DO LIPIDS CONTRIBUTE TO THE LACK OF CARDIO-PROTECTIVE EFFECT OF BINGE DRINKING: ALCOHOL CONSUMPTION AND LIPIDS IN THREE EASTERN EUROPEAN COUNTRIES

ANNE PEASEY*, MARTIN BOBAK, SOFIA MALYUTINA1, ANDRZEJ PAJAK2, RUZENA KUBINOVA3, HYNEK PIKHART, SVETLANA KURILOVITCH1, RUDOLF POLEDNE4 and MICHAEL MARMOT

International Centre for Health and Society, Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 6BT UK, 1Institute of Internal Medicine, Novosibirsk, Russia, 2Jagiellonian University, Krakow, Poland, 3National Institute of Public Health, Prague, Czech Republic and 4Institute of Clinical and Experimental Medicine, Prague, Czech Republic

(Received 11 November 2004; first review notified 16 February 2005; in revised form and accepted 16 March 2005; advance access publication 6 June 2005)

Abstract — Aims: The cardio-protective effect of moderate alcohol consumption is partly mediated by HDL cholesterol. However, epidemiological studies suggest that binge drinking may not be associated with reduced risk of heart disease; a possible explanation is that the relationship of blood lipids with binge drinking is different from that with moderate intake. We investigated this hypothesis in a population study in three eastern European countries. Methods: We conducted a cross-sectional study in random population samples in Novosibirsk (Russia), Krakow (Poland) and Karvina (Czech Republic). A sub-sample of 282 men aged 45–64 years who provided a fasting blood sample were analysed. Annual alcohol intake and the frequency of heavy binge drinking (>140 g of ethanol per session) were estimated from a graduated frequency questionnaire. Results: Annual intake of alcohol was positively associated with total and HDL cholesterol. After controlling for annual intake, the frequency of heavy binge drinking was associated with increased concentrations of total and HDL cholesterol. By combining annual intake and drinking pattern, we found that men consuming >81 l of alcohol per year who had a heavy binge at least once a month had the mean total, HDL and LDL cholesterol 1.69 (SE 0.35), 0.61 (0.11) and 0.97 (0.34) mmol/l, respectively, higher than non-drinkers; this resulted in more favourable ratios of total and LDL cholesterol relative to HDL cholesterol in frequent heavy bingers. Conclusions: Blood lipids do not seem to explain the apparent lack of the cardio-protective effect of binge drinking reported in epidemiological studies.

INTRODUCTION

Moderate alcohol drinkers have a lower risk of coronary heart disease than abstainers (Corrao et al., 2000; Rehm et al., 2003b). The cardio-protective effect of alcohol is partly mediated by blood lipids, because moderate alcohol intake is associated with several biochemical parameters, including increase in HDL cholesterol (HDL-C) and reduction in blood coagulation (Rimm et al., 1999).

However, in addition to average volume of alcohol intake, there is a growing interest in the effects of pattern of drinking on coronary heart disease (Rehm et al., 1996). Several studies indicated that binge drinking is not associated with a reduced risk of cardiovascular disease and that it may, in fact, increase the risk of cardiac death or stroke (Kauhanen et al., 1997; Mazzaglia et al., 2001; Murray et al., 2002; Rehm et al., 2003a). These studies raise questions about the effect of binge drinking on lipids; it has been suggested that, contrary to regular moderate drinking, binge drinking is associated with an unfavourable lipid profile (McKee and Britton, 1998). So far, however, the evidence on binge drinking and blood lipid concentrations is sparse and inconsistent (Puddye et al., 1999).

The aim of this paper is to contribute to the understanding of the biological effects of binge drinking. To do so, we examined the association between average drinking volume, binge drinking behaviour and lipid profile in population samples from the Czech Republic, Poland and the Russian Federation.

SUBJECTS AND METHODS

Subjects

The data come from the pilot HAPIEE (Health, Alcohol and Psychosocial factors In Eastern Europe) study, a cross-sectional study of men and women aged 45–64 years in Novosibirsk (Russia), Krakow (Poland) and Karvina-Havírov (Czech Republic). The subjects were randomly selected from local population registers (more details have been described elsewhere; Bobak et al., 2004). The total size of the study was 2466 subjects; a small random subsample of subjects provided a fasting blood sample. This report is based on the 282 men in the subsample; women were excluded because the rates of binge drinking were too low (Bobak et al., 2004) for meaningful analyses.

