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Stopping drinking and risk of oesophageal cancer

K K Cheng, S W Duffy, N E Day, T H Lam, S F Chung, P Badrinath

Abstract

Objective—To examine the effect of stopping drinking on the risk of oesophageal cancer.

Design—Hospital based case-control study.

Setting—Surgical departments of four district general hospitals and general practices in Hong Kong.

Subjects—Cases were 400 consecutive admissions of patients with histologically confirmed diagnosis of oesophageal cancer during a 21 month period in 1985-90 (87% response rate). Controls were 150 patients selected from the same surgical departments as the cases and from the general practices from which the cases were originally referred (95% response rate).

Main outcome measure—Relative risk of developing oesophageal cancer after stopping drinking (adjusted for age, education, place of birth, smoking, and diet).

Results—Current light drinking (<200 g ethanol/week) was not associated with significant increase in risk. Among former drinkers risk fell more quickly in moderate (200-599 g/week) than heavy (>600 g/week) drinkers. Even among heavy drinkers, however, risk had dropped substantially after five to nine years of not drinking. The results suggest that the time taken for risk to return to that in subjects who never drink was 10-14 years for moderate drinkers and 15 years or more, if ever, for heavy drinkers.

Conclusion—Risk of oesophageal cancer decreases fairly rapidly with time after abstaining from drinking. This new finding could be used in health promotion to encourage behavioural changes, especially in heavy drinkers, who have a very high risk of developing oesophageal cancer. It also suggests that alcoholic beverages have a strong effect on the late stage of carcinogenesis.

Introduction

Alcoholic beverages have been shown by many epidemiological studies to increase the risk of oesophageal cancer.1 Largely on the basis of epidemiological findings, a working group of the International Agency for Research on Cancer concluded that alcoholic beverages are carcinogenic to humans and causally related to cancers of the oral cavity, pharynx, larynx, oesophagus, and liver.2 One factor, however, which previous studies have not studied in detail is the effect of stopping drinking on the risk of developing cancer. This will be important for several reasons. Firstly, although several different carcinogenic mechanisms of alcoholic beverages have been proposed, their relative importance is still unclear. Laboratory experiments might have been expected to be illuminating, but the evidence of the carcinogenicity of ethanol and alcoholic beverages on experimental animals is much less strong than the epidemiological findings in humans and was judged to be inadequate by the working group.3 Information on how risk changes after the removal of exposure should shed some light on this issue. Secondly, demonstrating a reduction in risk when someone stops drinking will be useful for the purpose of prevention and health promotion. Lastly, evidence of a decrease in risk on cessation will provide further evidence on the causal role of alcohol.

A recent case-control study on oesophageal cancer in Hong Kong Chinese has shown a very strong effect of drinking alcoholic beverages.4 The large sample and the number of former drinkers allowed us to examine the effect of stopping drinking.

Patients and methods

The study was a hospital based case-control study conducted during the period between March 1989 and December 1990. Eligible cases were consecutive admissions of patients with histologically confirmed diagnoses of oesophageal cancer to surgical departments of four general hospitals in Hong Kong. For each case, two controls were selected from patients admitted to the same departments and a further two controls were recruited in the general practice from which the case was originally referred to the care of surgical specialists. Both types of controls were matched by age and sex (within 5 years) to the case. Patients with diabetes mellitus and cancers of the trachea, bronchus and lung, oral cavity, pharynx, larynx, stomach, pancreas, liver, kidney, and bladder, all of which could be related to tobacco and alcohol intake, were excluded. Details of the methods have been reported elsewhere.5

A structured questionnaire was used by trained interviewers to interview subjects in hospital (cases and hospital controls) or general practice. Information was sought on patient characteristics, personal and family medical history, smoking and drinking habits, and diet. On alcohol drinking, details were asked about age at starting to drink, usual amount consumed, duration of drinking different types of beverages, and date of stopping for former drinkers. Using this information we calculated the average weekly amount of alcohol consumed as the mean quantity of ethanol consumed during the entire period of drinking.

