JURA
Journal of Undergraduate Research in Alberta • Volume 3 • 2013

Evaluating the effect of fructose ingestion on arterial stiffness and the renin-angiotensin system in healthy humans

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Introduction

Consumption of sugar, particularly in the form of fructose, has increased exponentially over the past three decades and it has been shown to adversely affect the renal and cardiovascular systems as it results in obesity and hypertension[1,2,3]. Animal studies suggest a role for the vascular renin angiotensin system (RAS) in response to fructose intake, activation of which is deleterious to cardiovascular outcomes, though the mechanism remains elusive in humans[4]. We will measure the arterial stiffness response to Angiotensin II (Ang II) challenge as a surrogate marker of vascular RAS activity and cardiovascular disease[5,6].

Methods

A randomized, blinded, two-period crossover study will be performed to determine the effect of fructose ingestion on arterial stiffness in 30 healthy, normotensive men and women adults.
Subjects will be studied in high-salt balance to ensure maximum RAS suppression[7]. Arterial stiffness, expressed as pulse wave velocity (PWV) and aortic augmentation index (AIX), will be measured during each study day by tonometry at baseline and in response to 60min of graded Angiotensin II infusion, an index of RAS activity. After undergoing study day 1, which is a no sugar treatment day, participants will be randomized to either a 2-week period of daily ingestion of 200g fructose or glucose and will undergo an identical study day to measure arterial stiffness. After a minimum 1 week washout period, subjects will then cross over to the other sugar treatment for the third study period during which they will undergo a third identical study day (Figure 1). Six subjects have been recruited and four have completed the study to date (75% male, 25% female; Age: 49±8 years, BMI: 25±5kg/m2). Ingestion of fructose is expected to increase baseline arterial stiffness but due to the blinded nature of the study, the order at which participants received different sugars are still unknown to us. Thus, the effect of each sugar on arterial stiffness and RAS activity could not be determined. As an alternative, the role of sugar in general in modulating arterial stiffness and RAS activity was examined.

Results

Based on the results obtained from four participants, it was observed that baseline arterial stiffness in response to ingestion of sugar in general is similar to baseline arterial stiffness when no sugar is ingested (AIX: 13.2±8.8% vs. 11.3±11.5%; PWV: 8.7±2.2 m/s vs. 8.5±2.6 m/s, respectively). This suggests that a compensatory mechanism is reducing the arterial stiffness to its "normal" level. It was also hypothesized that ingestion of fructose results in a blunted arterial stiffness response to Ang II infusion compared to

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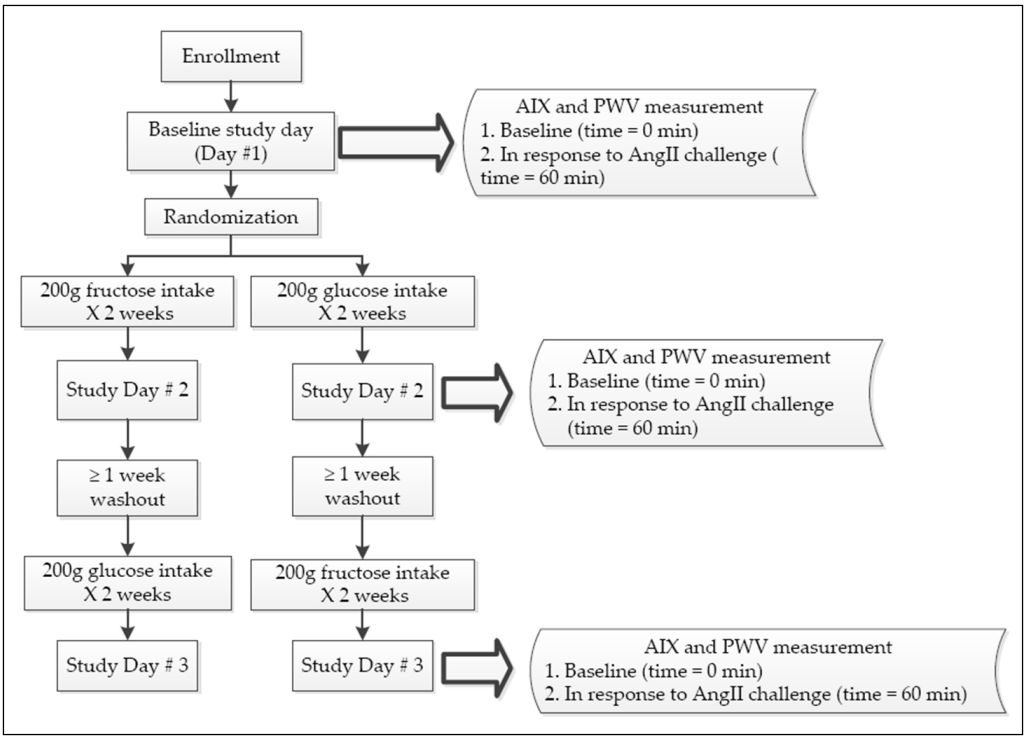

Figure 1:
Overview of this crossover study which allows each participant to serve as his/her control. During the washout, participants are not receiving fructose or glucose to prevent carry over effect.

glucose ingestion, implying a more activated RAS since fructose, but not glucose, draws out water into the colon resulting in a loss of water and therefore RAS activation[8]. Our results suggested a much more blunted increase in arterial stiffness in response to Ang II infusion for sugar treatments combined, compared to participants that did not receive any sugar (ΔAIX: 15.0$\pm$1.0 % vs. 8.8$\pm$0.61 %; ΔPWV: 8.8$\pm$0.24 m/s, 1.1$\pm$0.16 m/s, respectively), suggesting that sugar in general results in the activation of RAS in healthy humans. This will suggest that the increased fructose-associated cardiorenal risk may be mediated, in part, by changes in vascular RAS activity.

Conclusion

If consistent with the recent observations, this novel program of research may provide physicians with an intervention to alter the otherwise poor outcomes in patients with cardiovascular disease.

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