Swedish Moist Snuff and Myocardial Infarction Among Men

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Background: Previous studies have provided inconsistent results on possible increased risk of cardiovascular disease with the use of smokeless tobacco. The aim of this study was to assess whether long-term use of Swedish moist snuff (widely used among Swedish men) increases the risk of acute myocardial infarction.

Methods: This case-control study was conducted in 2 Swedish counties. We identified 1760 men, age 45–70 years, who had a myocardial infarction in 1992–1994. We randomly selected male controls from the study base after stratification for age and hospital catchment area. Information about snuff consumption, smoking history, hypertension, and other factors was obtained by mailed questionnaire and medical examination. The participation rate was 77% among cases and 78% among controls, with tobacco use data available for 1432 cases and 1810 controls.

Results: After adjustment for age, hospital catchment area, and smoking, the relative risk of first acute myocardial infarction was 1.1 (95% confidence interval = 0.8–1.5) for former snuff users and 1.0 (0.8–1.3) for current snuff users. Analyses limited to either nonfatal or fatal cases did not change the results. Among the controls, the consumption of smokeless tobacco was strongly associated with certain risk factors for myocardial infarction such as smoking, hypertension, and high body mass index.

Conclusion: The hypothesis that smokeless tobacco increases the risk for myocardial infarction is not supported in the present study.

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Tobacco smoking is a well-documented risk factor for cardiovascular disease. Nicotine is one of the substances in tobacco that has a cardiovascular effect. The acute effects of nicotine include an increase in heart rate and higher blood pressure.[1–3] Studies show that snuff users are exposed to at least the same doses of nicotine as smokers, but exposure to many other substances may differ substantially between snuff users and smokers.[4–6] The nicotine content as well as the content of other substances in smokeless tobacco varies, partly as a consequence of different production methods.[7,8] This study is focused on Swedish moist snuff. Sweden has a high consumption of snuff among men (845 g per capita per year for males over 15 years old). Approximately 20% of the adult men in Sweden are daily snuff users, but only 1% of the women.[9,10]

The results from the few studies available on cardiovascular effects in long-term users of smokeless tobacco are ambiguous. Some show an increase in heart rate and blood pressure, as well as a higher prevalence of hypertension.[11–14] Other studies have not confirmed these findings.[15,16] Fibrinolytic variables and blood lipids do not seem to be affected by snuff use,[17–20] and no association with carotid and femoral atherosclerosis has been found.[20,21] There are to date no definitive findings indicating that snuff users have increased morbidity or mortality from cardiovascular diseases. One Swedish study reported an increased prevalence of circulatory disorders as well as cardiovascular mortality among snuff users.[11,22] However, more recently published studies show no increased risks of myocardial infarction from use of Swedish snuff, although there is a tendency toward increased risk of fatal myocardial infarction.[23–25] The aim of the present study is to assess whether long-term use of Swedish smokeless tobacco increases the risk of first-time acute myocardial infarction in men.

Subjects

The present study is based on 2 methodologically equivalent case-control studies using identical questionnaires: the Stockholm Heart Epidemiology Program and the Västernorrland Heart Epidemiology Program. The Stockholm study base consists of Swedish citizens with no previous myocardial infarction, age 45–70 years, and living in Stockholm

County in 1992–1993; participants in the second study were men age 45–65 years living in Västernorrland County in 1993–1994. We included only men in this study because the reported use of smokeless tobacco among women was negligible.

Cases were defined as all events of first acute myocardial infarctions (nonfatal and fatal) that could be identified from departments of medicine at all hospitals in Stockholm as well as from the hospital discharge register and the mortality register at Statistics Sweden. We randomly selected male controls from the study base after matching for age and hospital catchment area. To maintain the power of the study, 5 control candidates per case were sampled so that potentially nonresponding controls could be replaced by another control. Cases still alive 28 days after falling ill were classified as nonfatal and those with a survival less than 28 days were classified as fatal. In Stockholm County, 1485 men with first acute myocardial infarction were identified, and in Västernorrland county, 275 cases were identified (total 1760 cases). Detailed description of the study design, data collection, and exposure information can be found in a previous report.[26] The study was approved by the Ethics Committee at the Karolinska Institutet.

