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Research Article

A pilot study on the impact of a low fructose diet and allopurinol on clinic blood pressure among overweight and prehypertensive subjects: a randomized placebo controlled trial

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Abstract

Fructose and sodium intake have been associated with hypertension and metabolic syndrome. Although various mechanisms are involved, fructose causes hypertension partly through rising intracellular and serum uric acid. To date, there are no studies in adults that have evaluated the impact of low fructose diets and allopurinol on prehypertensive and overweight subjects. The objective of this study was to compare the effect of low fructose diet and allopurinol or placebo on blood pressure (BP) and metabolic syndrome components The study was a controlled clinical trial and consisted of two phases; in the first phase of intervention (4 weeks), patients were randomized to either low fructose diet (34 patients) or control diet (38 patients). In the second phase of intervention (weeks 4–8), the same groups continued with the same diet prescriptions but were further randomized to receive placebo or allopurinol (300 mg/d). Clinic and 24-hour ambulatory BP, anthropometric measures, and laboratory data were determined at baseline, weeks 4 and 8. Seventy-two patients were included in the trial. At the end of the dietary phase, both diet groups significantly reduced their BP, but there were no between-group differences. Compared to placebo, at the end of follow-up, subjects in the allopurinol group had a lower clinic systolic blood pressure and this was significant within- and between-group comparisons. The percentage of dippers was higher in the allopurinol group, and weight was reduced significantly despite the absence of caloric restriction Allopurinol was associated with a significant reduction in clinic BP, an increase in the percentage of dippers, and significant weight loss. Larger studies with longer follow-up are needed to confirm our findings. J Am Soc Hypertens 2015;9(11):837–844. © 2015 American Society of Hypertension. All rights reserved.

Keywords: Diet; fructose; hypertension; uric acid.

Introduction

Fructose consumption, in the form of added sugars such as high fructose corn syrup or sucrose, has increased markedly in the past 30 years.[1,2] The excessive intake of fructose is one proposed cause of increased metabolic syndrome (MS) and obesity, and both conditions in turn are associated with the development of systemic hypertension.[2] Although various mechanisms are involved, fructose causes hypertension partly through raising intracellular and serum uric acid. An elevated serum uric acid is common in subjects

Conflicts of interest: L.G.S-L and R.J.J. are members of Colorado Research Partners LLC that is developing inhibitors of fructose metabolism. R.J.J. also has shares and is on the Scientific Board of XORT therapeutics. M.M. has received honorarium payments from Abbott, Amgen, and Sanofi and has served in advisory boards for Baxter and Sanofi. A.V-R has received honorariums and served in advisory boards for Baxter.

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with prehypertension,[3–5] with new onset hypertension,[6] with gestational hypertension,[7] and with advanced hypertension.[8] Pilot studies also suggest that lowering uric acid can result in an improvement in blood pressure (BP) in obese adolescents with hyperuricemia and prehypertension[9] and in adolescents with newly diagnosed hypertension.[10] Data from our group have demonstrated that high fructose intake administered to healthy adults resulted in significant increase in BP and worsening of MS parameters, and the increase in BP was prevented with allopurinol.[11] The opposite was also demonstrated when fructose was restricted in humans and this associated with lowering uric acid, a decrease in BP, and improvement in MS parameters.[12]

To our knowledge, there are no studies that have evaluated the impact of low fructose diets plus allopurinol in adult prehypertensive and overweight subjects. The objective of this study was to compare the effect of a low fructose diet plus allopurinol or placebo on BP and MS components.

Methods

The study is a controlled clinical trial and consisted of two phases; in the first phase of intervention (4 weeks), patients were randomized to either low fructose diet or control group. In the second phase of intervention (weeks 4–8), the same groups continued with the same diet prescriptions but were further randomized to receive allopurinol (300 mg/d) or placebo. The trial was conducted between July 2010 and May 2013 at the Instituto Nacional de Cardiología Ignacio Chávez, México. The study was approved by the human subjects committee at the institution and was registered at ClinicalTrials.gov (NCT01157936). All participants gave written informed consent.

Participants

To participate in the trial, patients had to be 18 years or older, overweight (body mass index [BMI] >25 kg/m^2) or obese (BMI >30 kg/m2), with systolic blood pressure >120 to 140 mm Hg and diastolic 80 to 90 mm Hg, and with a history of high fructose consumption from sources of added sugar (excluding fruits) of >70 g/d. Subjects were excluded if they had a history of diabetes, chronic kidney disease, liver disease or abnormal liver function tests, hematologic abnormalities, malignancy, were taking any medications, or were pregnant. Patients were eliminated from the study if during the study period required any medications, if the BP during the study period became greater than 160/100 mm Hg, fasting blood glucose greater than 200 mg/dL, low-density lipoprotein cholesterol greater than 190 mg/dL, triglycerides greater than 500 mg/dL, serum uric acid levels less than 2 mg/dL or greater than 12 mg/dL, became pregnant, had severe disease in the study period (infectious, neoplastic, cardiovascular, and neurologic), or required hospitalization for medical or surgical causes. In addition, patients were eliminated from the study if they had adverse clinical or biochemically derived from the study medication (allergic reaction, decreased cell blood count, or elevated liver function tests).

Dietary and Pharmacologic Intervention

All subjects were followed in a prerandomization phase before randomization where they did not have dietary restrictions. If subjects weight did not vary more than 2 kg and ambulatory blood pressure monitoring (ABPM) results remained within the inclusion criteria, then patients were recruited for the study. The allocation of patients to each intervention group was performed using a random number table.

Diet Intervention

The first intervention consisted of 4 weeks of randomization to either an isocaloric control diet where the proportion of macronutrients and fructose intake was maintained as their baseline diet or an isocaloric low fructose diet. Fructose in the form of added sugars and fruits was restricted to <20 g/d, and the proportion of other macronutrients was matched to the baseline diets. To match their baseline carbohydrate consumption in the low fructose group, starches such as bread, cereals, and tortillas were added to the diet in the amounts required to preserve this macronutrient balance. Study subjects in both groups were counseled to reduce sodium intake to <2.5 g/d. Patients completed a frequency of consumption questionnaire that was adapted from the food questionnaire used for the US National Health and Nutrition Examination Survey but was modified to include the types of foods that are specific to the Mexican diet.[12] For a more specific baseline fructose determination, fructose intake was implemented based on reference tables (The Sugar Fix, 2008, by Richard J Johnson with Tim Gower, Rodale Press, NYC, USA). After randomization, patients were followed every other week. Participants were provided weekly with a daily meal plan and were instructed to record their food and beverage intake at least once a week in a food diary. Adherence was defined as attending at least 80% of the scheduled clinic visits and having blood work during this last visit. Physical activity was assessed by asking the patients if they performed any specific aerobic or anaerobic exercise besides their daily routine. No additional physical activity was prescribed for any group. Random 24 urinary collections were performed to assess for low sodium diet adherence.

Pharmacologic Intervention

After week 4, patients were further randomized to receive either allopurinol (300 mg/d) or placebo in the

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