Alcohol sensitivity, alcohol use and high-sensitivity C-reactive protein in older Chinese men: The Guangzhou Biobank Cohort Study

Shao Jun Xu [a,b], Chao Qiang Jiang [a], Wei Sen Zhang [a,*], Kar Keung Cheng [c], Catherine Mary Schooling [d], Lin Xu [d], Bin Liu [a], Ya Li Jin [a], Kin Bong Hubert Lam [c], Tai Hing Lam [d]

[a] Molecular Epidemiological Research Centre, Guangzhou No.12 Hospital, Guangzhou, China
[b] Guangzhou Medical University, Guangzhou, China
[c] Unit of Public Health, Epidemiology and Biostatistics, University of Birmingham, UK
[d] School of Public Health, The University of Hong Kong, Hong Kong Special Administrative Region

ARTICLE INFO

ABSTRACT

Compared to other ethnic groups Asians are more likely to be sensitive to alcohol, due to polymorphisms of alcohol-metabolizing enzymes. Although previous studies have found positive association between regular alcohol use and high-sensitivity C-reactive protein (HsCRP), whether this association is modified by alcohol sensitivity has not been clarified. We therefore sought to examined this potential effect modification in a cross-sectional community sample with high prevalence of alcohol sensitivity, using data from 2903 men aged ≥50years recruited during phase 1 of the Guangzhou Biobank Cohort Study. Information on alcohol consumption and sensitivity (facial flushing, palpitation or dizziness after drinking) was obtained by questionnaire and HsCRP was measured by an immunoturbidometric assay. Elevated HsCRP was defined as HsCRP level equal to or higher than 2.81 mg/L(median). Excessive alcohol use was defined as use of ≥210 g ethanol per week. After adjustment for age, educational level, occupation, smoking status, physical activity and history of cardiovascular disease, alcohol use was associated with HsCRP in a dose-response pattern. The risks of elevated HsCRP were higher in those who drank daily (odds ratio (OR) = 1.38 (1.10, 1.72)) or drank excessively (1.57 (1.22, 2.02)), and were even higher in alcohol users with alcohol sensitivity (1.82 (1.24, 2.65) for daily users and 2.34 (1.48, 3.71) for excessive users). Results of this study have showed an important role of alcohol sensitivity in modifying the association between alcohol use and HsCRP level. Reduction of alcohol use should be an important public heath target, particularly among populations with high prevalence of alcohol sensitivity.

© 2016 Elsevier Inc. All rights reserved.

1. Introduction

Animal and epidemiological studies have suggested an association between chronic alcohol use and atherosclerosis and cardiovascular mortality(Romelsjo, Allebeck, Andreasson, & Leifman, 2012; Shirpoor, Salami, Khadem-Ansari, Heshmatian, & Ilkhanizadeh, 2012; Tang et al., 2013), but the underlying mechanism has not been fully elucidated. Previous research has focused on lipids and genetic factors, purported to be potential mediators of the vascular

effects of alcohol(Brinton, 2010; Yao et al., 2011). However, accumulating evidence suggests alcohol may modify other factors through complex pathways that remain to be clarified (Brinton, 2010; Mukamal et al., 2001); as such alternative mechanisms of alcohol on atherogenesis may exist.

High-sensitivity C-reactive protein (HsCRP) is a marker of systemic inflammation and a predictor of cardiovascular risk (Cushman et al., 2009; Kaptoge et al., 2012; Otsuka, Kawada, Katsumata, Ibuki, & Kusama, 2008). Population-base studies have shown an association between alcohol use and HsCRP(Albert, Glynn, & Ridker, 2003), but the shape of the relationship remains inconclusive, with some earlier studies showing a J-shaped association between alcohol use and HsCRP(Imhof et al., 2001; Stewart, Mainous, & Gilbert, 2002), while a linear dose-response

relationship was reported in a more recent study (Oliveira, Rodriguez-Artalejo, & Lopes, 2010). Although the reason behind such discrepancy is not clear, it is possible that the effects of alcohol are modified by intrinsic genetic differences. For example, compared to other ethnic groups Asians are more likely to have lower alcohol tolerance, due to polymorphisms of alcohol-metabolizing enzymes, such as acetaldehyde dehydrogenase(Wakabayashi, 2005). We have previously shown that alcohol sensitivity plays important role in the association between alcohol use and hypertension(Zhang et al., 2009, 2013). Therefore, we sought to investigate whether alcohol sensitivity modifies the association of alcohol use with HsCRP in older Chinese males, using the data from the ongoing Guangzhou Biobank Cohort Study (GBCS).