Measurements

Participants completed a questionnaire and attended a medical examination. Annual alcohol consumption and drinking pattern were estimated from a graduated frequency questionnaire, which assessed the frequency of consuming different amounts of alcohol per day in the past year (Rehm, 1998). For the present analyses, annual alcohol intake was classified into five categories; the following cut-off points were selected to make sure that sufficient numbers of men were in each group: non-drinkers; 1–200; 201–2000; 2001–8000 and >8000 g of ethanol per year. We used two measures of binge drinking. First, (any) binge drinking was defined as consumption of ≥100 g ethanol per occasion; second, heavy binge drinking was defined as consuming ≥140 g ethanol per occasion. The frequency of any or heavy binge drinking in the past year was defined as never, <1 per month, 1–3 per month and ≥1 per week.
Serum samples were analysed centrally in one batch in the WHO Regional Lipid Reference Centre, Institute of Clinical and Experimental Medicine, Prague. Lipid concentrations in serum were measured on a Roche COBAS MIRA auto-analyser, using a conventional enzymatic method with reagents from Boehringer Mannheim Diagnostics and Hoffman-La Roche. LDL cholesterol (LDL-C) was calculated by the Friedewald formula (Friedewald et al., 1972).

Statistical analysis
To investigate the association between lipid concentrations and alcohol drinking patterns, we estimated the differences in the mean concentrations of total, HDL-C and LDL-C and triglycerides (TG), and in the total/HDL-C and LDL-C/HDL-C ratios, between categories of annual alcohol intake binge drinking, using linear regression and controlling for age, country, body mass index (BMI) and smoking status. We initially conducted country-specific analyses; since the associations between blood lipids and alcohol variables were similar between countries, data from all three countries were pooled and were adjusted for country in the analyses. There were some differences in the concentrations of serum lipids between countries; levels of HDL-C were somewhat higher (reflected in a slightly lower total/HDL-C ratio) and concentrations of TG were considerably lower in Russia than in the other two countries. To avoid the problem of different absolute concentrations, subsequent results are reported as differences in concentrations and ratios between categories, rather than adjusted means and ratios, and all analyses are adjusted for country.

In the next step, we first examined the differences in serum lipids by categories of annual intake. Second, we investigated the differences in serum lipids by frequency of drinking (the pattern of results mirrored those for annual intake). Third, we analysed differences in serum lipids by the frequency of any and heavy binge drinking; we have additionally controlled for annual alcohol intake in these analyses. Finally, we analysed the differences in serum lipids between categories of annual intake after stratifying for heavy binge drinking behaviour. Likelihood ratio test P-values for linear trend were presented. All statistical analyses were performed using Stata 6.0.

RESULTS
The characteristics of the sample are shown in Table 1. The proportion of non-drinkers and drinkers was similar in all three countries (not shown in Table). Drinking patterns, however, differed between countries. The volume of alcohol that Czech men reported consuming each year was nearly double that reported by Polish and Russian men. Heavy binge drinking was most frequent among Russians and least common among Poles. Annual alcohol intake and binge drinking were not associated with age, BMI or smoking (not shown in Tables).

The associations between annual alcohol intake and mean concentration of blood lipids are shown in Table 2. There was a suggestion of total cholesterol increasing with alcohol intake but most of this association was owing to an increase in HDL cholesterol. Annual intake of alcohol was not associated with

