

Null Results in Brief

Risk of Brain Glioma not Associated with Cigarette Smoking or Use of Other Tobacco Products in Iowa

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Introduction

The hypothesis that various *N*-nitroso compounds, which are potent nervous system carcinogens in animal studies, may also increase the risk of human brain cancer (1) has been of great interest in recent etiological studies of this disease. In the United States, it is estimated that cigarette smoking gives rise to at least a 20-fold greater daily exposure to *N*-nitroso compounds than any other consumer product (2), and the use of tobacco products is considered to be the greatest and most widespread source of human exposure (3). Epidemiological studies of cigarette smoking and risk of brain cancer (including gliomas and/or astrocytomas) have been inconclusive (4). To clarify the role of using various tobacco products in the risk of brain cancer and to examine the risk of brain cancer by type of cigarette smoked, as suggested by earlier studies, we analyzed the data from a population-based case-control study of brain glioma in Iowa.

Materials and Methods

A total of 375 histologically confirmed incident glioma cases, 40–85 years of age, participated in the study (201 males and 174 females), and a total of 2434 (1601 males and 833 females) population-based controls were frequency-matched by sex and 5-year age groupings with a matching ratio of approximately 6.5:1. Controls <65 years of age were randomly selected from computerized state drivers' license records. Controls ≥65 years of age were selected from the United States Health Care Financing Administration listings. Persons with a previous cancer diagnosis were excluded from consideration as controls. The participation rate was 91% for glioma cases, 82% for controls <65 years of age, and 80% for controls ≥65 years of age. A postal questionnaire on use of cigarettes and other tobacco products and several potential confounding factors was used to collect detailed information from study subjects or from their next of kin. Unconditional logistic regression models were used to estimate the association between tobacco product use and the risk of brain cancer and to control for confounding.

Results and Discussion

As shown in Table 1, there was no overall association between brain cancer risk and cigarette smoking among either men or women. There was also no increased risk of brain cancer associated with current or past smoking, age at first smoking, duration of smoking, daily number of cigarettes, or life-time pack-years of smoking. Analysis by type of cigarette smoked showed an 80% increased risk for ever-smokers of nonfilter cigarettes among females. This, however, was limited to ex-smokers, and no increased risk was found for those with longer durations and larger pack-years of smoking. Use of pipe, cigar, snuff, or chewing tobacco was also not associated with a significantly increased risk of brain cancer for either men or women in this study (data not shown).

This is one of a few studies with adequate statistical power to examine the risk of a specific histological type of brain cancer (glioma) with the use of several types of tobacco products, including cigarettes, cigars or pipes, snuff, and chewing tobacco, among both males and females. The use of proxy respondents for patients who were too ill or had died may have resulted in misclassification of exposure information. However, two recent reliability studies have concluded that proxy-reported smoking status is an accurate and effective means to estimate smoking status among adults (5, 6). Considering that brain cancer is among the most rapidly fatal of all cancers and a disease with a devastating impact on a person's memory, use of proxy respondents in population-based case-control study of brain cancer seems inevitable and, perhaps, preferable to self-respondents.

In summary, the findings of this study do not support a major effect on the risk of brain cancer associated with cigarette smoking or the use of other tobacco products. However, it should be noted that several studies have implicated dietary intake of *N*-nitroso compounds as a risk factor for brain tumors as recently reviewed by Giles (7). Therefore, although the use of tobacco products is a major source of human exposure to various *N*-nitroso compounds, the route of exposure may be important (absorption through the gastrointestinal tract *versus* through inhalation). Laboratory studies have also shown that various *N*-nitroso compounds are potent nervous system carcinogens, particularly when animals are exposed transplacentally, as cited by Preston-Martin *et al.* (1). The lack of association between tobacco product use and risk of brain cancer found here and in other epidemiological studies may also be attributable to the human blood-brain barrier, which may limit the amount of *N*-nitroso compounds reaching the brain tissue. It is also possible that human brain tissue may differ from other organs in susceptibility to tobacco carcinogens, including the ability to form carcinogen-DNA adducts, to metabolically activate precarcinogens, and to further convert carcinogenic metabolites into nontoxic, water-soluble metabolites. Future molecular epidemiological studies may help to clarify these issues.

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Table 1 Risk of brain glioma associated with cigarette smoking in Iowa

Cigarette smoking	Men		Women	
	Case/Control	OR ^a (95% CI)	Case/Control	OR ^a (95% CI)
Never	69/533	1.0	121/574	1.0
Ever	132/1068	0.9 (0.6–1.2)	53/259	0.8 (0.6–1.2)
Ex-smoker	71/742	0.8 (0.5–1.1)	27/120	1.0 (0.6–1.6)
Current smoker	61/326	1.0 (0.7–1.6)	26/139	0.7 (0.4–1.1)
Duration (yr)				
<30	49/358	0.8 (0.5–1.2)	22/76	1.1 (0.7–2.0)
30–40	42/305	0.9 (0.6–1.4)	15/84	0.6 (0.3–1.2)
>40	37/402	0.9 (0.5–1.4)	10/99	0.4 (0.2–0.9)
Unknown	4/3			6/0
Number of cigarettes per day:				
<11	23/197	0.9 (0.6–1.6)	16/94	0.7 (0.4–1.3)
11–20	49/448	0.8 (0.5–1.2)	25/103	1.0 (0.6–1.7)
>20	60/423	0.9 (0.6–1.4)	12/62	0.7 (0.3–1.4)
Pack-years:				
<25	41/337	0.8 (0.5–1.3)	23/110	0.8 (0.5–1.4)
25–49	40/341	0.8 (0.5–1.3)	16/94	0.6 (0.3–1.2)
>49	47/387	0.9 (0.6–1.4)	8/55	0.6 (0.3–1.3)
Unknown	4/3			6/0

^a OR, odds ratio. Adjusted for age (40–54, 55–64, 65–74, and 75–85 years), body mass index (<24, 24–26, >26 kg/m²), level of education (≤8, 9–11, 12–15, ≥16 years), strenuous or moderate exercise (≤1×/day, 2–6×/week, 1–4×/month, <1×/year), duration of living in a residence served by chlorinated surface water (0, 1–19, 20–39, ≥40 years), and having a first-degree relative with brain cancer (yes/no).

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