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Alcohol Consumption and Breast Cancer... Is there a link?

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In 1993, breast cancer was diagnosed in 182,000 U.S. women and caused the death of 46,000 U.S. women.¹ Breast cancer incidence in the United States has continuously risen throughout the past several decades. According to statistics from the National Cancer Institute, incidence rates rose by 24% between 1973 and 1991.² Research has shown that some of the rise in breast cancer incidence is due to an increase in mammography use during the mid-1980's, however, this alone does not explain the continuous rise in incidence.³ It is likely that gradual increases in the prevalence of lifestyle risk factors for breast cancer also account for the rise in incidence.

Established risk factors for breast cancer include family history of breast cancer, nulliparity, later age at first birth, and higher socioeconomic status. These four risk factors combined are thought to account for approximately 40% of U.S. breast cancer cases.⁴ In addition, early menarche, cumulative exposure to exogenous and endogenous estrogen, central or abdominal obesity, and increased alcohol consumption, have also been implicated as possible risk factors. To what extent these additional risk factors contribute to breast cancer incidence is not clear.

With the exception of alcohol consumption, the majority of these risk factors can not be easily modified. According to the National Center for Health Statistics, 60.7% of women 18 years of age reported being "current drinkers." Of these, 39.4% were considered light (up to three drinks per week); 27.4% were considered moderate (4-13 drinks per week); and 9.1% were considered heavy drinkers (14 or more drinks per week).⁵ The fact that alcohol consumption is so common suggests that if it could be causally related to breast cancer development, then alterations of drinking patterns might be able to influence the morbidity and mortality stemming from this disease.

The History of Alcohol as A Risk Factor for Breast Cancer

The first evidence that a link between alcohol and breast cancer might exist came in 1977 from a large case-control study. The study compared 600 breast cancer patients to patients with other cancers thought not to be linked to alcohol and found that after adjusting for age, smoking and education level, women drinking more than 51 ounce-years (defined as the number of ounces of ethanol consumed per week multiplied by the number of years of consumption) had a relative risk of developing breast cancer of 1.55.⁶ Little attention was given to these findings until 1982, when a second large case-control study of 1152 patients with breast cancer and 519 control subjects with ovarian and endometrial cancer and 2702 nonmalignant control patients was carried out. The study found that women who drank four or more drinks per week had a breast cancer relative risk of 2.0 compared to malignant control subjects and 2.5 compared to nonmalignant control subjects. Moreover, the study found an increased breast cancer risk in light drinkers who consumed less than four drinks per week of 1.5 and 1.9 compared to malignant and nonmalignant control subjects respectively. This study set of intense research on the possibility of a causal relationship between alcohol consumption and breast cancer and since then more than 50 epidemiological studies of alcohol and breast cancer have appeared.⁷

The majority of epidemiological studies investigating the relationship between alcohol and breast cancer have indicated an increased risk of breast cancer. However, this increased risk has generally been subtle and results have varied widely. A review of eighteen case controlled studies deemed to be informative based on their size and efforts to control for the major reproductive and dietary risk factors found that twelve of the studies showed positive associations between alcohol and breast cancer, four showed no association between alcohol and breast cancer, and one study suggested an inverse relationship between alcohol consumption and breast cancer. In 1994 Longenecker and colleagues performed a metaanalysis of 28 case-control and 10 cohort studies. Their results indicated a dose-response association between the amount of alcohol consumed and the relative risk for breast cancer. On average the breast cancer risks associated with alcohol consumption were small. Women who consumed one drink of alcohol per day (13 g of ethanol) had a 1.14 breast cancer risk relative to non-drinkers, while women who consumed three drinks per day (39 g of ethanol) had a 1.37 breast cancer risk relative to non-drinkers.

Although the relative risks reported have been small this does not make them insignificant. Most studies have been careful to adjust for other known risk factors (confounding factors), such as socioeconomic status and diet, which could appear to be making alcohol the culprit when it is really not. Because epidemiological studies are often based on alcohol questionnaires there was some concern with regards to the accuracy of these questionnaires in accessing alcohol consumption. Studies performed to determine the accuracy of these questionnaires have found that although substantial underreporting of heavy drinking does occur, moderate and lesser levels of alcohol consumption carry very little error.⁸ Considering the fact that few confounding factors are believed to be present in the epidemiological studies and that the methods of reporting alcohol consumption appear to be fairly accurate, the presence of a "small" increased risk of breast cancer with alcohol consumption could suggest a causal relationship. Because alcohol consumption is so common, this small increased risk could be of public health significance.

Modification of the Link between Alcohol and Breast Cancer

Several studies have looked at the link between alcohol and breast cancer with respect to other factors and many interesting results have emerged.

Does the type of alcohol consumed matter?