<table>
<thead>
<tr>
<th>Variable</th>
<th>Russia</th>
<th>Poland</th>
<th>Czech Republic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute number of men</td>
<td>136</td>
<td>56</td>
<td>92</td>
<td>282</td>
</tr>
<tr>
<td>Age (years) mean (SE)</td>
<td>54.7 (0.53)</td>
<td>55.1 (0.76)</td>
<td>55.3 (0.55)</td>
<td>55.0 (0.34)</td>
</tr>
<tr>
<td>BMI (kg/m²) mean (SE)</td>
<td>26.5 (0.004)</td>
<td>27.3 (0.006)</td>
<td>28.2 (0.004)</td>
<td>27.2 (0.003)</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>64 (48)</td>
<td>26 (46)</td>
<td>35 (38)</td>
<td>129 (45)</td>
</tr>
<tr>
<td>Annual alcohol intake, grams of ethanol, mean (SE)</td>
<td>4677 (633)</td>
<td>4113 (1148)</td>
<td>8274 (1207)</td>
<td>5738 (342)</td>
</tr>
<tr>
<td>Binge drinking, ≥100 g of alcohol per occasion at least once a month (%)</td>
<td>36 (26)</td>
<td>4 (7)</td>
<td>15 (16)</td>
<td>55 (19)</td>
</tr>
<tr>
<td>Total cholesterol, mean (SE)</td>
<td>5.83 (0.11)</td>
<td>6.13 (0.12)</td>
<td>5.89 (0.12)</td>
<td>5.91 (0.07)</td>
</tr>
<tr>
<td>HDL cholesterol, mean (SE)</td>
<td>1.22 (0.04)</td>
<td>1.10 (0.03)</td>
<td>1.09 (0.04)</td>
<td>1.15 (0.02)</td>
</tr>
<tr>
<td>LDL cholesterol, mean (SE)</td>
<td>3.96 (0.10)</td>
<td>4.04 (0.11)</td>
<td>3.84 (0.12)</td>
<td>3.94 (0.07)</td>
</tr>
<tr>
<td>Triglycerides, mean (SE)</td>
<td>1.38 (0.06)</td>
<td>2.32 (0.18)</td>
<td>2.50 (0.19)</td>
<td>1.93 (0.08)</td>
</tr>
<tr>
<td>Total:HDL cholesterol ratio (SE)</td>
<td>5.31 (0.17)</td>
<td>5.86 (0.22)</td>
<td>5.89 (0.20)</td>
<td>5.61 (0.11)</td>
</tr>
<tr>
<td>LDL:HDL cholesterol ratio (SE)</td>
<td>3.64 (0.14)</td>
<td>3.88 (0.18)</td>
<td>3.73 (0.15)</td>
<td>3.72 (0.09)</td>
</tr>
</tbody>
</table>

SEs in parentheses; adjusted for age, sex, country, smoking and BMI.

Values shown for ratios are the difference in the ratio from the non-drinking reference group.
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<table>
<thead>
<tr>
<th>Heavy binge drinking</th>
<th>n</th>
<th>Total cholesterol</th>
<th>HDL-C</th>
<th>TG</th>
<th>LDL-C</th>
<th>Total:HDL cholesterol ratio</th>
<th>LDL:HDL cholesterol ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>202</td>
<td>0 (reference)</td>
<td>0 (reference)</td>
<td>0 (reference)</td>
<td>0 (reference)</td>
<td>0 (reference)</td>
<td>0 (reference)</td>
</tr>
<tr>
<td>Less than 1/mth</td>
<td>51</td>
<td>-0.15 (0.20)</td>
<td>0.08 (0.06)</td>
<td>-0.07 (0.23)</td>
<td>-0.22 (0.19)</td>
<td>-0.40 (0.31)</td>
<td>-0.35 (0.26)</td>
</tr>
<tr>
<td>1–3/mth</td>
<td>21</td>
<td>0.38 (0.27)</td>
<td>0.18 (0.08)</td>
<td>-0.38 (0.32)</td>
<td>0.36 (0.26)</td>
<td>-0.42 (0.43)</td>
<td>-0.12 (0.35)</td>
</tr>
<tr>
<td>1+/week</td>
<td>8</td>
<td>1.34 (0.44)</td>
<td>0.53 (0.14)</td>
<td>-0.07 (0.51)</td>
<td>0.81 (0.78)</td>
<td>-0.85 (0.69)</td>
<td>-0.60 (0.56)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td>0.022</td>
<td>&lt;0.0001</td>
<td>0.36</td>
<td>0.13</td>
<td>0.087</td>
<td>0.21</td>
</tr>
</tbody>
</table>

SEs in parentheses; adjusted for age, sex, country, BMI, smoking and annual alcohol intake. Values shown for ratios are the difference in the ratio from the non-bingers reference group.

LDL or TG concentrations, nor with the total/HDL or LDL-C/HDL-C ratios.

