Impact of artificial sweeteners on glycaemic control in healthy humans

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Background and aims: Prospective epidemiological studies indicate that a high habitual intake of beverages sweetened with non-caloric artificial sweeteners (NAS) increases the risk of developing type 2 diabetes (T2DM), but the underlying mechanisms are unknown. In animals, acute exposure to NAS activates intestinal sweet taste receptors (STRs) to trigger the release of glucose-dependent insulinotropic polypeptide (GIP) from proximal K-cells, and glucagon-like peptide-1 and 2 (GLP-1, GLP-2) from more distal L-cells, while dietary NAS supplementation increases the function of the sodium-dependent glucose co-transporter-1 (SGLT-1) to augment glucose absorption and increase postprandial glycaemia. It is not known whether NAS alters glucose absorption in humans, and if so, whether this affects postprandial glycaemic control adversely.

Materials and methods: 27 healthy subjects (age 27 ± 2 years, body mass index 24 ± 1 kg/m², 14 male) were randomised, in double-blind fashion, to dietary supplementation with a NAS combination (92 mg sucralose plus 52 mg acesulfame-K, equivalent to ~1.5L of diet beverage/day, N=14) or placebo (N=13), taken in capsules three times daily before meals over 2 weeks. Subjects then attended the laboratory after an overnight fast and underwent non-sedated endoscopy incorporating a 30 min intraduodenal glucose infusion (30g/150ml, 3 kcal/min, including 3g of the glucose analogue 3-O-methyl glucose, 3-OMG) and biopsy collection, before and immediately after the intervention. Glucose absorption (serum 3-OMG), plasma glucose, insulin and gut peptides (total GLP-1, GLP-2 and GIP) were measured, and the incremental areas under the curve (iAUC, over 120 min) compared by 2-way ANOVA.

Results: NAS supplementation augmented the iAUC for glucose absorption (23%, P ≤ 0.05) and blood glucose (27%, P ≤ 0.05), and attenuated the iAUC for GLP-1 (35%, P ≤ 0.05) compared to baseline, while none of these measures were altered with placebo. The GLP-2, GIP, and insulin responses to enteral glucose were similar between NAS and placebo groups, although GLP-2 and insulin were lower at 40 and 60 min, respectively, in the NAS group (37% for both vs. baseline, P ≤ 0.05).

Conclusion: In healthy humans, 2 weeks of dietary NAS supplementation (i) enhances glucose absorption, (ii) augments blood glucose responses to enteral glucose, and (iii) attenuates GLP-1 release, the latter possibly reflecting reduced glucose exposure to more distally located L-cells. This study supports the concept that NAS have a deleterious impact on acute glycaemic control, and highlights the potential for exaggerated postprandial glycaemic excursions in high habitual NAS consumers, which could predispose to T2DM.