Effect of drinking on adiponectin in healthy men and women: A randomised intervention study of water, ethanol, red wine and beer with or without alcohol.

Armin Imhof MD, Ines Plamper MS, Steffen Maier MS, Gerlinde Trischler and Wolfgang Koenig MD

Dept. of Internal Medicine II, Cardiology, University of Ulm, Ulm, Germany

Address for correspondence:
Armin Imhof MD
E-mail. armin.imhof@uni-ulm.de

Clinical trial reg. no. NCT00764426, clinicaltrials.gov

Submitted 14 October 2008 and accepted 20 February 2009.
**Objective:** Moderate alcohol consumption is associated with reduced incidence of type 2 diabetes and cardiovascular mortality and increases adiponectin concentrations but effects might be differ according to gender and beverage consumed.

**Research design and methods:** Seventy-two healthy individuals (22-56 years) were enrolled in this randomised controlled cross-over trial. After wash-out, two interventions for 3 weeks followed: ethanol (concentration 12.5 %), beer (5.6 %), or red wine (12.5 %) equivalent to 30 grams of ethanol per day for men and 20 g/d for women or the same de-alcoholised beverages, or water. Adiponectin was measured by sandwich ELISA.

**Results:** Among females adiponectin significantly increased after with red wine (29.8%, p<0.05), among men after ethanol solution (17.4%, p<0.05) and beer (16.1%, p<0.05). De-alcoholised beverages had no substantial effect on adiponectin concentrations.

**Conclusion:** Moderate amounts of ethanol-containing beverages increased adiponectin concentrations but gender specific effects might depend on type of beverage consumed.
Moderate alcohol intake is associated with lower risk for type 2 diabetes, fatal and nonfatal cardiovascular disease (CVD)(1; 2). It has been suggested that alcohol in moderate doses – in addition to favourable changes of blood lipids, the haemostatic profile, and insulin resistance – exhibit anti-inflammatory mechanisms, thus potentially modulating atherosclerosis development (3). Adiponectin might represent an important link between insulin resistance, type 2 diabetes and atherosclerosis. Adiponectin improves insulin sensitivity and has several anti-inflammatory properties (4) and high concentrations of adiponectin were associated with lower risk of type 2 diabetes (5; 6) and future cardiovascular events (7). Moderate alcohol consumption is associated with increased adiponectin concentrations in healthy individuals, in obese males and in women with impaired glucose tolerance and type 2 diabetes (8-11). Recently, adiponectin has been proposed to be the most important mediator between moderate alcohol consumption and lower incidence of type 2 diabetes among middle-aged women (12). However, neither of these studies assessed potential varying effects of different types of alcoholic beverages in a randomised setting in men and women thus might be prone to selection bias because of personal preferences of study participants. Moreover, there is still controversial debate about potential favourable effects of non-alcoholic ingredients such as polyphenols.

We investigate the effect of short term moderate consumption of either low-concentrated ethanol solution, red wine, and beer with or without alcohol on adiponectin in a randomised controlled cross-over intervention trial.

RESEARCH DESIGN AND METHODS

Seventy-two non-smoking healthy Caucasian men and women of German nationality, aged 22-56 years were recruited. They were moderate alcohol consumers and had a family history free of alcohol dependencies. Liver disease was excluded measuring liver enzymes. All participants gave written informed consent to all procedures. The study was approved by the local ethics committee.

After a wash-out period of at least 2 weeks participants were randomly allocated – stratified by age and gender – to the following interventions over 3 weeks: Beer (5.6 %), red wine (12.5 %), or ethanol (concentration 12.5 %), equivalent to 30 grams of ethanol per day for men and 20 g/d for women or the same amount of de-alcoholised beer or de-alcoholised red wine (same brand) or pure water (control-group). Following the second wash-out period of three weeks a further intervention with the corresponding beverage followed (beer/de-alcoholised beer, wine/de-alcoholised wine, ethanol/water and vice versa). The rational for this study design was avoidance of selection bias caused by preferences in drinking behaviour. All participants were asked not to change their dietary habits and habitual physical activity during the study period.