Data were analysed by using conditional logistic regression, producing odds ratios and deviance χ² tests for effects.6 We analysed hospital and general practice controls separately but as findings were similar we have reported results on the combination of the two series of controls.
Results

Of the 461 eligible cases, 49 were too ill or senile to be interviewed and 12 refused to participate, leaving 400 cases (345 men, 55 women; 87% of eligible cases). The number of controls interviewed was 1598 out of 1682 selected, giving a response rate of 95%. Among the cases, 341 patients had squamous cell carcinoma, 46 had adenocarcinoma, and other rarer histological types made up the remainder. Table I shows information on age, sex, and education attainment of cases and controls.

Principal results of the study have been reported previously. In summary, alcohol consumption and a number of other variables were found to be important in multivariate modelling. These variables included educational attainment; place of birth; meal pattern; consumption of fresh vegetables, citrus fruits, and pickled vegetables; and tobacco smoking. While the emphasis of this paper is on the effect of stopping drinking, all odds ratios of alcohol related factors were adjusted for these other variables. For tobacco smoking, two variables were included in the adjustment: average amount smoked a day and smoking status (never smokers, current smokers, former smokers by years since stopping).

Among the subjects, the three commonest types of drinks were beer, spirits, and various Italian beverages which were similar in ethanol content to Western style fortified wines and spirits. Most of the current and former drinkers used a combination of the three types of drinks. Very few subjects drank wine.

Table II shows the effect of average amount of alcohol used (in g ethanol) on risk of oesophageal cancer in all subjects, including former drinkers. The equivalent of 40 g ethanol is about 2 pints (1.13 l) beer, 2 fl oz (440 ml) wine, or 0.5 fl oz (112 ml) spirit. There was a clear trend, and those who drank 600 g or more a week were at more than nine times the risk. On the other hand, the effect of duration of drinking habit was less strong (table III). The risk associated with longer duration of drinking habit was not much higher than that due to shorter duration. The two dimensional classification shown in table IV also suggests that it was amount rather than duration which had a stronger effect on risk: there were clear rises in risk within duration categories when amount increased. In contrast, the pattern within amount categories was much less clear. Although there seems to be an interaction between the two variables, it was not significant on testing.

Table V shows the risks associated with drinking status. There was significant increase in risk among current drinkers. Former drinkers were at a similar overall risk to current drinkers. The picture becomes more clear when the effect on risk of time since stopping among former drinkers is examined (table VI). The results show that apart from an increased risk among those who recently stopped, there was a clear decrease in risk with longer periods of abstinence. To further examine the effect of stopping we looked at the changes in risk after quitting in different categories of amount consumed a week (table VII). In current drinkers and those who stopped within the past 10 years, there was a dose-response relation between amount used and risk. Among current drinkers who used less than 200 g a week, there was no significant.
increase in risk compared with never drinkers, although those who stopped recently were at a higher risk. In the other two amount categories, risk clearly fell with time after stopping. The rate of decline was greater among the moderate (200 to 599 g a week) than heavy (600 or more a week) drinkers. The risk estimates in table VII were more or less unchanged by adjustment for duration of habit.

**Discussion**

The aetiological role of alcoholic beverages in a number of cancers is well established. On the other hand, few epidemiological studies have looked at the effect of stopping exposure on risk. We were able to identify six such studies. None of them, however, provided information on the rate of change in risk in relation to amount used and duration of habit. The sites examined in these studies included oesophagus, mouth, pharynx, pancreas, and breast. While it is now generally accepted that alcoholic beverages cause cancer in the first three sites, evidence on the role of alcohol in the pancreas and breast is still inconclusive.

Those studies were all case-control in design apart from one cohort study on breast cancer. In Puerto Rico, Martinez showed a fall in risk of cancers of the oesophagus, mouth, and pharynx after alcoholic beverages had been discontinued for 10 years or more, but the estimates were not adjusted for other risk factors (for example, smoking) reported. Victoria et al reported an adjusted relative risk of 0.78 (90% confidence interval 0.36 to 1.69) of oesophageal cancer after stopping cachaça (a popular alcoholic beverage in southern Brazil) for 10 or more years. No information on the relation with amount consumed or duration of habit was reported. A study on pancreatic cancer in England found a higher risk among former drinkers than current drinkers and attributed this to stopping of habit after the development of symptoms. In the three studies on breast cancer, there was suggestion of a lower risk among former drinkers, but no further details were given.