We found no association between the frequency of any binge drinking (≥100 g alcohol per session) and lipid concentrations after controlling for annual intake (not shown in Table). However, further analyses indicated that frequent heavy bingeing (≥140 g alcohol per session) was related to lipid concentrations even if annual intake was controlled for (Table 3). The frequency of heavy binge drinking was significantly associated with total and HDL cholesterol, and was marginally associated with a reduced total/HDL-C ratio.

The associations between lipid concentrations, alcohol intake and binge drinking are summarized in Table 4. Since we found no association between any bingeing and lipids, non-bingers and less heavy bingers (100–139 g alcohol per session) were amalgamated; the other group consists of heavy binge drinkers. There were no binge drinkers who consumed <2000 g of ethanol per year, and these cells in the Table are therefore empty. The concentrations of HDL-C and LDL-C were significantly higher among frequent heavy binge drinkers than in non-drinkers, non-bingers or less frequent binge drinkers. As a result, frequent heavy drinkers had total cholesterol 1.7 mmol/l higher than non-drinkers and >1 mmol/l higher than less frequent heavy drinkers or non-bingeing drinkers. Because the increase in HDL concentration in frequent heavy bingers was proportionally higher than the increase in LDL, the ratios of total/HDL-C and LDL/HDL-C were lower (more favourable) in these heavy drinkers than in non-drinkers.

DISCUSSION

In this study of eastern European men, we have assessed the relationship between lipid concentrations and alcohol consumption, in terms of both annual alcohol intake and binge drinking patterns. We found that total and HDL-C increased with annual alcohol intake, and frequent heavy drinking was associated with increased levels of both HDL-C and LDL-C.

Several limitations of this study should be considered. First, the cross-sectional design complicates the assessment of causality. It is likely that the abstainer group contains some former heavy drinkers; if these drinkers had different levels of blood lipids than other abstainers, the difference between drinkers and non-drinkers would be inaccurate. We do have some data on former drinkers in the Russian sample, and we found no significant differences between current non-drinkers and non-drinkers who used to drink 6 years before. However, the sample size was small (57 persons only), and the possibility of reverse causation cannot be entirely excluded.

Second, the size of the study was modest and the numbers of men in the high alcohol intake categories were relatively small. The statistical power of the study was therefore limited and some of the confidence limits around the point estimates are wide, although associations were found.

Third, the inaccuracy with which individuals report drinking could result in an under- or over-estimate of drinking patterns. Graduated frequency measures seem to underestimate alcohol consumption to a lesser extent than the ‘average’ quantity and frequency measures commonly used in epidemiology (Rehm and Gmel, 2003). Self-reported drinking correlated well with the serum GGT concentrations in a subset of the Russian subjects (Malyutina et al., 2002) and with self-reported problem drinking (Bobak et al., 2004). Repeated interviews with a subsample added further support to the reliability of the alcohol measurement. Nevertheless, some misclassification of alcohol intake certainly occurred which, if random, would tend to underestimate the association between drinking and lipids.

Finally, there were differences between the three countries in drinking patterns, serum TG and BMI. The differences between populations, both in the high frequency of binge drinking and in the low levels of triglycerides in Russia, are consistent with other reports (Malyutina et al., 2002; Averina et al., 2003; Bobak et al., 2004). Laboratory bias is unlikely, as all lipid concentrations were determined in a central laboratory using a single methodology. The associations between alcohol and lipids were similar between countries and were not affected by the absolute levels of lipid concentrations, drinking rates or BMI. Inclusion of waist-to-hip ratio, a measure of central adiposity, did not influence the association between alcohol and lipids. This strongly suggests that the pattern of results is not specific or due to one particular country.

The association between overall alcohol intake and the lipid profile has been investigated in many studies (for reviews see, for example: McKee and Britton, 1998; Puddey et al., 1999; Rehm et al., 2003b). The main finding of these studies is that a moderate intake of alcohol is associated with a beneficial effect on the lipid profile, in particular with elevated concentrations of HDL-C (Rimm et al., 1999). Some investigators found a reduction in LDL-C (Nakanishi et al., 2001) while others found an increase in TG levels (Chrysohosou et al., 2003) in moderate drinkers. Our results are consistent with the literature with respect to HDL-C but we did not observe any reduction in LDL-C among non-binge drinkers.
Table 4: Differences in mean concentrations of blood lipids (mmol/l) by annual intake and binge drinking pattern