Questionnaire

Inquiry about participation and information on exposure was collected by mailed questionnaires sent to all nonfatal cases and all the controls followed by a telephone interview. The nonfatal cases and their controls also attended a medical examination approximately 3 months after recruitment. This examination included assessment of blood pressure and cholesterol. In fatal cases, next of kin answered the questionnaire. The participation rate was 77% among all the cases, 89% among the nonfatal cases, 65% among the fatal cases, and 78% among the controls. In the analysis, we divided the exposure data into 3 categories (never used snuff, former snuff users, and current snuff users). Subjects who had stopped using snuff more than 2 years before enrollment were classified as former snuff users. Subjects who at enrollment had been using snuff within the last 2 years were classified as current snuff users.

The questionnaire also collected information on other cardiovascular risk factors, including socioeconomic factors, marital status, educational level, work and work environment, physical activity, smoking, dietary habits, alcohol consumption, height, and weight. Classification criteria for these risk factors are described elsewhere.[26–28] Smoking was divided into 3 categories (never smokers, former smokers, and current smokers), classifying subjects who had stopped smoking more than 1 year before as former smokers and those who had smoked within the past year as current smokers.

Statistical Methods

The subjects were divided into 9 groups according to combinations of smoking and snuff habits. We calculated odds ratios (ORs) with 95% confidence intervals (CIs) of myocardial infarction in relation to use of snuff by smoking status through logistic regressions with never smoking, never snuff users as the reference group. Adjustment for age (5-year groups) and hospital catchment area was made with dummy variables. We also included variables for potential confounders (diabetes, hyperlipidemia, hypertension, overweight, physical inactivity, and job strain).

RESULTS

There were 1432 cases (1173 nonfatal and 259 fatal) and 1810 controls who provided data about tobacco use (Table 1). The consumption of smokeless tobacco was similar among cases and controls. Approximately 5% were former snuff users and approximately 10% were current snuff users. Smoking habits were similar among nonfatal and fatal cases of myocardial infarction. Among the controls, those who used both snuff and cigarettes smoked slightly fewer cigarettes than those who exclusively smoked (16.4 compared with 18.6 cigarettes per day). This was also true for the former smokers

TABLE 1. Number of Cases (Nonfatal and Fatal) and Controls by Smoking Status and Use of Swedish Moist Snuff

	Cases								Controls			
	Never Smoked		Former Smoker*		Current Smoker		All					
	Nonfatal	Fatal	Nonfatal	Fatal	Nonfatal	Fatal	Nonfatal	Fatal	Never Smoked	Former Smoker*	Current Smoker	All
Never used snuff	248	45	239	64	502	114	998	223	598	480	460	1538
Former snuff user†	6	1	30	6	26	4	62	11	12	66	12	90
Current snuff user	7	3	62	9	53	13	122	25	28	94	60	182
All	261	49	331	79	581	131	1173	259	638	640	532	1810

*Stopped smoking 1 year before inclusion.
†Stopped using snuff more than 2 yr before inclusion.

(18.4 cigarettes per day with snuff use and 20.6 cigarettes per day without snuff).

Consumption of smokeless tobacco was strongly associated with smoking among controls (Table 2). Snuff use was also associated with hypertension and obesity, 2 other known risk factors for myocardial infarction. In general, the associations appeared stronger in current snuff users than in former snuff users.

No increased risk of acute myocardial infarction was observed among former or current snuff users (Table 3). Odds ratios were 1.1 (95% CI = 0.8–1.5) for former snuff users and 1.0 (0.8–1.3) for current snuff users. The odds ratio based on nonfatal cases was 1.0 (0.7–1.5) for former snuff users and 1.0 (0.8–1.3) for current snuff users. For the fatal cases, the risk was 1.0 (0.5–2.1) for former snuff users and 1.0 (0.7–1.6) for current users.

