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A case-controlled study of the current role of cigarette smoking and alcohol consumption in primary liver cell carcinoma in Nigerians

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Summary

This paper describes the findings of a case-controlled study of 100 patients with primary liver cell carcinoma, sex- and age-matched with another 100 patients seen at the orthopaedic clinic of the University College Hospital, Ibadan. Contrary to widespread belief, the relative risks of cigarette smoking and alcohol consumption were not found to be statistically significant. The implication of this on the possible aetiology of primary liver cancer is discussed.

Résumé

Cet article décrit les constatations d'une étude d'observation-témoin de 100 malades avec le carcinome hépatique primordiale, le sexe et l'âge égalés avec 100 malades de la consultation externe orthopédique de UCH, Ibadan. Contraire à la croyance générale, les cigarettes et l'alcool étaient trouvés de ne pas être statistiquement significatifs. L'implication de ceci en considérant la cause du carcinome hépatique primordiale est discuté.

Introduction

In developed countries of the world, such as Greece, Japan and North America, cigarette smoking and alcohol consumption have been reported to be aetiologically important causes of primary liver cell carcinoma (PLCC) [1–4]. While previous studies in Nigerians have suggested an association between hepatitis B virus (HBV) or aflatoxin and PLCC [5–7], there are no known controlled studies on the suspected risks of the use of cigarettes and alcohol.

This paper, therefore, examines the relative risks of cigarette and alcohol consumption in a case-controlled study of 100 histologically proven patients with PLCC seen over a 2-year period at the University College Hospital, Ibadan.

Subjects and methods

The case group were 100 histologically proven patients with PLCC. All these patients were interviewed at the gastroenterological clinic of the University College Hospital, Ibadan during a 2-year period (1987–1988). For each patient a sex- and age- (±5 years) matched control subject who was seen at the orthopaedic clinic of the same hospital with a diagnosis of trauma was interviewed. Prior to the interview, the controls were screened by physical examination and routine liver tests to exclude the possibility of any occult PLCC. All control interviews took place within 1 month of the patient interviews. All subjects were interviewed in person by one interviewer (I.O.O.). The data collected included information on cigarette smoking and drinking habits, use of drugs, occupational history and family history of cancer. The smoking habits were classified into two categories: (a) non-smoker (never in life smoked cigarettes, pipes or cigars) and (b) smoker. The drinking habits were also classified into two main categories, i.e. non-drinker (never had any alcoholic drinks) and drinker. The drinkers were further categorized as light (equivalent to

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less than 10 grams of alcohol/day), moderate (equivalent to 10–35 grams of alcohol/day) or heavy drinkers (equivalent to more than 35 grams of alcohol/day). All the subjects with moderate and heavy alcohol use were then interviewed with four clinical questions to make a diagnosis of alcoholism [8]. The questions focused on 'Cutting down', 'Annoyance by criticism', 'Guilty feeling' and 'Eye-opener' (CAGE). The CAGE questionnaire has been found reliable in discriminating between alcoholics and non-alcoholics and requires at least three positive responses out of the four questions for a diagnosis of alcoholism [9].

The relative risks of smoking and drinking habits were estimated by calculating the odds ratio. The confidence intervals of the odds ratio were also calculated and its significance in the development of PLCC examined by the chi-square test. The effect of the CAGE-positive response was examined between patients and controls using the Mantel-Haenszel chi-square test.

Results

There were 85 (85%) male cases of PLCC with a mean age of 46.6 years and a standard deviation (SD) of 4.2 years. The 15 (15%) female cases had a mean age of 50.1 ± 5.1 years. Eighty-five (85%) control subjects were males with a mean age of 46.2 ± 3.6 years; the 15 (15%) female controls had a mean age of 49.8 ± 3.0 years. Patients and controls were similar with respect to religion, marital status, education, dietary habits, use of drugs, occupational history and family history of cancer.