A baseline history of alcohol consumption, dietary habits, medical history, sociodemographic parameters were obtained by standardized interview. At each visit, symptoms of concurrent inflammatory processes/infections including fever, cough or antibiotic therapy were carefully assessed and, if present, the participant or the respective intervention period was excluded from analyses. Fasting blood was collected
from the antecubital vein in a sitting position with minimal suction and short-term occlusion. Plasma and serum was stored within 90 minutes at -80 °C until analysis. Laboratory analyses were blinded. Plasma adiponectin concentrations were measured before and after intervention by sandwich ELISA (Quantikine®, R&D Systems, Wiesbaden, Germany).

**Statistical analyses:** Each intervention group contained 12 males and 12 females undergoing two interventions in random sequence. Data sets of 16 intervention periods were removed before analyses because of concurrent infections or drop out leaving 128 data sets for analyses. Numbers of excluded data sets were similar in all groups and did not substantially differ between males and females. Analysis of variance (ANOVA) with mixed linear models were used to assess effect of interventions on adiponectin. (PROC MIXED in SAS®, SAS Institute Inc., Cary, North Carolina, USA) All tests performed were two-sided, and a p-value <0.05 was considered statistically significant using SAS software, Release 8.2 (SAS Institute Inc. Cary, NC, USA).

**RESULTS**
Compliance was excellent according to self-report and counting of empty bottles returned. One participant was excluded because of protocol violation. Baseline characteristics including age, BMI, and liver enzymes did not differ within genders and between intervention groups. Adiponectin concentrations were substantially higher among females (means 7.6-8.8 µg/ml) compared to males (means 4.8-6.3 µg/ml) but did also not differ between the intervention groups within each gender. Among females adiponectin significantly increased after intervention with red wine (29.8%, p<0.05), among men after ethanol solution (17.4%, p<0.05) and beer (16.1%, p<0.04). De-alcoholised beverages had no substantial effect on adiponectin concentrations (Figure).

**CONCLUSION**
In this open, randomized cross-over intervention study we found a substantial increase of plasma concentrations of adiponectin after consumption of moderate doses of alcoholic beverages for three weeks. Among women, this effect was statistically significant after intake of red wine, among men after beer and ethanol solution.

This is the first study assessing effects of different alcohol-containing and corresponding de-alcoholized beverages in a randomised study in both genders. We confirm and extent findings from other studies. Adiponectin exhibit a bundle of various favourable metabolic effects boldering the hypothesis of its pivotal role in affecting risk of diabetes and cardiovascular disease (4). Given the robust increasing effect of consumption of moderate doses of alcoholic beverages on adiponectin concentrations in our and previous studies makes it an intriguing candidate for mediating beneficial effects of these beverages on the respective diseases (8-12). Most strikingly, effects differ with respect to gender and type of beverage. However, drinking preferences of participants might substantially affect our findings by incomplete adherence to the study protocol. Among females 50% reported to drink preferably wine but only 11% preferred beer in daily life. Among males first choice was beer for one third and wine for 22%. All others denied strong preferences. Furthermore, experimental and clinical data suggest
that sex hormones affect adiponectin concentrations and among healthy males effects of alcohol on sex hormones varied by drinking pattern and between beer and wine indicating a potential explanation for our findings (13-15).

In summary, our results suggest that alcohol containing beverages have robust increasing effects on adiponectin concentrations but effects might differ between genders depending on type of beverage consumed.

ACKNOWLEDGEMENTS

This study was supported by a grant from the European Research Advisory Board (ERAB), Ligne, Belgium. We also thank Sascha Wunderlich and Prof. Back from the Institute of Brewery Technology, Technical University Munich, Weihenstephan, Germany for providing us with the beer and Euresis GmbH, Aachen, Germany for providing us with the wine.

Disclosure: There are no conflicts of interest.
REFERENCES


pre- and post-menopausal women: the European Prospective Investigation into Cancer and Nutrition. *Cancer Causes Control* 17:1033-1043, 2006
Figure: Mean percent change with standard deviation of adiponectin concentrations from baseline after intervention with beer (B+), de-alcoholized beer (B-), red wine (RW+), de-alcoholized red wine (RW-), ethanol solution (EtOH) and water (W). (*p<0.05)