Further adjustment for diabetes, hyperlipidemia, hypertension, overweight, physical inactivity, and job strain in the analyses had negligible influence on the results.

DISCUSSION

Our results do not indicate an increase in risk of myocardial infarction among users of Swedish moist snuff. These results are unchanged when possible confounders are taken into account. Evidence from the few earlier studies on snuff use and cardiovascular disease is conflicting. In 1 case-control study, conducted within the framework of The Northern Sweden MONICA project (585 male cases, 589 controls), the age-adjusted relative risk of myocardial infarction among snuff users was 0.9 (0.6–1.3).[24] In a later analysis within this study (687 cases of first myocardial infarctions, nonfatal and fatal, 687 controls), the relative risk after adjustment for multiple cardiovascular risk factors was 0.6 (0.4–0.9) for nonfatal and 1.5 (0.5–5.0) for fatal events.[25] These results are consistent with a cohort study based on 135, 036 Swedish male construction workers that showed an increased risk of dying of cardiovascular diseases among snuff users (1.4, 1.2–1.6).[22] There are several possible explanations for this range of results, including differences between an occupational cohort and general population samples, differences of the composition of control groups, and differences resulting from use of mortality compared with morbidity as an end point. In the cohort study, the baseline exposure information was from the early 1970s, and changes in snuff and smoking habits during the follow up as well as changes in the composition of snuff from the 1970s to the 1990s[29] could influence the results. Furthermore, all these studies were based on small numbers of cases who used snuff, which makes random variability a possible explanation as well.

The strength of our study is the quality of diagnosis and case identification. The combination of the sources used to find cases and uniform diagnostic criteria contributed to the high quality of diagnosis and minimized the number of unidentified cases.[26] Tobacco consumption was measured by a self-reported questionnaire, and this may have introduced some misclassification. Tobacco use is usually more common among nonresponders.[25,30] Bias would be introduced if participation was related to the exposure; this could give a misrepresentation of the true exposure prevalence among cases and controls. In our study, 81% of the cases and 75% of controls answered questions about their tobacco habits. There were fewer consumers in the

TABLE 2. Associations Between Certain Risk Factors for Myocardial Infarction and Snuff Use Among Controls*

		Snuff Use				
		Never (n = 1538)	Former (n = 90)		Current (n = 90)	
	No.	%	%	OR (95% CI)	%	OR (95% CI)
Diabetes	1808	5	4	1.1 (0.40–3.3)	6	1.5 (0.76–2.9)
Hyperlipidemia†	1292	21	23	1.1 (0.63–2.0)	23	0.99 (0.66–1.5)
Hypertension‡	1810	26	23	0.98 (0.58–1.6)	35	1.8 (1.3–2.5)
Overweight (BMI ≥30 kg/m^2)	1809	10	14	1.5 (0.79–2.8)	18	1.9 (1.2–2.9)
Physical inactivity§	1789	34	28	0.90 (0.56–1.5)	35	1.2 (0.85–1.7)
Job strain‖	1808	4	4	1.2 (0.42–3.5)	6	1.8 (0.88–3.5)
Former smoker¶	1810	31	73	8.1 (4.3–15.4)	52	4.4 (2.8–6.9)
Current smoker	1810	30	13	1.2 (0.50–2.7)	33	2.5 (1.6–4.1)

*Odds ratios adjusted for age group, hospital catchment area, and smoking.
†6.5 mmol/L at examination or treatment with lipid-lowering medication.
‡170/95 mm Hg at examination or hypertension in questionnaire.
§No physical activity or very little activity during leisure time 5–15 yr before inclusion.
‖Ratio between the demand sum score and the decision sum score, subjects with ratio >0.765 were classified as exposed to job strain.
¶Stopped smoking 1 year before inclusion.

