Int J Diabetes & Metab (2010) 18:95-98

Acute red wine consumption elevates plasma insulin and decreases plasma glucose in women during an oral glucose tolerance test

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Abstract
Epidemiological studies have shown that moderate wine consumption is associated with a reduced risk of developing type 2 diabetes, but the physiological mechanisms have not been elucidated. While relatively few studies have evaluated the effects of chronic wine consumption on glucose metabolism, the acute effects of wine have not been described. Therefore, we evaluated the glucose and insulin responses during oral glucose tolerance tests (OGTT) in six healthy women, 60 min after ingestion of either water or red wine (2.5 ml/kg BW). Blood samples were taken 0, 15, 30, 60, 90, and 120 min after ingestion of 75 g glucose and plasma was analyzed for glucose and insulin concentrations at each time point. Red wine elevated the plasma insulin response at 30 min (23%, $p = 0.003$) and resulted in lower plasma glucose concentrations at 60, 90, and 120 minutes ($p < 0.05$). Area under the curve for glucose was significantly reduced after wine consumption ($p = 0.01$) while area under the curve for insulin was similar after each treatment. Although insulin sensitivity was seemingly unaltered, ingestion of red wine resulted in significantly lower plasma glucose levels between 1 and 2 hours after ingestion of glucose, which may at least partially explain the improved glucose tolerance associated with moderate wine consumption.

Key words: *wine, plasma insulin, plasma glucose, glucose tolerance test*

Introduction

Epidemiological studies have consistently reported that moderate alcohol consumption, defined as 10-30 g/day, is associated with a reduced incidence of type 2 diabetes mellitus.[1,2] In a meta-analysis of prospective observational studies, Koppes and associates reported that moderate drinking reduces the relative risk of diabetes by approximately 30%.[3] Similarly, Hodge et al. observed an inverse association between alcohol intake and diabetes risk, but only in women and only if wine was the alcoholic beverage.[1] Wannamethee and associates reported that the inverse association was most apparent in women who drank wine or beer, as opposed to liquor,[2] which suggests that non-alcoholic components of these beverages are important in mediating their effects. Despite the apparent relationship between wine intake and diabetes risk, no definitive physiological mechanism explaining this link has been described.

The few experimental studies that have assessed the effects of moderate wine consumption on glucose tolerance have reported either no change[4,5,6] or an enhancement[7] in insulin sensitivity. While the equivocal results have no immediate explanation, the subjects in these previous three studies consumed wine daily for two to ten weeks, with testing performed after an overnight fast. The acute effect of wine consumption on glucose disposal and insulin action has been reported only once, but the study involved wine consumption during a mixed-nutrient meal.[8] Thus, the purpose of this study was to evaluate the effect of acute red wine ingestion on glucose metabolism in women during an oral glucose tolerance test (OGTT).

Materials and Methods

Subjects

Six apparently healthy women (23-43 years of age) were recruited and signed written consent before participation in the study, which was approved by the Institutional Review Board at Transylvania University. Subjects were included in the study if they reported being non-diabetic and nonsmokers. The subjects' average weight, height, and BMI were 66.9 ± 4.5 kg (range: 54.3-83.3 kg), 1.67 ± 0.03 m (range: 1.60-1.78 m), and 23.9 ± 1.5 (range: 20.3-30.0), respectively. Alcohol consumption averaged 3.6 drinks/wk, with intake occurring on 0-4 days/wk. All subjects were asked to abstain from exercise and alcoholic beverages for 72 hours prior to each OGTT, and this was verified via activity and diet questionnaires that were collected prior to each session.

Study Design

All subjects completed two OGTTs, one following ingestion of water and the other following ingestion of red wine (Cabernet Sauvignon Grand Estates, Columbia Crest, Paterson, WA; 13.5% alcohol/volume). Each OGTT was separated by at least one week, and the beverage was given in random order.

Received on:8/9/2010
Accepted on 3/11/2010
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Subjects reported to the laboratory at 9:00 AM following an overnight fast and consumed 2.5 ml/kg body weight of either water or wine. After 60 min, subjects began the OGTT by ingesting a 75 g glucose solution (Limondex). Blood samples (4-5 ml) were obtained from an antecubital vein using non-treated evacuated blood tubes at 0, 15, 30, 60, 90, and 120 minutes after glucose ingestion. Each sample was centrifuged immediately and the plasma fraction was isolated and stored at -55°C for subsequent analysis.

Plasma glucose concentration was determined at each time point using a glucose analyzer (YSI 2300, Yellow Springs, OH) and plasma insulin concentration was determined with a human insulin ELISA kit (Millipore, Billerica, MA).

Calculations

Areas under the curve for glucose (AUCg) and insulin (AUCi) were determined using the standard trapezoid method. Whole body insulin sensitivity was assessed from the OGTT data by determining the reciprocal of the glucose-insulin index, which is the product of AUCg and AUCi.[9] Statistical differences between treatments were determined using the paired

Student's *t* test, with significance set at $P \leq 0.05$. In the text, data are reported as the mean ± SE.

