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CONCISE REPORT

The effect of moderate alcohol consumption on bone mineral density: a study of female twins

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Background: Osteoporosis is associated with morbidity and mortality, particularly in postmenopausal women. The effect of moderate alcohol intake on bone mineral density (BMD) and fracture risk remains unclear.

Objective: To carry out a twin study to investigate this effect while controlling for genetic effects and other confounding variables.

Methods: BMD was determined at the hip and lumbar spine in 46 pairs of monozygotic twins discordant for alcohol consumption. Biochemical evidence of altered bone metabolism was sought.

Results: A positive association between alcohol consumption and BMD was shown, in contrast to the negative effect of smoking on BMD. Markers of bone turnover were not associated with alcohol or BMD.

Conclusions: Moderate alcohol consumption is not harmful to bone health in women and may even be beneficial. Beneficial effects do not appear to be mediated through an action on bone metabolism.

The effect of moderate alcohol consumption on bone mineral density (BMD) and fracture risk remains unclear despite a growing number of epidemiological studies.^{1–3} BMD is known to be influenced by age, sex, menopausal status, and smoking habits, and population samples differing in these variables may in part account for the discrepant results. Many published studies were not specifically designed to investigate alcohol consumption but were part of a broad lifestyle assessment. Differing methods of quantifying alcohol intake have been used. Furthermore, most studies fail to address possible biological mechanisms to account for an association between alcohol consumption and BMD. Alterations in markers of bone turnover,⁴ for example, indicate whether alcohol primarily influences bone formation or bone resorption. In developed countries, osteoporosis and fractures are associated with considerable morbidity and mortality in postmenopausal women. The use of alcohol is widespread and is thought to be increasing among women. It is of public health importance, therefore, to determine what level of alcohol intake should be recommended for optimal bone health.

Many of the limitations associated with conventional epidemiological studies may be overcome by the study of monozygotic twins. Such twins are uniquely matched for age, sex, and genetic factors, all of which are known to influence both BMD and the propensity to consume alcohol. In addition, the study of monozygotic twins enables a powerful study to be conducted using a relatively small sample. We carried out a study specifically to investigate the effect of alcohol consumption on BMD and bone metabolism, using monozygotic twin pairs who were discordant for alcohol consumption. In this co-twin control study, BMD was

determined at the hip and lumbar spine. Evidence of an effect of alcohol on bone metabolism was sought using markers of bone turnover measured in serum and urine. The difference in BMD between alcohol discordant monozygotic pairs reveals the influence of alcohol intake on BMD while controlling for the important confounding variables of age, sex, and genetic factors.

METHODS

Questionnaires were sent to 1358 monozygotic female twin pairs registered with the St Thomas' UK adult twin registry.⁵ Ethical approval had been obtained and these well studied twin volunteers gave informed consent but were unaware of the precise question being addressed by the study. Demographic data were collected as well as various health and lifestyle details, including detailed information about alcohol intake over the last 12 months and current smoking status. Of those mailed, 911 pairs returned the questionnaires. Questionnaire frequencies of recalled intake of beer, wine, fortified wine, and spirits were converted into units of alcohol per week (with one unit equal to half a pint of beer, one glass of wine, or one measure of spirits). Forty six monozygotic pairs identified as discordant for alcohol consumption, with one twin drinking minimal alcohol (≤ 1 unit/week) and the other drinking more (>1 unit/week), were recruited to the study. BMD at hip and lumbar spine was determined in both twins in a twin pair on the same day, using a Hologic QDR 4500 DXA scanner. Evidence of altered bone metabolism was sought using fasting morning serum and urinary bone turnover markers (osteocalcin and bone specific alkaline phosphatase for bone formation; urinary C terminal cross links (CTX) as a measure of bone resorption).

RESULTS

The "minimal drinkers" consumed (mean (SD)) 0.2 (0.4) units/week, range 0 to 1, while the "drinkers" consumed 8.0 (7.8) units/week, range 2 to 28. There were no significant differences between the "minimal drinkers" and "drinkers" in height (162.4 v 162.9 cm, respectively, $p = 0.23$), weight (68.7 v 67.3 kg, $p = 0.19$), proportion who smoked (11.6% v 21.7%, $p = 0.07$) or were ex-smokers (28.0% v 37.0%, $p = 0.15$), and the proportion who were postmenopausal (60.0% v 62.2% $p = 0.56$) or using hormone replacement therapy (HRT) (26.1% v 23.9%, $p = 0.65$). None of the twins had taken a bisphosphonate. Alcohol consumption and BMD data were available for all 92 twins, and smoking data for 89. Bone marker data were available for osteocalcin in 72 twins, alkaline phosphatase in 63, and CTX in 59.