One recent study found that postmenopausal women who consumed wine had a decreased breast cancer risk.⁹ Other studies have found that wine consumption had no effect on breast cancer risk.^{10, 11, 12} However, several investigations have showed that wine did increase breast cancer risk.^{13, 14} It is possible that wine could have a different effect on mammary tissue than beer and spirits because some wine contains phenolic compounds that may have antioxidant activity.¹⁵ In addition, some investigations have suggested that beer and spirits may contain substances with estrogenic activity which

could directly effect mammary tissue.¹⁶ More research needs to be done before beverage-specific associations can be made.

Is consumption at an early age (as opposed to recent/ current intake) associated with risk?

Many studies have tried to determine whether women who drink in early life are at greater risk for developing breast cancer than women who drink in later life. Several early studies suggested that alcohol consumption before age 30 was more strongly associated with breast cancer risk than recent consumption.⁷ This led to the speculation that there might be some period of biologic vulnerability earlier in life. More recent studies have not supported this speculation and point to a cumulative effect of alcohol rather than an age dependent effect.¹⁰

Are the risks greater for premenopausal or postmenopausal women?

Studies of the effects of menopausal status on the link between alcohol consumption and breast cancer have yielded mixed results. Approximately the same numbers of studies have found the link to be stronger in premenopausal women as have found the link to be stronger in postmenopausal women. In general, studies of premenopausal women with breast cancer have been difficult because of the relatively small number of cases.

Are alcohol related risks greater for women who are taking exogenous estrogen?

Recent studies have found that the alcohol-breast cancer link may be stronger in women who have taken or are taking exogenous estrogen.^{17, 18} One study of postmenopausal women using estrogen based hormone replacement therapy found that acute alcohol ingestion caused a 327% increase in the levels of circulating estradiol while only a minimal increase was observed with ingestion of an equivalent carbohydrate drink. Although further research is needed to confirm these results, the fact that the levels of estradiol in this study were dramatically higher than the targeted levels for hormone replacement therapy suggests that it is important to consider potential health risks, such as breast cancer, when placing women who consume alcohol on hormone replacement therapy.

Pathophysiological Evidence of a link between Alcohol and Breast Cancer

Up to this point the majority of the evidence suggesting an association between alcohol and breast cancer has been from epidemiological studies. Pathophysiological evidence of a link between alcohol and breast cancer would greatly substantiate this association. It has been suggested that alcohol might influence breast cancer risk by effecting pituitary prolactin secretion¹⁹ or by affecting the integrity of the plasma membranes of breast tissue cells and allowing for transport of carcinogens to breast tissue.²⁰ However, the mechanism which has been supported by the most evidence is the possibility that alcohol may increase hormonal levels of estrogen or other reproductive steroid hormones which have a commonly accepted role in the breast.²¹

Do hormones link alcohol to breast cancer?

As I discussed above, alcohol has been shown to increase levels of exogenous estrogen in women taking hormone replacement therapy. A recent study looked at the levels of plasma and urinary hormones in premenopausal women. The study found evidence that peri-ovulatory plasma estradiol levels were increased by 27.5% and urinary estradiol levels were increased by 31.9% when the women consumed 2 drinks of alcohol per night as compared to when they consumed no alcohol.²² The "alcohol induced" increase in estrogen level observed in this study suggests a possible mechanism for alcohol related breast cancer risk which warrants further investigation.

Animal Studies

Six studies on alcohol induced mammary carcinogenesis in rodents have been conducted. Of the six studies only one showed an increase in mammary tumors in animals receiving alcohol. According to an analysis by Longnecker et al.⁷ at least two of the studies which showed no result were flawed because the alcohol-treated animals weighed less than the control animals. In another of the null experiments the control animals had a very high rate of mammary tumors and this may have obscured the results. Although more evidence is needed to confirm a pathophysiological basis for breast cancer, the existence of one study which shows that alcohol leads to mammary tumors in rats suggests that alcohol could lead to breast cancer in women.

Conclusion

The majority of epidemiological studies have shown a small increase in relative risk of breast cancer from alcohol consumption. Furthermore, this increase in breast cancer risk has shown to grow with greater alcohol consumption. Recent studies have shown that alcohol increases estradiol levels in both premenopausal and postmenopausal women suggesting a plausible mechanism by which alcohol might promote breast cancer. In addition, one study in rats has shown that alcohol augments mammary carcinogenesis, giving further support to the hypothesis that alcohol may promote breast cancer. Although further research is necessary to explain the variation between epidemiological studies observed and determine what other risk factors for breast cancer might be modified by alcohol consumption, women with other risk factors for breast cancer may want to consider consuming less alcohol. Of course, in making this decision it is important that they consider other factors such as the evidence that suggests that cardiovascular disease is negatively associated with moderate wine consumption.

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