EXPERIMENTAL INVESTIGATION OF THE EFFECTS OF NON-CALORIC SWEETENERS ON TESTOSTERONE IN MALE MICE

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Relevance of the study: Increasing prevalence of obesity and diabetes over the past decade has stimulated the global rise in consumption of noncaloric sweeteners as alternatives to sugar. Noncaloric sweeteners are the synthetic or naturally derived food and beverage additives that provide negligible caloric content while possessing high sweetening potency. Although they are publicly perceived to be safe, recent data has begun to challenge assumptions.

Objective of the study: This study aimed to examine the endocrine and metabolic impacts of non-caloric sweeteners. The goals were to figure out how exposure to non-caloric sweeteners affects testosterone levels and to look at morphometric changes that go along with it. The research examined the fluctuations of testosterone levels in liver homogenates and plasma, in conjunction with an extensive biochemical profile analysis.

Methods and Materials: Mice were divided into 4 groups according to the sweetener: stevia, saccharine, sucrose and distilled water. Their effects were analyzed during the 70- day period with living conditions and the feeding patterns being similar among all 4 experimental groups. Biochemical blood assay, liver homogenate analysis on day 70 and morphometric studies every 10 days were recorded. This experimental study was conducted on healthy adult male mice (20 days old). Animals were maintained under standard laboratory conditions approximately 22 ± 2 °C, 12-hour light/dark cycle. Mice were divided into four groups: control (water), stevia, saccharin, and sucrose. Sweeteners were administered orally with water in supraphysiological doses for 75 days. All groups were kept under identical environmental and feeding conditions. Body weight and body length were detected every 10 days to assess changes in body composition. On day 70, blood samples were collected under anesthesia, and plasma was separated for biochemical analysis. Total testosterone levels were measured using enzyme-linked immunosorbent assay (ELISA). Data were expressed as mean ± standard deviation. Statistical analysis was performed using one-way ANOVA followed by post hoc Tukey's test. A p-value < 0.05 was considered statistically significant.

Results and Discussion: Liver homogenate and blood plasma analysis of noncaloric sweetener groups, as well as, sugar group revealed testosterone reduction by 1.5-2-fold magnitude in comparison to the control group. Physical measurements demonstrated severe obesity for the sugar group and irregular weight loss for the noncaloric sweeteners.
This study shows that long-term exposure to both non-caloric sweeteners and sugar at very high doses can lower testosterone levels significantly, which could mean that the endocrine system is being disrupted. The 1.5–2-fold reduction noted in liver homogenate and plasma indicates that

these substances may disrupt steroidogenesis or the regulation of the hypothalamic–pituitary–gonadal axis. Although sugar intake correlated with severe obesity, non-caloric sweeteners resulted in erratic weight loss, underscoring unique metabolic effects despite yielding a comparable hormonal response.

The obesity noted in the sugar group aligns with established correlations between elevated sugar consumption and adiposity, insulin resistance, and modified lipid metabolism. Conversely, the weight variations in the non-caloric sweetener groups may indicate metabolic dysregulation, modifications in gut microbiota composition, or compensatory adjustments in appetite-regulating hormones. These results indicate that the absence of calories does not inherently imply metabolic neutrality.

The significant decrease in testosterone levels across all experimental groups raises concerns about possible effects on reproductive health, adipose tissue function, and behavior. Changes in body composition may make endocrine imbalance worse because adipose tissue is involved in hormonal metabolism and aromatization. Consequently, both direct and indirect systemic effects must be taken into account when assessing the long-term safety of sugar and its substitutes.

These results highlight the necessity for additional mechanistic investigations to elucidate the involved pathways and to reevaluate the prevalent belief that non-caloric sweeteners are metabolically innocuous.

Conclusion: The changes elicited distinct consequences of chronic consumption of non-caloric sweeteners and sugar in their supraphysiological doses on body composition, healthy metabolism, as well as physiological endocrine functioning compared to the control group. The findings raise concerns not only regarding the direct effects of analyzed parameters but also towards the potential indirect effects on related systems, such as adipose tissue structure and appetite regulating hormones, reproductive system and behavioral changes. Collectively, these observations underscore the need for further investigations and increased awareness related to the use of sugar alternatives commonly perceived as safe.

Abstract:

The global rise in obesity and diabetes has increased the use of non-caloric sweeteners as sugar substitutes. The aim of the present study was to examine the endocrine and metabolic effects of stevia, saccharin and sucrose in male mice. Mice were divided into four groups: water control, stevia, saccharin, and sucrose. Sweeteners were administered orally in supraphysiological doses for 70 days under identical conditions. Body weight and length were measured every 10 days, while blood and liver samples were analyzed on day 70. Testosterone levels were measured using ELISA, and statistical analysis was performed using ANOVA. Results showed a 1.5–2-fold decrease in testosterone levels among all groups in comparison to reference range, as well as, in experimental groups in comparison to controls. The sucrose group developed severe obesity, while non-caloric sweetener groups showed irregular weight loss. Findings suggest that both sugar and non-caloric sweeteners may disrupt endocrine and metabolic functions, possibly affecting steroidogenesis and hormonal regulation. The study highlights the need for further research on the long-term safety of commonly used sugar substitutes.

Key words: Saccharine, sucrose, stevia, testosterone, weight, length, endocrine changes, metabolic alterations, obesity, weight loss**.**