2. Materials and methods

2.1. Sources of data

The GBCS is a three-way collaborative project between Guangzhou No. 12 Hospital and the Universities of Hong Kong and Birmingham, and has been described elsewhere in detail(Jiang et al., 2006). Briefly, about 30,000 older (≥50 years) men and women from Guangzhou, the third largest city in China, were recruited from a community social and welfare association in three phases (2003–04, 2005–06, and 2006–08), with around 10,000 participants included in each phase. The Guangzhou Medical Ethics Committee of the Chinese Medical Association approved the study and all participants given written, informed consent before participation. All participants underwent a structured computer-assisted interview, as well as fasting biochemical and anthropometric measurements. HsCRP was measured during the first phase of recruitment of 10,413 participants, but not in the subsequent phases due to the limited resources. Hence the present analysis is restricted to phase 1 male participants (n = 3064). We excluded females as only 8.6% reported to have ever used alcohol (0.4% being excessive users, defined in the following section). We also excluded former drinkers (n = 98) to avoid reverse causation due to poor health status. A total of 2903 men with all variables information on all variables of interest were included.

2.2. Alcohol use and sensitivity

During the interview, participants were asked about their frequency of alcoholic beverage consumption and the usual quantity per occasion, from which we calculated the amount of alcohol use (g ethanol per week). We categorized alcohol use based on frequency into never, occasional, regular, and former drinkers. Occasional drinkers were those drinking less than once per week, or only on special occasions, such as wedding or major festival. Regular drinkers were people who drank at least once per week, and were further divided into moderate (less than 210 g of ethanol per week) and excessive (drinking 210 g or more ethanol per week) drinkers(Au et al., 2012). Former drinkers were those who stopped drinking for more than one year. We also categorized participants using another scheme into never, occasional, 1–6 times per week and daily drinkers. Self-reported alcohol use has been found to be reliable and valid in different populations(Midanik, 1988). For the GBCS, content and predictive validity of our exposure variables has been confirmed previously elsewhere(Schooling et al., 2009). Alcohol sensitivity was assessed by the question 'Do you usually experience facial flushing, palpitation or dizziness after drinking alcohol?' Participants who gave an affirmative response were considered to have alcohol sensitivity(Itoh et al., 1997).

2.3. HsCRP

Blood samples were drawn using a vacutainer tube in the morning after an overnight fast. We used a latex agglutination turbid metric test with a detection limit of 0.06 mg/L (BioSystems SA, Costa Brava30, Barcelona, Spain) to measure HsCRP. Further details of this test were given previously (Lao et al., 2010).

2.4. Statistical analysis

HsCRP levels were logarithmically transformed and their geometric means are presented. We created a dichotomized variable for HsCRP using the median (2.81 mg/L) as the cut-off value. We first compared the demographic characteristics across alcohol use status and sensitivity (never drinkers, current drinkers without alcohol sensitivity, and current drinkers with alcohol sensitivity). We then performed logistic regression analyses to assess the association of alcohol sensitivity and alcohol use with the elevated HsCRP (≥2.81 mg/L) adjusting for potential confounders, which included age, occupation (manual, non-manual, others), educational level, physical activity (as assessed by the International Physical Activity Questionnaire and categorized into active, moderate, and inactive)(Deng et al., 2008), smoking (never, former, current) and history of cardiovascular diseases. All analyses were performed using SPSS 16.0(SPSS Inc., Chicago, IL, USA).

3. Results

The mean age of the 2903 men included was 66.2 years (SD 5.8), with two-third (67%) being never drinkers, 13% occasional drinkers, and 20% regular drinkers. Of the regular drinkers, 69% reported to drink daily and 53% consumed at least 210 g of ethanol every week. About 40% of the drinkers were sensitive to alcohol. Table 1 shows the characteristics of the participants according to drinking status and broken down by alcohol sensitivity. There was no difference in terms of age, education level and occupation between never and current drinkers, although drinkers were more likely to be current smokers and less likely to reported a history of cardiovascular disease.

Mean HsCRP levels were similar in never (2.51 mg/L; 95% CI 2.42, 2.61) and occasional (2.48; 2.27, 2.72) drinkers, but were significantly higher in regular drinkers (2.84; 2.65, 3.06; P = 0.009) and those with alcohol sensitivity (2.87; 2.64, 3.12; P = 0.03).

Table 2 shows the associations between alcohol use and elevated HsCRP (≥median, which is 2.81 mg/L), adjusting for age (Model 1)and additionally for other potential confounders (Model 2). Regular drinkers, particularly those who consumed daily or those who had ≥210 g ethanol per week had a significantly higher odds of having elevated HsCRP, when compared to never drinkers, with adjusted odds ratios being 1.38 (95%CI 1.10, 1.72) and 1.57 (1.22, 2.02), respectively. There was a statistically significant trend for elevated HsCRP risk with more frequent and heavy alcohol use (P for trend = 0.01 and 0.004, respectively). Drinkers with alcohol sensitivity had a 40% increased odds of elevated HsCRP (95%CI 12%, 75%) compared to never drinkers. When compared to drinkers who were insensitive to alcohol, the odds ratio for elevated HsCRP was 1.32 (1.01, 1.72).

We further explored the potential effect modification by alcohol sensitivity. The results are shown in Table 3. Regular users with alcohol sensitivity had higher risk of elevated HsCRP compared to those who were insensitive. This effect was more marked among those consuming ≥210 g ethanol per week, with adjusted adds ratios being 2.34 (95%CI 1.48, 3.71) for the alcohol-sensitivity individuals, and 1.34 (1.00, 1.79) for those being insensitive to alcohol.