.5	4.7	12.5	43.5
Rectum	65.2	64.2	4.4	14.5	68.0
Larynx	62.3	95.7	4.1	31.3	195.2
Lung	61.1	92.3	4.4	30.7	140.4
Breast	60.2	-	5.5	3.9	6.4
Cervix uteri	49.3	-	5.7	7.1	8.1
Prostate	70.9	100.0	4.0	17.9	95.6
Bladder	67.3	85.8	4.2	19.1	83.1
Kidney	60.0	63.8	4.9	15.0	70.9
Lymphoma	55.1	52.4	5.3	10.7	44.5
All cases	62.6	74.9	4.6	17.8	88.3
All controls	58.9	54.0	5.0	12.9	60.6

[1]Percentage; [2]Mean years of study; [3]Mean number of cigarettes smoked per day; [4]Mean mililiters of alcohol drunk per day

Table 3. Odds ratios of Cancers by Salted Meat Consumption[1]

	I	II		III		
Cancer site	OR reference	OR	95 % CI	OR	95 % CI	p-value trend
Oral cavity	1.0	1.51	1.05-2.17	1.15	0.75-1.79	0.15
Pharynx	1.0	1.05	0.72-1.51	1.39	0.89-1.90	0.21
Oral cavity & pharynx	1.0	1.21	0.92-1.59	1.19	0.88-1.61	0.14
Oesophagus	1.0	1.11	0.82-1.51	2.28	1.75-2.97	<0.0001
Stomach	1.0	0.99	0.67-1.46	0.82	0.53-1.27	0.42
Colon	1.0	0.76	0.47-1.24	1.50	0.99-2.25	0.19
Rectum	1.0	0.78	0.52-1.16	1.52	1.07-2.15	0.09
Colon & rectum	1.0	0.80	0.58-1.11	1.53	1.16-2.03	0.03
Larynx	1.0	0.78	0.54-1.11	1.24	0.89-1.73	0.55
Lung	1.0	1.59	1.30-1.95	1.57	1.26-1.97	<0.0001
Female breast	1.0	1.28	0.96-1.69	1.16	0.87-1.53	0.12
Cervix uteri	1.0	2.03	1.23-3.33	1.76	1.05-2.25	0.003
Prostate	1.0	1.10	0.83-1.47	1.60	1.18-2.17	0.005
Bladder	1.0	1.12	0.79-1.60	2.23	1.63-3.04	<0.0001
Kidney[2]	1.0	1.18	0.75-1.85	1.62	1.03-2.54	0.03
Non-Hodgkin lymphoma	1.0	0.98	0.57-1.69	1.81	1.12-2.95	0.04
Total	1.0	1.19	1.02-1.37	1.50	1.28-1.75	<0.0001

[1]Adjusted for age, sex (when applicable), residence, urban/rural status, education, smoking status, years since stopping smoking, number of cigarettes among current smokers, alcohol drinking, total food intake, total vegetables and fruit consumption; [2]Renal-cell carcinoma

95 % CI 1.18-2.17), bladder cancer (OR 2.23, 95 % CI 1.63-3.04), renal-cell carcinoma (OR 1.62, 95 % CI 1.03-2.54), and non-Hodgkin's lymphoma (OR 1.81, 95 % CI 1.12-2.95). Salted meat was also directly associated with all cancers combined (OR=1.50, 95 % CI 1.28-1.75). There was a tendency for a dose-response relationship for several of these cancers and for all cancers combined, although for lung cancer and cervical cancer there seemed to be a threshold effect. The remaining cancer sites (oral cavity, pharynx, stomach, larynx and breast) were not significantly associated with salted meat intake.

Discussion

The present study found positive associations between the intake of salted meat and risk of cancers of the oesophagus, colon and rectum, lung, prostate, cervix uteri, urinary bladder, renal-cell carcinoma, and non-Hodgkin's lymphomas and all cancers combined.

Evidence is emerging for an elevated risk of several cancers with high red and processed meat intake, however few previous studies have been conducted on the relationship between salted meat intake and cancer risk. Salted meat intake was not significantly associated with risk of oral and pharyngeal cancer in this study. A Chinese study reported an almost three-fold increased risk of oral and pharyngeal cancer with high intake of salted meat and fish (Zheng et al., 1992a) and in a previous report we also found a >2-fold increased risk with high salted meat intake (De Stefani et al., 1994). However, a few other studies reported only non-significant weak positive associations (Zheng et al., 1993) or no association (De Stefani et al., 1999). We found a >2-fold increased risk of oesophageal cancer with high salted meat intake in this study and these results are in line with two previous studies conducted in Uruguay (De Stefani et al., 1999; 2003), one study conducted in Brazil (Gimeno et al., 1995) and one from China (Zhou et al., 1999), although another Chinese study reported no association (Takezaki et al., 2001). In a combined analysis of 5 case-control studies in South America, high salt intake was associated with increased oesophageal cancer risk (Castellsague et al., 2000). Craddock suggested that salted meat could be a carcinogen for oesophageal mucosa due to its content of salt and exogenous nitrosamines (Craddock, 1992). In addition, red and processed meat may increase oesophageal cancer risk (Cross et al., 2007; World Cancer Research Fund/ American Institute for Cancer Research, 2007; Navarro Silvera et al., 2008; Aune et al., 2009) by increasing the formation of nitrosamines in the upper digestive tract (Lunn et al., 2007) and nitrosamines are known to be potent carcinogens in the oesophageal mucosa (Craddock, 1992).