Results

Plasma glucose concentrations did not differ between the groups at baseline and remained at similar levels until at least 30 min after glucose ingestion (Fig. 1). While there was no difference in peak glucose concentration between the water and wine treatments (7.6 ± 0.44 vs. 7.3 ± 0.59 mM, respectively), ingestion of wine resulted in significantly reduced plasma glucose concentrations at 60, 90, and 120 min (P = 0.02, 0.02, and 0.03, respectively).

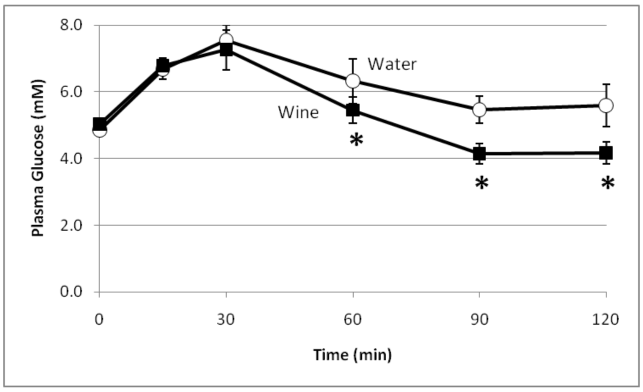

Figure 1: Plasma glucose responses during oral glucose tolerance tests. Either water or wine was consumed 60 minutes prior to the test and 75 g glucose was ingested at time 0. Values are means ± SE. *P < 0.05 compared to water treatment at same time point.

Plasma insulin concentrations did not differ among trials at baseline, or at any other time point except 30 min after glucose ingestion (Fig. 2). Wine ingestion prior to the test resulted in a significantly elevated (23%) plasma insulin concentration at 30 min (P = 0.003).

Glucose and insulin areas under the curve are presented in figure 3. Wine ingestion significantly reduced AUCg by 10% (P = 0.01), due entirely to the reduced plasma glucose concentrations at 60, 90, and 120 min. Despite the significantly elevated plasma insulin concentration after wine ingestion at 30 min, there was no difference between groups in AUCi.

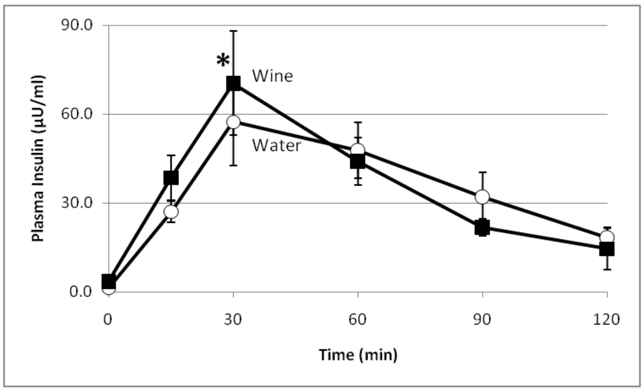

Figure 2: Plasma insulin responses during oral glucose tolerance tests. Either water or wine was consumed 60 minutes prior to the test and 75 g glucose was ingested at time 0. Values are means ± SE. *P < 0.05 compared to water treatment at same time point

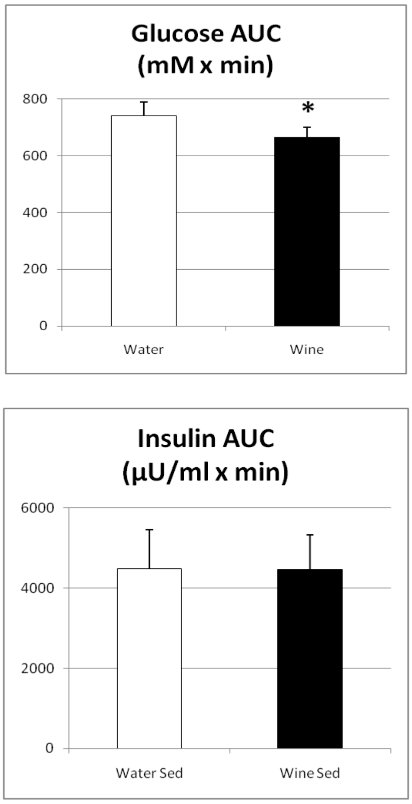

Figure 3: Glucose (a) and insulin (b) areas under the curve during oral glucose tolerance tests. Values are means ± SE. *P < 0.05 compared to water treatment.

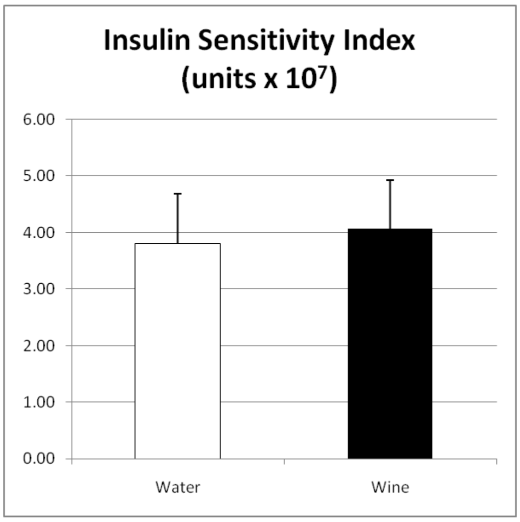

Figure 4: Insulin sensitivity index. Insulin sensitivity was calculated as the inverse of the product of AUC_g and AUC_i. Values are means ± SE.