<table>
<thead>
<tr>
<th>Annual intake (g)</th>
<th>Non-drinkers</th>
<th>Bingers</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (reference)</td>
<td>0 (reference)</td>
<td>0 (reference)</td>
</tr>
<tr>
<td>20–200</td>
<td>0.54 (0.30)</td>
<td>0.48 (0.30) **</td>
</tr>
<tr>
<td>201–2000</td>
<td>0.48 (0.38)</td>
<td>0.46 (0.38) *</td>
</tr>
<tr>
<td>&gt;2000</td>
<td>0.46 (0.27)</td>
<td>0.46 (0.27) *</td>
</tr>
</tbody>
</table>

The numbers give the difference between each category and non-drinkers (reference group); SEs in parentheses; adjusted for age, country, smoking and BMI.

Only recently have drinking patterns been included in the studies of alcohol intake and lipid concentrations (Puddey et al., 1999; Rehm et al., 2003a). So far, the results are inconclusive. Some of the early studies on binge drinking found that binge drinkers had lower HDL-C and higher LDL-C than non-bingers (Gruchow et al., 1982). A study on squirrel monkeys revealed no change in HDL-C and an increase in LDL-C with increased alcohol intake (Hojnacki et al., 1991) but interpolation to humans is not straightforward. An intervention study by Rakic et al. (1998) found an increase in HDL-C and a reduction in LDL-C in binge drinkers and an increase in HDL-C in moderate drinkers. The increase in HDL in both groups of drinkers in our results are consistent with the intervention study; however, we also observed that drinking alcohol was related to an increase in LDL-C in heavy binge drinkers.

It is not clear at what level of binge drinking changes in blood lipids occur. The usual definition of binge drinking is ≥80 g of alcohol in one session but this is an arbitrary cut-off point. It ignores the frequency of bingeing. We found no changes in the lipid profile among drinkers who consumed ≥100 g of ethanol per session at least once per month. In contrast, drinkers consuming ≥140 g of ethanol per session at least once per month had elevated concentrations of HDL and LDL. While elevation of HDL among drinkers is thought to be a consequence of increased hepatic production and secretion of apolipoproteins and lipoproteins (Rimm et al., 1999; Sierksma et al., 2004), the increase in LDL cholesterol in heavy drinking could also be confounded by dietary fat intake (Rumpler et al., 1999; Richter et al., 2004). We assessed this possibility, using data from a food frequency questionnaire, but fat intake was similar in non-binge and binge drinkers. This suggests that confounding by dietary fat was unlikely.

A possible confounder is whether drinking occurred with a meal, since drinking with meals has been associated with a reduction in cardiovascular risk compared with those drinking without food (Trevisan et al., 2004). Unfortunately, in this study we did not assess the relation between dietary and drinking patterns.

The interpretation of our results in terms of cardiovascular risk is not unequivocal. On the one hand, the finding of elevated LDL-C in heavy binge drinkers may help explain reports of increased cardiovascular mortality in heavy or binge drinkers (Kauhanen et al., 1997; Mazzaglia et al., 2001; Murray et al., 2002; Rehm et al., 2003a). In this study, the group of heavy binge drinkers with high annual intake was relatively small, accounting for ~7% of the men. This appears consistent with a cohort study in Russia in which cardiovascular mortality in frequent heavy drinkers was about double of that in moderate drinkers but this group was also relatively small, ~5% of the cohort (Malyutina et al., 2002). On the other hand, the ratios of total and LDL to HDL-C were lower in heavy drinkers. Although the Apo B/Apo A-I ratio may be a more sensitive measure of future cardiac risk than LDL/HDL-C ratio (Yusuf et al., 2004), the total and LDL to HDL-C ratios are well established predictors of cardiovascular risk (Kinosian et al., 1994; Meisnger et al., 2005). On the basis of our data on total, HDL and LDL-C, the results do not indicate a more atherogenic lipid profile in heavy binge drinkers.

In summary, our findings suggest that both HDL and LDL concentrations are affected by heavy binge drinking but the role
of lipids in potentially mediating the relation between binge drinking and cardiovascular disease remains to be clarified.

Acknowledgements — The study was funded by the Wellcome Trust. M.M. is recipient of the UK MRC Research Professorship.

REFERENCES


