Cardiovascular Physiology

Four days of Fructose Supplementation Affected the Vascular Function of Rats in a Sex-Dependent Manner without Changing Glucose Metabolism

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Introduction: Fructose consumption has been increased in the last few decades, raising the concern about the effects of this sugar on the organism. It is already known that fructose induces metabolic disturbances as insulin resistance and lipid accumulation and it may affect cardiovascular function. In addition, it has been demonstrated that high fructose diet affected differently cardiovascular parameters in males and female rats, however the mechanisms involved in these alterations remain unclear.

Objective: To determinate how fructose dietary supplementation, in a non-insulin resistance stage, could affect the vascular function of male and female rats.

Material and Methods: In order to stablish a fructose supplementation model with no changes on glucose metabolism, we provide 10% fructose solution (Fr Group) or tap water (Ct Group) to Wistar male and female rats during four days and performed glucose intraperitoneal tolerance test or insulin sensitivity test. The results confirmed that 4 days of fructose supplementation did not change neither the glucose tolerance nor insulin sensitivity comparing to the Ct Group. Once stablished the experimental model, we investigated whether fructose overload could alter the vascular function. For this, the animals were euthanized and thoracic aorta responses induced by phenylephrine (PE) were analyzed by iron myography. We observed that rats treated with high fructose showed a decreased response to PE when compared with those from Ct Group.

Results: To address the influence of the sex on the vascular dysfunction induced by high fructose diet, we analyzed separately the PE responses from female and male rats. Interestingly, on male rats, fructose did not alter the the contractility of aortic segments. However, female population preserved the vascular phenotype of decreased response to PE after fructose supplementation observed on the overall population. This lack os

response to PE was accompanied by an exacerbated endothelial anti-contractile action not connect to NO bioavailability. Also in females treated with high fructose, the modulation of vascular contractility by superoxide anion was pronounced, which can be responsible for the reduced Na^+K^+ATPase activity observed in this group. Despite of male rats treated with fructose did not show increased vascular response to PE, it seems to reduce superoxide dismutase enzyme function. Consequently, less hydrogen peroxide resembles to be available reverberating in reduced potassium channel activity in that population. **Conclusions:** Together, the results obtained in the present study demonstrated that fructose dietary supplementation, in an early stage as four days, affect the vascular function independently of the metabolic alterations. This effect seems to be sex-dependent and may involve alterations on redox signaling on smooth muscle cells.

Keywords: Fructose, vascular function, rats, sex, glucose metabolism