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Letter to the Editor

Evolutionary physiology shows the need for an unprecedented study on sugar

Dear Editor,

It is with much interest that we read the fascinating Opinion Paper by Riccardo Baschetti [1]where he highlights the fact that rapid absorption of sugars (a result of the extremely concentrated sugars in our industrialised diets as well as high salt intake) may represent an underappreciated cause of pathology. This is an intriguing hypothesis but does not directly invoke a mechanism of action. Specifically, because sucrose is digested into is its glucose and fructose monomers, it is not directly evident which of these sugars are responsible for a toxic effect following a concentrated surgery meal/beverage. Also, how could such a detrimental effect be mediated?

Following a meal, fructose is rapidly absorbed by the liver, where it is primarily consumed during the synthesis of lipid, glycogen, as well as various glycolytic and TCA intermediates. The reason why serum fructose levels are maintained at extremely low levels, compared to glucose, likely relate to the fact that glucose is a very stable sugar and less likely to form advanced glycation end-products (AGEs).

Notably, recent finding [2] have implicated the small intestine as playing a pivotal role in shielding the liver against hepatotoxic effects of fructose [2]: In mice, fructose absorbed by the small intestine is metabolised into glucose as well as a range of other metabolic intermediates. In fact, intravenous injection with fructose results in its accumulation in the kidneys, pancreas, small intestine, and liver, whereas orally administered fructose results in fructose accumulating primarily in the small intestine, with only a small amount in the live [2]. This highlights the efficacy with which the small intestine metabolise fructose. However, the ability of the small intestine to metabolise fructose increase linearly up to a dose of 0.5 g/kg before reaching fixation: At high dose fructose ($\geq$1 g/kg), the clearance mechanisms of the small intestine are overwhelmed, and fructose slipover occurs [2].

The observation that fructose levels increase proportionately to the amount of fructose ingested, and exhibit lower clearance as fructose load increases, have also been observed in humans [3]. Indeed, fructose-derived AGE is percent in diabetic patients [4], suggesting that, similar to mice, high-dose (i.e. consecrated) fructose can overwhelm clearance systems. Finally, elevated intracellular glucose levels can stimulate the in situ formation of fructose from glucose (via the polyol pathway) in the liver, and have been argued to underlie the cause of hepatotoxicity [5]. Taken together, these observations support the notion that concentrated sugars may hold an underappreciated danger.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2019.07.016.

References

[1] Baschetti R. Evolutionary physiology shows the need for an unprecedented study on sugar. Clin Nutr ESPEN 2019;31:23–7. https://doi.org/10.1016/j.clnesp.2019.03.012.
[2] Jang C, Hui S, Lu W, Cowan AJ, Morscher RJ, Lee G, et al. The small intestine converts dietary fructose into glucose and organic acids. Cell Metabol 2018. https://doi.org/10.1016/j.cmet.2017.12.016.
[3] Kim HS, Paik HY, Lee KU, Lee HK, Min HK. Effects of several simple sugars on serum glucose and serum fructose levels in normal and diabetic subjects. Diabetes Res Clin Pract 1988. https://doi.org/10.1016/S0168-8227(88)80030-5.
[4] Takeuchi M, Iwaki M, Takino JI, Shirai H, Kawakami M, Bucala R, et al. Immunological detection of fructose-derived advanced glycation end-products. Lab Investig 2010. https://doi.org/10.1038/labinvest.2010.62.
[5] Lanaspa MA, Ishimoto T, Li N, Cicerchi C, Orlicky DJ, Ruzycki P, et al. Endogenous fructose production and metabolism in the liver contributes to the development of metabolic syndrome. Nat Commun 2013. https://doi.org/10.1038/ncomms3434.

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