ORIGINAL

Cancer incidence in alcoholics cared for in a public university hospital: a report of case series

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Abstract

Objective: To evaluate the incidence of cancer in patients treated in the Alcoholism Outpatient Clinic of the Clinical Hospital of the Federal University of Uberlândia, in the city of Uberlândia, MG, Brazil. **Methods:** Medical records of 490 out of 511 patients, treated between January 1995 and December 2006, were reviewed. This search was conducted in the hospital's Medical Archive Service and in the Mortality Information System of the city of Uberlândia's Civil Registry Office. **Results:** No patients were referred with a confirmed or suspected diagnosis of cancer. Among the 490 patients, 23 (4.7%) developed some form of cancer during the study period. All these were men, with a mean age of 48.7 ± 9.6 years (33 to 65 years), and 18 (78.3%) were smokers. Upper aerodigestive tract cancer was the most frequent (10/23 - 43.5%) and in all of them, the histological type was squamous cell carcinoma; 5 (21.7%) had gastric cancer (adenocarcinoma); 2 (8.7%), lung (carcinoma); 2 (8.7%), liver cancer (hepatocellular carcinoma and cholangiocarcinoma); 2 (8.7%), central nervous system cancer; 1 (4.3%), acute myeloid leukemia (FAB M2); 1 (4.3%), rhabdomyosarcoma; and 1 (4.3%), poorly differentiated carcinoma with undefined primary site. **Conclusions:** During the study period, at least 4.7% of patients developed some form of cancer, predominantly in the upper aerodigestive tract. This is an alarming fact, considering that 12.3% of Brazilians aged over 12 years may be dependent on alcohol and another 24% make heavy and/or frequent use of alcoholic beverages.

Keywords: alcohol consumption, alcoholics, incidence, neoplasms, smoking.

INTRODUCTION

It is estimated that upwards of 80%, to even 90%, of cancers in Western populations can be attributable to environmental causes, among which are poor dietary habits (a diet low in fruits and vegetables and high in animal fat) and social and cultural practices, including alcohol consumption and smoking[1].

The association of alcohol with an increased incidence of esophageal cancer was described 100 years ago by Lamu[2] and several studies have been published since then, showing the relationship between chronic use of alcohol and various types of cancer. Currently, there is sufficient evidence that chronic consumption of alcoholic beverages can cause cancer of the oral cavity, pharynx, larynx, esophagus (squamous cell carcinoma), liver, colon and rectum, and among women, breast; there is limited evidence that this could cause pancreatic cancer[3,4].

Epidemiologic evidence on the association between smoking and cancer could be observed in the 1920s and the causal relationship between tobacco and lung cancer was established in the 1950s[5]. Nowadays, when considered individually, tobacco smoking is the leading cause of cancer worldwide and there is sufficient evidence that it causes cancer in the oral cavity, oropharynx, nasopharynx, hypopharynx, esophagus (adenocarcinoma and squamous cell carcinoma), stomach, colon, rectum, liver, pancreas, nasal cavity and paranasal sinuses, larynx, lung, uterine cervix, ovary, urinary bladder, kidney, ureter and bone marrow; there is limited evidence of its association with breast cancer in women[4].

The purpose of this study was to report the incidence of cancer in patients cared for in an alcoholism outpatient clinic.

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METHODS

In this retrospective study, the medical records of 511 patients were reviewed, all of whom were cared for at least once in the Alcoholism Outpatient Clinic of the Clinical Hospital of the Federal University of Uberlândia (CH-FUU), in the city of Uberlândia (Brazil) from January 1995 to December 2006. Appointments in this clinic are scheduled by the city's Appointment Scheduling Center. Requests to make these appointments are conducted by professionals in primary health care, emergency rooms and hospitals, and sometimes by the patients' own recommendations for their acquaintances. Many of these patients arrived for their first appointment with severe liver, pancreatic, cardiac or neuro-psychiatric disorders, among others.

The records for analysis were requested from the CH-FUU's medical files, based on the number of existing records in the appointment books to schedule return appointments. In addition, a search was conducted through the CH-FUU's Hospital Information System to analyze data on patients who might have died in the hospital, while another search was conducted through the Mortality Information System of the city of Uberlândia's Civil Registry Office for those who might have died outside of the hospital environment.