Figure 4 depicts whole body insulin sensitivity calculated from AUCg and AUCi. There was no difference in insulin sensitivity between the groups.

Discussion

This study examined the hypothesis that red wine alters glucose metabolism and improves the glucose-insulin response during an OGTT. The novel finding of this investigation is that acute wine consumption, 60 minutes prior to an OGTT, results in an elevated plasma insulin concentration at 30 min and lower plasma glucose concentrations during the last hour of the test. While an extended time course of the glucose response was beyond the scope of this study, it is apparent that ingestion of approximately one glass of red wine one hour before consuming sugar can lower subsequent plasma glucose levels, and this response may at least partially explain the consistently-reported relationship between moderate wine consumption and reduced risk of type 2 diabetes.

Because insulin sensitivity was similar in the two trials (Figure 4), the wine-induced reduction in plasma glucose at the end of the OGTT was likely the result of the enhanced insulin response. Indeed, the glucose and insulin time courses (Figures 1 and 2) show that the glucose concentrations in the wine trial became significantly reduced only after the large insulin spike at 30 min into the OGTT. Although the increased insulin level was short-lived, the effect on glucose concentration was sustained for at least 60 minutes. Similar results regarding an enhanced insulin response after ingestion of alcoholic beverages have been reported.[10,11,12] Koivisto and associates[10] showed elevated insulin and lower glucose levels in type 2 diabetics after ingestion of a vodka aperitif, red wine with a meal, and cognac after the meal. Trojan[11] and Nikkila[12] reported enhanced glucose-stimulated insulin secretion in the presence of ethanol. Conversely, Avogaro and associates,[13] Bantle and associates[14] and Gin and associates[8] found no difference in the insulin responses to an intravenous glucose load[13] or a meal[14,8] when vodka, white wine, or red wine, respectively, was used as the alcoholic drink. Unfortunately, the use of different alcoholic beverages at various time points in these studies precludes definitive interpretations regarding the specific action of wine. Whether the enhanced insulin response in the presence of red wine resulted from increased insulin release and/or decreased insulin clearance is unknown. Avogaro and associates[13] reported that acute alcohol (vodka) consumption enhanced insulin action without affecting β–cell secretion.

However, based on elevated C-peptide levels, Trojan and associates reported an increased insulin secretion in response to acute ethanol ingestion.[11] The C-peptide response was not determined in this study, but it is a factor that should be analyzed in future experiments.

The absence of improved insulin sensitivity from this acute dose of red wine was unexpected. It was hypothesized that insulin sensitivity would increase, based on two lines of evidence. First, in a 12-year prospective study, Conigrave and associates[15] found that the frequency of alcohol consumption was inversely associated with diabetes, and that consumption on at least five days per week provided the greatest protection. This suggests that the health benefit of alcohol, regarding diabetes, is short-lived and must be "replenished" on a regular basis.

Accordingly, most empirical studies of chronic moderate alcohol consumption[4,5,6,16] found no change in insulin sensitivity, perhaps because alcohol's effect is acute, and the time lag between alcohol consumption and the test for insulin sensitivity was too great.

Second, the antioxidant action of red wine may enhance glucose uptake in skeletal muscle. Red wine contains several antioxidants, including quercetin and resveratrol, and has been shown to enhance plasma antioxidant defenses[17] and preserve plasma from meal-induced oxidative stress in type II diabetic subjects.[18] Resveratrol improves glucose transport in cultured myotubes,[19,20]and the biological antioxidant α–lipoic acid enhances insulin-stimulated glucose uptake in humans[21] and rats.[22] Additionally, drinking red wine or tannic acid, a phenolic antioxidant compound in red wine, with lunch resulted in a lower glucose excursion after the meal, while ethanol had no effect on insulin or glucose levels.[8] Thus, some non-alcoholic components of red wine may contribute to improved insulin sensitivity.

This study has several limitations that should be addressed. First, the small sample size may have limited our ability to detect small changes in the measured variables, such as insulin sensitivity. However, we did detect significant differences in insulin and glucose levels, and the values for insulin sensitivity were almost identical between the two treatments, suggesting that additional subjects would not change the result. Second, consumption of alcohol was not blinded. Given the distinct taste of red wine and the known physiological effects of alcohol, this would have been difficult to achieve. Finally, the two hour duration over which glucose and insulin were analyzed prevented the determination of longer term effects.

In summary, this study showed that consumption of red wine by women prior to ingestion of glucose enhances the insulin response and produces a lower plasma glucose level without affecting insulin sensitivity. While the mechanism of the elevated insulin level is not known, this response to acute wine consumption may at least partially explain the association between moderate wine consumption and the lower risk of developing type 2 diabetes.

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