Therefore, it seems from the literature review that the present study may be able to provide some insight into a topic not previously dealt with.

We have shown that whereas the risk of oesophageal cancer among former drinkers as a group was similar to that in those who continued to drink (table V); a fall in risk with time after stopping was found on more detailed analysis. Thus the group of former drinkers was not homogeneous with respect to risk. As duration of drinking habit was found to be less important in determining risk than average amount of consumption, we examined the change in risk on drinking cessation in relation to average consumption. The results show that risk tended to drop more quickly among moderate than heavy drinkers. Even among heavy drinkers, however, the risk had fallen substantially after five to nine years of not drinking. Although some risk estimates shown in table VII had wide confidence intervals because of small numbers, the general pattern suggests that among moderate drinkers it would take 10-14 years for risk to return to that in subjects who never drink. For heavy drinkers, it is likely to require 15 years or more, if it reduces at all.

The results in table VII on the effect of time since stopping, stratified by weekly intake, classify the data into 18 categories. This leads to sparse data and hence to a degree of instability in some categories. This might be avoided by more parsimonious modelling—for example, estimating parametric relation between the actual numerical values for years since stopping and weekly consumption and risk. The drawback in this case would be that this would necessitate curvilinear models and possibly multiplicative terms between the two explanatory variables, giving rise to problems of modelling and interpretation.

We found an increase in risk among recent abstainers. This was probably because of subjects who stopped drinking after diagnosis or developing symptoms. This result is similar to findings in prospective and case-control studies on stopping smoking and risk of lung cancer. The retrospective design of a case-control study gives the opportunity to assess temporal hypotheses in relation to reported history over the period of interest before diagnosis (or recruitment of control subjects), in contrast with cohort studies, in which the status at only one fixed baseline time point (or at a small number of fixed points) is known. Problems of recall and sampling, however, are potential sources of bias. The close age matching, good response rates, and similar results from the two groups of controls indicated that our results were reliable.

All results presented in this paper were adjusted for average amount smoked a day and smoking status (current smokers, former smokers by years since stopping, and never smokers). An attempt was made to examine the effect of changes in smoking habit by amount smoked in the same fashion as changes in drinking shown in table VII. This failed, however, because of sparseness of data. On the other hand, we did not have information on recent changes in dietary habits. Drinkers who stopped may also have acquired a more healthy diet, although our finding that adjustment for dietary intake did not make substantial differences to the risks associated with drinking (data not shown) does provide some indirect evidence against it. The question will remain an open one until detailed longitudinal data on both dietary and drinking habits are available in a cohort study. Also changes in certain other aspects of lifestyle not examined in our study might have an effect. This is unlikely to be very important as the combined attributable risk due to alcohol, tobacco, and diet was almost 90% in the study population.

**CONCLUSIONS**

Results from our study are of clear importance in health promotion. Alcohol drinking is a major risk factor for oesophageal cancer, which has a poor prognosis. While drinking less than the equivalent of 200 g of ethanol a week was not found to be associated with a higher chance of developing the condition, risk increases as intake goes up, with a more than 11-fold risk among current heavy drinkers. For this group the fairly rapid reduction of an extremely high risk could

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**Key messages**

- Alcohol is a major cause of oesophageal cancer but little is known about the effect of stopping drinking on risk.
- Current light drinking (<200 g ethanol a week) was not associated with significant increase in risk.
- Among former drinkers, risk had dropped substantially after five to nine years of cessation.
- The time taken for risk to return to that of people who never drink was 10-14 years for moderate drinkers (200-599 g a week) and 15 years or more, if ever, for heavy drinkers (>600 g a week).
- This new finding could be used in health promotion to encourage behavioural changes. It suggests that alcoholic beverages have a strong effect on the late stage of carcinogenesis.
encourage change. Although it is difficult to be certain how long it will take for risk to return completely, if at all, to baseline after stopping, the benefits of a substantial fall in risk after a mere five to nine years could provide a useful incentive for behavioural change. We have not directly studied the effect of reducing intake rather than total cessation, but results on the relation between amount and risk indicate that there is probably a decrease in risk on cutting down drinking as well.