While reviewing medical records, data that normally appear in these records were collected, such as patients' age, gender, smoking status, amount and duration of alcohol intake and initial diagnostic hypotheses, and whether they developed some form of cancer during the study period.

The present study project was approved by the Ethics Committee of the Federal University of Uberlandia (Official Opinion 701/08).

RESULTS

Of all the 511 records included in this study, 490 were analyzed and 21 were excluded because they did not include data from the clinic. Of all the 490 patients, 435 (88.8%) were male and 55 (11.2%) were female, with a mean age and standard deviation (SD) of 43.5 ± 10.4 years (33 to 65 years). Among those analyzed, the diagnosis of a certain type of cancer was made in 23 (4.7%) patients, and the body locations, histological types, ages and frequency of concomitant smoking are shown in Table 1. These patients suffered from heavy alcoholism, drinking more than 100 grams of ethanol per day for a period longer than 14 years. Among them, 13 (56.5%) reported drinking *cachaça* (distilled alcoholic beverage made from sugarcane); 5 (21.7%), beer and *cachaça*; 2 (8.7%), beer; and 3 (13%) had no records of types of beverages consumed. The frequency of smoking among the 490 patients was 67% and that among patients with cancer was 78.3%.

Table 1. Frequency of body locations, histological types of cancers and smoking in the chronic alcoholic patients evaluated (all male).

N	Location	Histological types	Age (years)	Smoking
1	Amygdala	Squamous cell carcinoma	43	+
2	Tongue	Squamous cell carcinoma	58	+
3	Tongue	Squamous cell carcinoma	35	-
4	Base of tongue	Squamous cell carcinoma	56	-
5	Oral mucosa/ esophagus	Squamous cell carcinoma	41	+
6	Mouth/Lung	Squamous cell carcinoma/poorly differentiated carcinoma	48	+
7	Larynx	Squamous cell carcinoma	38	+
8	Esophagus	Squamous cell carcinoma	33	+
9	Esophagus	Squamous cell carcinoma	49	+
10	Esophagus	Squamous cell carcinoma	48	+
11	Stomach	Gastric adenocarcinoma, diffuse type	65	+
12	Stomach	Gastric adenocarcinoma, intestinal type	58	+
13	Stomach	Gastric adenocarcinoma, intestinal type	36	+
14	Stomach	Gastric adenocarcinoma, intestinal type	57	+
15	Stomach	Gastric adenocarcinoma, intestinal type	50	+
16	Lung	Bronchogenic carcinoma	47	+
17	Liver	Hepatocellular carcinoma	63	+
18	Liver	Cholangiocarcinoma	62	+
19	CNS	Glioblastoma multiforme	34	+
20	CNS	Cerebellopontine angle schwannoma	45	-
21	Bone Marrow	Acute myeloid leukemia (FAB M2)	53	-
22	Skeletal muscle	Rhabdomyosarcoma	49	-
23	Undefined	Poorly differentiated carcinoma metastatic to cervical lymph node	53	+

CNS: central nervous system.

In their first consultation in the Alcoholism Outpatient Clinic, mean age and SD of patients with cancer was 48.7 ± 9.6 years (varying between 33 and 65 years).

No patients had been referred for treatment in the clinic with a confirmed or suspected diagnosis of cancer, and the mean time between the first consultation and diagnosis of cancer was 4.3 ± 3.0 years (varying from one to nine years). Among these, 16 (69.6%) had died, four (17.4%) were under treatment, and progress could not be found for three patients (13%), probably due to changing their place of treatment. Mean age of patients who died was 50.6 ± 7.5 years (varying from 39 to 66 years). The 16 patients who had died from cancer accounted for 16.7% of the 96 patients whose death could be confirmed in the study period.

DISCUSSION

In the present study, 4.7% of patients treated in the CH-FUU's alcoholism outpatient clinic developed some type of cancer during the study period. The incidence of cancer may have been even higher than that observed, because it is not uncommon for alcoholics to abandon follow-up or change their place of treatment and, as a result, such diagnosis would not be included in the medical records evaluated. This shows the extent of the problem that may exist in Brazil, where it is estimated that 12.3% of the population aged between 12 and 65 years are alcoholics[6], another 24% are frequent and/or heavy drinkers[7] and 17.5% of the population aged over 15 years are smokers[8].