We found no association between salted meat intake and stomach cancer risk in this study, although in three previous studies in this population there was an elevated risk (De Stefani et al., 1990; 1998b; 2004). Most studies from other populations, including China (Takezaki et al., 2001; Lu et al., 2002; Bao et al., 2003; Ding et al., 2008;), Taiwan (Lee et al., 1990), India (Phukan et al., 2006), Mexico (Ward and Lopez-Carrillo, 1999) and Lithuania (Strumylaite et al., 2006) also reported an elevated stomach cancer risk with high salted meat intake, although in two of these studies the results were not statistically significant (Ward and Lopez-Carrillo, 1999; Bao et al., 2003). A meta-analysis found an elevated stomach cancer risk with high processed meat intake (Larsson et al., 2006) and the report from the World Cancer Research Fund/ American Institute for Cancer Research (2007) stated that there was limited suggestive evidence for an association between processed meat intake and risk of stomach cancer (World Cancer Research Fund/American Institute for Cancer Research, 2007). A high salt intake is suspected to increase stomach cancer risk as well (World Cancer Research Fund/American Institute for Cancer Research, 2007). In addition, nitroso-compounds formed either exogenously in meats or formed endogenously due to high

heme-iron intake may increase stomach cancer risk (Jakszyn and Gonzalez, 2006; Jakszyn et al., 2006). Although both red and processed meat intake are established risk factors for colorectal cancer (World Cancer Research Fund/American Insitute for Cancer Research, 2007), we are not aware of any previous studies that specifically addressed the association between salted meat intake and colorectal cancer risk.

Salted meat intake was not significantly associated with risk of laryngeal cancer in this study. A Chinese case-control study reported a strong association between salted meat and fish intake and laryngeal cancer (Zheng et al., 1992b) and a previous study from Uruguay also suggested an elevated risk, albeit not significant (De Stefani et al., 1995), while a more recent study found no association (De Stefani et al., 1999).

To our knowledge only two previous studies from Uruguay assessed the association between salted meat intake and lung cancer and reported significant (De Stefani et al., 1996) or non-significant (De Stefani et al., 2002) positive associations, consistent with our present results. In a previous study, lung cancer was directly associated with nitrosodimethylamine, which may be present in salted meats (De Stefani et al., 1996). Also, high red and processed meat intake has been associated with increased risk of lung cancer (Cross et al., 2007; World Cancer Research Fund/American Institute for Cancer Research, 2007; Hu et al., 2008; Aune et al., 2009a; 2009b; Lam et al., 2009; Tasevska et al., 2009) perhaps through effects of heme-iron and heterocyclic amines (Tasevska et al., 2009).

We found positive associations between intake of salted meat and cancers of the cervix, prostate, bladder, kidney, non-Hodgkin's lymphoma and all cancers combined, but no association with breast cancer. Except for two previous studies from Uruguay which found a positive association between salted meat and bladder cancer (Balbi et al., 2001) and non-Hodgkin's lymphoma (De Stefani et al., 1998), we are not aware of any previous studies specifically on salted meat intake and these cancers, although a number of studies have found associations between red and processed meat intake and some of these cancers (Tavani et al., 2000; Cross et al., 2007; World Cancer Research Fund/American Institute for Cancer Research, 2007; Hu et al., 2008; Aune et al., 2009a; 2009b). Because we are not aware of any association between salt intake and these cancers, it is quite possible that these associations may reflect other more general mechanisms of meat-related carcinogenesis.

As with any-case-control study we cannot exclude the possibility that recall and selection bias may be present. However, the response rate was rather high both among the cases and the controls. Recall bias may be less of a problem because salted meat is a less frequently consumed meat item in Uruguay and therefore should be easy to remember. Our study has strengths as well; the large number of cases made it possible to detect moderate-sized odds ratios. We adjusted for the most important risk factors for cancer, but cannot exclude the possibility that residual confounding from unmeasured or unknown risk factors could explain some of the results.

In summary, this study suggests that salted meat consumption is a risk factor for a number of cancer sites. It is possible that salt and exogenous nitrosamines may explain some of these results, but other mechanisms may also play a role.

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