The mean (SD) BMD values in the drinkers and minimal drinkers were, for total hip, 0.982 (0.116) and 0.964 (0.104)

Abbreviations: BMD, bone mineral density; CTX, C terminal cross links; DXA, dual energy x ray absorptiometry; HRT, hormone replacement therapy

Table 1 Regression coefficients (95% confidence intervals) of the intrapair differences in bone mineral density and alcohol consumption

Site	Unadjusted			Adjusted		
	β^*	95% CI	p Value	β^*	95% CI	p Value
Total spine	0.21	-0.02 to 0.44	0.08	0.33	0.14 to 0.53	<0.01
Total hip	0.21	0.01 to 0.41	0.04	0.24	0.04 to 0.44	0.02
Hip neck	0.18	-0.03 to 0.4	0.1	0.19	-0.05 to 0.42	0.11
Trochanter	0.002	0.00 to 0.004	0.05	0.24	-0.03 to 0.51	0.08
Intertrochanteric	0.25	0.04 to 0.46	0.02	0.29	0.08 to 0.50	0.01
Ward's triangle	0.31	0.01 to 0.62	0.04	0.32	-0.02 to 0.67	0.065

Intrapair differences in BMD were calculated as a percentage of the mean BMD and intrapair differences in alcohol expressed as units per week. Significant p values (<0.05) are shown in bold.

*Regression coefficient.

BMD, bone mineral density; CI, confidence interval.

g/cm², and for total spine, 1.020 (0.160) and 1.011 (0.168) g/cm², respectively. To take into account the pairing of the twins, intrapair differences in variables were examined. Associations between the variables were explored using regression analysis of these intrapair differences (STATA software).

Table 1 shows the regression coefficients (with 95% confidence intervals) of the intrapair differences in BMD and alcohol consumption. This analysis was carried out both unadjusted and adjusted for past and present smoking, body mass index, and current use of HRT. Alcohol consumption was found to be positively associated with BMD at the lumbar spine and sites at the hip reflecting both cortical and trabecular bone. There was no clear association between any of the bone markers and BMD or alcohol consumption (data not shown).

DISCUSSION

We used matched, exposure discordant identical twins specifically to look at the effects of alcohol on bone in women. This type of study is unique among epidemiological designs in its ability to control for multiple confounding variables. Identifying the alcohol discordant pairs in which one twin drank minimal alcohol was a major undertaking and was not conducted post hoc. There are, of course, limitations to such a cross sectional study and a clinical end point such as fracture would have been preferable, although extremely impractical to achieve. Questionnaire data on alcohol consumption may be influenced by recall bias but within a twin pair this is unlikely to have a significant effect. We are aware of no other published twin studies addressing the influence of alcohol on BMD.

This study confirms that consumption of moderate alcohol by women is not deleterious to bone health, and may even be beneficial. Clearly we cannot extrapolate to higher levels of consumption: only three subjects drank in excess of the UK current recommended limit for women (21 U/week). Even so, mean BMD across the sites of these three subjects was greater than the mean of the rest of the sample. Smoking is a major confounding variable in studies examining the effect of alcohol. There is good evidence that smoking has a negative effect on BMD,^{3,6} and this finding was reproduced in our study (data not shown). Bone marker data were incomplete, but no association was shown between bone markers and BMD or alcohol. This suggests that moderate alcohol exerts its positive effects on the BMD of different types of bone through mechanisms other than bone formation/resorption. Mechanisms by which alcohol might act include its reported oestrogenic effects⁷ (although this acts in part through bone turnover) and influence on the microarchitecture of bone,

which is increasingly recognised as an important determinant of bone strength.⁸

There remains much controversy over the importance of moderate alcohol exposure as a risk factor for osteoporosis. This study has controlled for important confounders such as smoking and lends weight to the growing evidence that moderate alcohol consumption is not detrimental to bone health in women. We think it unlikely that the benefits to BMD would be offset by an increased risk of falls at this moderate level of alcohol consumption. Indeed, in keeping with our results a reduction in hip fracture risk in drinking women has been shown in a large case-control study.⁹ The results presented here have a clear message for public health as well as for practising clinicians advising and managing patients at risk of osteoporosis.

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Authors' affiliations

F M K Williams, L F Cherkas, T D Spector, A J MacGregor, Department of Twin Research and Genetic Epidemiology Unit, St Thomas' Hospital, London SE1, UK

Correspondence to: Dr Frances M K Williams, Department of Twin Research and Genetic Epidemiology Unit, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH, United Kingdom; frances.williams@gstt.nhs.uk

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