The exact mechanisms by which chronic ethanol consumption stimulates carcinogenesis are not fully defined. There has been more evidence showing that acetaldehyde is predominantly responsible for alcohol associated carcinogenesis; acetaldehyde is carcinogenic, mutagenic, binds to DNA and proteins, destroys folate and results in secondary hyperregeneration[2]. Polymorphisms in acetaldehyde dehydrogenase 2 (ALDH2) are reported to be the key event in establishing the upper aerodigestive tract's (UADT) individual susceptibility to cancer; patients with inactive ALDH2, in whom facial flushing is usually seen after alcohol consumption, are those at a higher risk of squamous cell carcinoma and multiple UADT cancers[9]. Increases in the risk of cancers have been found to be associated with abusive consumption of beer, distilled beverages or wine[1,2].

In this study, among all patients with cancer, 10 (43.5%) had a neoplasm of the UADT, i.e. oral cavity, pharynx, larynx or esophagus, and the histological type in all of them was squamous cell carcinoma (SCC). Epidemiological studies have shown an association between heavy alcohol intake and SCC of the UADT in addition to a linear correlation with both duration and amount of alcohol consumption[3]. However, an increase in the risk of these cancers has been observed with an ethanol intake of 25 grams per day[10], which corresponds to two cans of beer or two drinks of a distilled beverage.

Among patients with cancer of the UADT, only two were not smokers. Smoking and chronic abuse of alcoholic beverages are independent and modifiable risk factors for head and neck cancers (oral cavity, pharynx and larynx), and at least 75% of these cancers are attributed to the combination of cigarette smoking and alcohol consumption[11]. With respect to the esophagus, alcohol consumption is associated with an increase in the risk of SCC exclusively, while smoking is associated with increased risks of SCC and adenocarcinoma[12].

A total of five patients had gastric adenocarcinoma and all were smokers. Presently, there is sufficient evidence that tobacco smoking is carcinogenic to the stomach,[1,4-5,12] while the association between stomach cancer and alcohol consumption is not clearly defined. Most studies revealed that there is no consistent evidence between alcohol consumption and gastric cancer[3], however, two recent studies showed evidence of an increased risk of gastric cancer among heavy alcohol drinkers[13,14].

One patient had hepatocellular carcinoma (HCC) and another, cholangiocarcinoma. Chronic alcohol abuse increases the risk of developing HCC and, in France, excessive alcohol consumption was described as the main risk factor for primary liver cancer[15]. However, the exact role of alcohol in the development of these cancers is still not completely defined. In Western countries, alcohol is a major cause of liver cirrhosis, which is a precancerous condition[2]. Changes in hepatic metabolism of carcinogens may also play a role and the risk of HCC by alcohol can be affected synergistically by an interaction with tobacco, hepatitis B virus or hepatitis C virus[3]. Some studies have also shown that heavy alcohol consumption is a risk factor for both intrahepatic[16,17] and extrahepatic cholangiocarcinoma[16].

Two patients had lung cancer and smoked. The causal relationship between smoking and lung cancer was established in the 1950s and, from the results of studies conducted in Europe, Japan and North America, between 87% and 91% of lung cancers in men were attributed to cigarette smoking[1]. In a meta-analysis study, no significant or consistent relationship was observed between chronic alcohol consumption and the increase in risk of lung cancer[10]. However, in a recent study conducted in Montreal, Canada, there was evidence of increased lung cancer risk associated with alcohol consumption[13]. Moreover, it has been observed that the continuous abuse of a drug increases preference for another. This interaction particularly exists between alcohol and tobacco, i.e. smoking is a risk factor for alcoholism and alcohol use is a risk factor to become a smoker[18].

One patient had acute myeloid leukemia (FAB M2) and was not a smoker. A recent study showed that alcohol consumption was a risk factor for acute myeloid leukemia and that this relationship was consistent for all

types of alcoholic beverages. The subtype with maturation, which was the case of the patient in this study, was most strongly associated with alcohol consumption[19].

