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Alcohol, tobacco and breast cancer: should alcohol be condemned and tobacco acquitted?

The first published report of an association between alcohol consumption and breast cancer risk was by Williams and Horm (1977). This investigation was hypothesis-generating, however, in that it examined multiple potential risk factors for several cancers and, apart from age, ethnic group and smoking habits, no account was taken of other potential confounding variables. A possible association between breast cancer and tobacco smoking was first proposed by Macmahon et al (1982). They hypothesised that cigarette smoking would reduce the risk of breast cancer, mainly on the basis of their observation that smoking was associated with a reduction in urinary oestrogen levels during the luteal phase of the menstrual cycle. However, Hiatt and Fireman (1986) proposed a contrary hypothesis. They postulated that tobacco smoke would have a direct carcinogenic effect as mutagens from cigarette smoke had been found in the breast fluid of non-lactating women.

Since these initial reports, a substantial number of epidemiological investigations have assessed these hypotheses. The overall evidence from the epidemiological data published so far seems to indicate that alcohol intake may be associated with a slight increase in the risk of breast cancer. By contrast, the evidence for smoking has been rather inconsistent, with some studies showing a slight increase in risk and others reporting no association or, even, a protective effect. Most of these studies have been based on relatively small numbers of breast cancer cases, however, thus yielding rather imprecise estimates of the true effects of these exposures. In addition many of them were unable to take account of the fact that alcohol and tobacco consumption are correlated, as smokers are more likely to drink alcohol than non-smokers.

Clarification of the independent effects, if any, of these exposures on the risk of breast cancer is of epidemiological relevance for various reasons. First, for populations where the prevalence of alcohol and/or tobacco consumption is high, even if the relative risk associated with these exposures is small, the effect of these exposures could still account for a substantial number of breast cancer cases. Second, unlike most of the known risk factors for breast cancer, alcohol and tobacco consumption are potentially modifiable behaviours and hence offer some scope for prevention. Third, clarification of the aetiological role of these exposures might yield light on the biology of breast cancer.

In this issue, the Collaborative Group on Hormonal Factors in Breast Cancer (2002) has published a reanalysis of individual data from over 80% of the worldwide epidemiological information on alcohol, tobacco and breast cancer risk in women. This reanalysis of data from 53 different studies, which included 58,515 women with breast cancer and 95,067 without, showed that the relative risk of breast cancer increased by 7.1% for each additional 10 g day$^{-1}$ intake of alcohol, i.e. for each extra unit (alcoholic drink) consumed on a daily basis. Relative to women who reported drinking no alcohol, the risk of developing breast cancer was 32% higher among those who reported drinking 35–44 g day$^{-1}$ and 46% higher among those who reported consuming 45 g day$^{-1}$ or more (average 57 g day$^{-1}$). The effect of alcohol was not found to be confounded by smoking or by any other known risk factor for breast cancer. The authors estimated that in developed countries the cumulative incidence of breast cancer by age 80 would be 8.8 per 100 women in non-drinkers and 9.4, 10.1, 10.8, 11.6, 12.4 and 13.3, respectively, per 100 women among women consuming an average of 1, 2, 3, 4, 5 and 6 alcoholic drinks each day. By contrast, the relationship between smoking and breast cancer was substantially confounded by the effect of alcohol and when the analysis was restricted to non-drinkers, no association was found between smoking and breast cancer.

So, can we now finally pass judgement on the alcohol- and tobacco-breast cancer hypotheses and lay them to rest? Unfortunately, the answer is not yet. As acknowledged by the authors the quality and validity of their exposure data were, to a certain extent, limited, as most of the individual studies were not set up with the primary purpose of addressing these hypotheses. Despite this caveat, the results strongly argue against an association between smoking and breast cancer but are in favour of a true positive association between alcohol and this tumour. Given the impossibility of conducting a randomised trial on this issue a causal relation between alcohol and breast cancer can never be established beyond any doubt, but the evidence provided by this reanalysis of practically all the available worldwide data, and the consistency of the findings across the various studies, strongly suggest that something is going on. As the relative risks involved are modest, it could be argued that the observed relationship between alcohol and breast cancer might be due to confounding by unknown risk factors, but it is hard to envisage an as yet unknown risk factor, which is consistently associated with alcohol intake in the relatively diverse populations studied.

Even if causal, the exact relationship with duration, timing, or indeed amount, of alcohol intake remains unclear. Self-reported information on alcohol consumption is known to be prone to measurement error and it is uncertain to what extent this might...
REFERENCES