Table 1 shows cigarette smoking and alcohol consumption among the patients and controls. The odds ratio, a good estimate of the relative risks, gave the risk of having PLCC as 1.7 times higher among smokers than non-smokers but this was not statistically significant ($P > 0.05$). When the analysis was stratified by sex, the risk increased to about four times in the females while it reduced to 1.4 times in males, although these positive and negative increases were not

Table 1. Cigarette smoking and alcohol consumption among patients and controls

Cigarettes/ alcohol use	Patients	Controls	Odds ratio	95% Confidence interval
Cigarette smoking				
Both sexes				
Non-smokers	51	64	1.0	
Smokers	49	36	1.7	(0.9–3.1)
Males				
Non-smokers	45	53	1.0	
Smokers	40	32	1.5	(0.8–2.8)
Females				
Non-smokers	6	11	1.0	
Smokers	9	4	7.1	(0.7–26.5)
Alcohol consumption				
Both sexes				
Non-drinkers	48	60	1.0	
Drinkers	52	40	1.6	(0.9–3.0)
Males				
Non-drinkers	35	46	1.0	
Drinkers	50	39	1.7	(0.9–3.2)
Females				
Non-drinkers	13	14	1.0	
Drinkers	2	1	1.4	(0.2–255.1)

statistically significant ($P > 0.1$). Similarly, there was a slightly higher risk, though not statistically significant ($P > 0.2$) among drinkers than non-drinkers. Again, no sex differential was observed. Although the sample of the CAGE-positive response was small (Table 2), the findings indicate that alcoholism and covert problem drinking is not common among the cases with PLCC ($\chi^2 = 2.97$; $P > 0.3$).

Discussion

The finding in this study that smoking and drinking may not be important risk factors in the aetiology of PLCC in Nigerians needs careful interpretation. Our result seems unlikely to be due to chance, given both the level of statistical significance and the CAGE-positive response pattern. There are, however, important limitations to this study which need to be mentioned. These are the uncertain reliability of obtaining information on cigarette smoking or alcohol use retrospectively and also the deliberate wrong estimation of use of these agents. As a result, some misclassification of cigarette or alcohol consumption from the sources considered in the study may possibly have occurred. If the misclassification was random, the non-association between cigarette or alcohol use and liver cancer would be stronger than indicated in the study. However, if the extent and direction of misclassification differed between cases and controls, erroneous conclusions could be reached.

Contrary to our observation of a non-association between smoking or drinking and PLCC, Trichopoulos *et al.* [1] in Greece and Yu *et al.* [4] in North America have suggested that excessive smoking or drinking are strongly associated with PLCC in patients frequently sero-positive for HBV infection.

During a study of haemoglobin genotypes and PLCC [10] we found that 40% of our patients with liver cancer had HBV markers, corroborating an earlier report [5]. This shows that even though no attempt was made to test the patients for HBV infection in the present study, there is some evidence that about the same proportion of patients with PLCC are HBV-related in these developed countries [1,4]. Assuming that HBV plays the same aetiological role in Nigeria as in these developed countries, what is the explanation for the non-association between smoking or drinking and the development of liver cancer in Nigerians? It may be due to the level of exposure to the hepatocarcinogens, a reflection of the dose of cigarette or alcohol consumed in Nigeria compared to that in the developed countries. It is important to note that up to now, there is no absolutely safe amount of cigarettes or alcohol for recommendation. The majority of smokers in Nigeria are light smokers with less than 25% exceeding 10 cigarettes per day and with only about 5% smoking for more than 5 years [11]. This correlates with the recent findings of Onadeko *et al.* [12] in students of our higher institutions. Similarly, the majority of the alcohol users are light drinkers, presumably for economic reasons and the fact that there are areas within the country where strict enforcement of religious laws against the use of alcohol still operates. However, the habit of smoking or drinking is on the increase in the general population as each factor is being promoted by widespread advertising which associates the habits with prestige and sophistication. The revenue accruing from the sale of cigarettes or liquour is enormous. Therefore with time,

Table 2. CAGE-positive response of cases with primary liver cancer and moderate or heavy alcohol consumption

CAGE-positive response	Controls (n = 26)	Patients (n = 29)
1	1	2
2	2	3
3	0	5
4	0	1
Total	3	11

smoking- or drinking-related liver cancer rates may be expected to rise in Nigeria as is the experience in other countries [1,3,4] unless the Government and non-governmental organizations such as the Nigerian Cancer Society take adequate steps to control the propaganda and sale of cigarettes and alcohol, in addition to educating the public on their hazards.

Clearly, our findings are preliminary. In view of the increasing widespread use of cigarettes and alcohol and because of the poor prognosis associated with PLCC [6] a further study of this issue is needed.

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