Two patients had neoplasia of the central nervous system. In two recent studies, no associations were found between smoking or chronic alcohol consumption and the increase in risk for gliomas[20] and glioblastomas[21].

Among the patients with cancer, at least 70% of them had died. Approximately two-thirds of patients with SCC of the head and neck present with advanced stage disease, frequently involving regional lymph nodes; distant metastasis at initial presentation is uncommon, comprising about 10% of patients[22].

Data from this study show a high incidence of cancers among patients who were treated in the Alcoholism Outpatient Clinic, of which 78% were also smokers. This reveals the need for alcoholics' complaints not to be neglected, so that the diagnosis of cancer can be made early.

To achieve this, the first step would be to diagnose abuse or alcohol dependence among patients. This diagnosis is rarely made during medical consultations, except for diseases strongly related to alcoholism, such as polyneuropathies, cardiopathies, liver cirrhosis or chronic pancreatitis[23]. The diagnosis of alcoholism can be made by asking the patient about their drinking habits and by using one of the several existing questionnaires for this purpose, such as the CAGE (Cut down, Annoyed by criticism, Guilty and Eye-opener) questionnaire, which mainly diagnoses chronic abuse of or dependence on alcohol[24], or the AUDIT (Alcohol Use Disorders Identification Test)[25], which diagnoses risk uses or dependence. These questionnaires can be used as an interview or they can be self-administered.

In patients who are alcoholics and/or smokers, symptoms such as hoarseness, sore throat, tongue pain, mouth ulcer, otalagia, dysphagia and odynophagia, cough, mouth bleeding and laryngeal stridor and/or, upon physical examination, findings of mass or ulceration in the oral cavity or oropharynx, cervical mass, vocal cord paralysis, and swallowing dysfunction may reveal cancer of the head or neck and need to be investigated[22]. People who have facial flushing after alcohol intake may be those who are at the greatest risk, because they metabolize acetaldehyde poorly[9].

In alcoholics, dyspeptic complaints and/or epigastric pain also need to be analyzed; apart from stomach and liver cancers, there is evidence, although limited, that alcoholics are at increased risk for pancreatic cancer, and this risk increases in the presence of chronic pancreatitis as a result of drinking alcohol[3]. Changes in bowel habits and/or rectal bleeding can indicate the presence of cancer. Chronic alcohol consumption also increases the risk of colon and rectal cancer[4,13]; alcohol consumption of ≥ 30g/day was positively associated with the risk of colorectal cancer as compared to abstaining[26].

Hepatic evaluation for alcoholic patients should also be conducted routinely; liver cirrhosis is a precancerous condition. Furthermore, it was determined that alcoholics that came for treatment at the Alcoholism Outpatient Clinic of the CH-FUU, had a high prevalence of serological markers of hepatitis B virus and hepatitis C virus[27,28], and these infections increase the risk of hepatocellular carcinoma.

After the diagnosis of alcoholism and/or smoking, patients must be advised to stop smoking and at least reduce alcohol intake. If necessary, they should be referred for specific treatment of these habits. Stopping to smoke or drink alcohol was found to reduce the risk of head and neck cancer. After one to four years without smoking, the risk of these cancers is reduced, with odds ratios of 0.70, compared with current smoking. Moreover, during a period equal to or greater than 20 years since smoking cessation, cancer risk reduces to levels equal to those who have never smoked; twenty years after stopping to drink alcohol, the risk for head and neck cancer is also reduced to the same level of those who have never drank[29]. Also there is clear evidence that the risk of esophageal cancer is reduced by 60% after stopping to drink alcohol for 10 years or more[1].

In conclusion, in the present study, a high incidence of cancer and mortality was found in the patients evaluated. Considering the fact that alcohol abuse and smoking are independent and modifiable risk factors for several types of cancer, researches of this study expect to emphasize the importance of raising people's awareness of the importance of not smoking and not drinking alcohol or, at least, drinking it moderately. In addition, the need to diagnose alcohol consumption and/or smoking in patients for subsequent counseling or treatment should be emphasized. As previously discussed, thorough physical exams and anamneses are required among alcoholic or smoking patients and their symptoms and signs should be valued, aiming to perform early diagnoses.

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