P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

# HerbClip™



**File: ■ Red Wine (*Vitis vinifera*, Vitaceae)**
**■ Diabetes**
**■ Blood Pressure**

**HC 101551-532**

**Date: November 13, 2015**

**RE: Moderate Red Wine Consumption May Lower Mean 24-Hour Blood Pressure and Pulse Pressure in Patients with Type 2 Diabetes with Rapid Ethanol Metabolism Genotype**

Gepner Y, Henkin Y, Schwarzfuchs D, et al. Differential effect of initiating moderate red wine consumption on 24-h blood pressure by alcohol dehydrogenase genotypes: Randomized trial in type 2 diabetes. *Am J Hypertens*. August 1, 2015; [epub ahead of print]. doi: 10.1093/ajh/hpv126.

One-quarter of adults in the world's industrialized countries have hypertension (elevated blood pressure). Observational studies show that heavy alcohol intake (definition not provided) is associated with hypertension. However, the effect of moderate alcohol intake on hypertension is inconclusive but it may reduce cardiovascular risk in patients with type 2 diabetes. Ethanol is metabolized by hepatic class 1 alcohol dehydrogenase (ADH1B). A genetic variant of ADH1B called rs1229984 has an increased reaction rate. The purpose of this randomized study was to evaluate the effect of 6 months of moderate red wine (*Vitis vinifera*, Vitaceae]) consumption on blood pressure dynamics in patients with type 2 diabetes who had previously abstained from alcohol.

This is a sub-analysis of the CaArdiovaSCulAr Diabetes & Ethanol (CASCADE) study. The CASCADE sub-study was conducted at the Nuclear Research Center Negev, Dimona, Israel, and Ben-Gurion University-Soroka Medical Center, Beersheba, Israel. The CASCADE study included 224 patients with type 2 diabetes who received either mineral water, white wine, or dry red wine 150 mL/dinner for 2 years. This sub-study (n = 54; mean age, 57 years) included only the patients from the Nuclear Research Center Negev who received mineral water (Mey-Eden; provided by Eden Springs Ltd; Golan Heights, Israel) or dry red wine (provided by Golan Heights Winery; Golan Heights, Israel) for 6 months. The wine and water were provided to the patients by the study administrators. The red wine contained 14.2% alcohol by volume and 270.1 mg gallic acid equivalents total phenols.

Patients included in the CASCADE study were 40-75 years old, diagnosed with type 2 diabetes according to the American Diabetes Association criteria, abstained from alcohol (≤ 1 drink/week), were nonsmokers, were clinically stable, and would drink wine if assigned. Excluded patients had hemoglobin A1c < 6.4% or > 10%; had > 2 daily

injections of insulin or used an insulin pump; had fasting serum triglycerides ≥ 400 mg/dL; had serum creatinine > 2 mg/dL; had liver dysfunction (defined as ≥ 3-fold increase in serum alanine aminotransferase and/or aspartate aminotransferase); had severe diabetic complications; had autonomic neuropathy manifesting as postural hypotension or hypoglycemia unawareness; used medications that might interact with moderate alcohol consumption; had active cancer or chemotherapy treatment in the past 3 years; had major illness that may cause hospitalization; had a high potential for addictive behavior or a family history of addiction or alcohol abuse; were women with first-degree relatives with breast cancer; or were pregnant or lactating women.

Ambulatory blood pressure was measured at baseline and 6 months. Diastolic and systolic blood pressures were measured, starting the morning the patient was fitted with the blood pressure cuff, and every 30 minutes during the day and every 60 minutes at night for 24 hours. All patients were told to eat a Mediterranean diet with unrestricted calories. The recommended diet was high in vegetables and low in red meat, and contained no more than 35% of calories from fat (mainly olive [*Olea europaea*, Oleaceae] oil and nuts). Blood was drawn for genotyping of the homozygous ADH1B*1 and ADH1B*2 variants and heterozygotes.

At 6 months, 92% of the patients remained in the study. Compliance in the wine group was 76.0% and compliance in the water group was 80.9%. A total of 61% of patients at baseline had hypertension, and 35% were taking antihypertensive therapy. The majority (85%) of patients were men. At 6 months, both groups had a mean weight loss of 1.3 kg (2.9 lbs). The changes in weight did not correlate with blood pressure changes. The average 24-hour blood pressure was not significantly different from baseline or between groups at 6 months. However, there was a transient decrease in blood pressure in the wine group at midnight (mean systolic blood pressure decreased 10.6 mmHg and diastolic blood pressure decreased 7.7 mmHg) and 7-9 am (the morning after consuming the wine, mean systolic blood pressure decreased 6.2 mmHg). In contrast, the water group had increased blood pressure at midnight (systolic blood pressure increased 2.3 mmHg and diastolic blood pressure increased 0.7 mmHg) and in the morning (systolic blood pressure increased 5.6 mmHg), which, for systolic blood pressure, was significantly greater than the wine group at midnight ($P = 0.03$) and in the morning ($P = 0.014$). Accordingly, the wine group also had a significant decrease in pulse pressure in the morning ($P = 0.032$). Users of antihypertensive medications had a greater decrease in hypertension at those 2 times compared with non-users (statistical significance not reported). Patients who were homozygous for the fast ethanol metabolism gene (ADH1B*2) had a significant decrease in mean 24-hour systolic blood pressure and pulse pressure compared with non-fast metabolizers (systolic blood pressure, $P = 0.002$, decrease of 8 mmHg vs. increase of 3.7 mmHg, respectively; pulse pressure, $P = 0.032$, decrease of 3.8 mmHg vs. increase of 1.2 mmHg, respectively).

The authors conclude that daily moderate red wine consumption did not affect 24-hour blood pressure in this study setting of patients with type 2 diabetes. However, there is a potential of a transient decrease at certain time intervals. Also, fast ethanol metabolizers, but not slow metabolizers, had a significant decrease in average 24-hour blood pressure. A limitation of this study is that it consisted mostly of men. Another limitation was the size of the subgroup analyses, e.g., there was a small population for the genetic variant analysis, which had $n = 12$ in the slow-metabolizer group and $n = 9$ in the fast-metabolizer group; also, the number of patients who were taking antihypertensive medications was only 35% of the total population. Because of these limitations, the

authors acknowledge that the study can be used only to generate hypotheses rather than generate firm conclusions. The clinical importance of the wine-associated transient decrease in blood pressure at midnight and in the morning is unknown. No conflicts of interest were reported.

*—Heather S. Oliff, PhD*