TABLE 3. Relative Risk of Acute Myocardial Infarction for Men Who Never Used Snuff and Former or Current Snuff Users, Stratified by Smoking Status

	Smoking Status			
	Never	Former*	Current	All
Snuff Use	OR (95%)	OR (95%)	OR (95%)	OR† (95% CI)
All cases (n = 1432)				
Never	1.0§	1.3 (1.1–1.6)	2.8 (2.3–3.4)	1.0§
Former‖	1.2 (0.46–3.1)	1.1 (0.73–1.7)	5.3 (2.7–10.6)	1.1 (0.78–1.5)
Current	0.73 (0.35–1.5)	1.6 (1.1–2.2)	2.3 (1.6–3.4)	0.98 (0.77–1.3)
All cases	1.0§	1.3 (1.1–1.6)	2.8 (2.4–3.4)	
Nonfatal cases (n = 1173)				
Never	1.0§	1.2 (0.98–1.5)	2.7 (2.2–3.3)	1.0§
Former‖	1.2 (0.43–3.2)	1.1 (0.68–1.7)	5.3 (2.6–10.7)	1.1 (0.79–1.6)
Current	0.59 (0.25–1.4)	1.6 (1.1–2.2)	2.1 (1.4–3.1)	0.98 (0.76–1.3)
All nonfatal cases	1.0§	1.3 (1.0–1.6)	2.7 (2.2–3.3)	
Fatal cases (n = 259)				
Never	1.0§	1.7 (1.6–2.6)	3.6 (2.4–5.2)	1.0§
Former‖	1.7 (0.21–13.6)	1.4 (0.55–3.3)	6.0 (1.8–20.3)	1.1 (0.54–2.1)
Current	1.7 (0.48–5.5)	1.5 (0.69–3.2)	3.8 (1.9–7.5)	1.0 (0.65–1.6)
All fatal cases	1.0§	1.6 (1.1–2.3)	3.5 (2.4–5.0)	

*Stopped smoking 1 year before inclusion.
†Adjusted for age, hospital catchment area, and smoking.
‡Number of controls, 1810 used for all analyses.
§Reference category.
‖Stopped using snuff 2 yr before inclusion.

older age groups and there was also geographic variation, with fewer consumers in the Stockholm area compared with Västernorrland area. These patterns are similar to those seen in other studies,[24,25,31] including a national survey.[1] The reported amount of tobacco consumption among the controls was consistent with national estimates.

Adjusting for diabetes, hyperlipidemia, hypertension, overweight, physical inactivity, and job strain had little impact on the risk estimates. It is unclear to what extent snuff use could influence some of these risk factors, which may be a reason to exclude them in the analyses. There could, however, be a residual effect of misclassification of smoking, resulting in negative confounding. Several studies indicate that the nicotine intake is relatively constant among tobacco users regardless of whether they smoke, use snuff, or mix the consumption.[30–33] Our data confirm that smokers who also use snuff tend to smoke less. The negative confounding would result in a lower observed excess risk from snuff among former smokers and current smokers because the effects from smoking on myocardial infarction are stronger. We found no clear evidence for an association of snuff use with fatal infarction. However, the results for the fatal cases should be interpreted with caution. The exposure information from the fatal cases was gathered from the next of kin, which increases the imprecision of the exposure information, although validation studies show that information on tobacco use may have a rather high quality using information from next of kin.[34] The nonparticipation rate was larger in this group and the results are based on few observations. Furthermore, the information about risk factors such as hyperlipidemia, hypertension, diabetes, and BMI were limited for the fatal cases and adjustments for some of these risk factors were not possible.

The difference in risks for myocardial infarction between smokers and snuff users could suggest that it is probably not the long-term exposure to nicotine in the smoking tobacco that increases the risk for myocardial infarction, but rather other components in cigarette smoke. Carbon monoxide, oxidant gases, and polycyclic aromatic hydrocarbons are substances in cigarette smoke that have a potential cardiovascular effect.[35] Another hypothesis would be that oral moist snuff contains substances such as fatty acids and flavonoids that could have a protective effect for myocardial infarction.

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