In comparison with epidemiological studies, animal investigations have been less conclusive on the carcinogenicity of alcoholic beverages, and alcohol per se does not seem to be carcinogenic. Furthermore, how alcoholic drinks cause cancer in the upper aerodigestive tract is still uncertain, although hypotheses have been put forward. The possibilities include action as solvents for other carcinogens, irritation of mucosa increasing cell turnover, nutritional deficiencies, depression of immune state, presence of other carcinoogens in beverages, and carcinogenicity of metabolites of ethanol. The hitherto absence of information on the effect of drinking cessation has hindered the understanding of this issue. Our present finding of a rapid fall in risk on cessation among moderate drinkers indicates that the predominant action is likely to be on the late stage of carcinogenesis. In heavy drinkers the large fall in risk after less than 10 years of cessation also indicates a strong effect of alcohol on the late stage of carcinogenesis, although one cannot be certain how long it will take for risk to return completely to that in those who never drink. These findings should be helpful in determining the relative importance of the possible carcinogenetic mechanisms and in the design and interpretation of further laboratory and epidemiological studies to elucidate the issue.

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Repeated oral vitamin K prophylaxis in West Germany: acceptance and efficacy

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Owing to concern that neonatal vitamin K prophylaxis might cause childhood cancer,1 parenteral vitamin K prophylaxis for all newborn infants has been abandoned in the United Kingdom2 and Germany.3 In its place three oral doses of vitamin K (0·5 mg in the United Kingdom, 1 mg in Germany) are now recommended for healthy neonates (at birth and during days 4-10 and weeks 4-6). We investigated whether these recommendations are being followed and whether three oral doses of vitamin K are as effective as parenteral vitamin K for preventing late haemorrhagic disease of the newborn.

Methods and results

We drew a random sample of 100 obstetric units from all 995 such units in West Germany. In August 1993 we sent questionnaires to the consultants in charge of these 100 units asking about their use of vitamin K prophylaxis.

Surveillance for late haemorrhagic disease was carried out by sending monthly postcards to heads of all paediatric hospitals in Germany.4 The average response rate during the observation period (West Germany) was 81%. Data from the postcards were validated by questionnaires. All cases of unexpected bleeding from severe, proved vitamin K deficiency in weeks 2-26 observed in West Germany from April 1993 to March 1994 were included in the case definition.

Ninety eight of the 102 questionnaires were returned (one unit was closed, one consultant refused to collaborate). Of these 98 units, 92 gave oral vitamin K (1 mg) twice to all healthy newborn infants in the first week of life as recommended. In 18 units intramuscular vitamin K was given for “at risk” conditions—for example, to infants delivered surgically. In 84 responding units the parents were alerted to the need for a third oral dose of vitamin K (three or more times in 45 units, twice in 27, and once in 12).

Twenty infants met the case definition for late haemorrhagic disease of the newborn (table), of whom 10 had intracranial haemorrhage. Fifteen infants had been breast fed exclusively. In five cases no additional diagnosis was known before and none was detected after the bleeding. Six infants had known conditions for which additional vitamin K prophylaxis was not generally recommended. In one of these additional mild cholestasis was found at bleeding, and one died before tests for cholestasis could be performed. In nine cases cholestasis (which remained “idiopathic” in four) was diagnosed after the bleeding.

Of the 20 infants who met the case definition, two had not received any vitamin K prophylaxis. Thirteen infants had received vitamin K according to the recommendations, but in five cases the third required dose had been overlooked. The time between the last dose of vitamin K and the occurrence of bleeding ranged between eight and 98 (median 28) days. The information about vitamin K prophylaxis was obtained from the well baby check up book (15 cases) or hospital delivery records (first two doses) plus parents’ recall of the third dose given by the paediatrician at the well baby check up at weeks 4-6 (four cases).

Conclusions

Acceptance of the new recommendations for vitamin K prophylaxis was high in German obstetric units,