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The impact of artificial sweeteners on the metabolic syndrome

Filip Czyżewski, Alicja Baranowska, Katarzyna Baranowska, Kinga Filipek, Jakub Kawka, Michał Muciek, Sebastian Mrugała, Waldemar Mrugała, Bartosz Skierkowski, Natalia Zalewska

Filip Czyżewski – corresponding author
Medical University Warsaw, ul. Żwirki i Wigury 61, 02-091 Warsaw
https://orcid.org/0009-0006-8556-6565; czyzewskifilip@gmail.com

Alicja Baranowska - Szpital Miejski w Siemianowicach Śląskich, https://orcid.org/0000-0002-0558-4194 alicja.baranowska.priv@gmail.com,

Katarzyna Baranowska - Medical University Warsaw, ul. Żwirki i Wigury 61, 02-091 Warsaw https://orcid.org/0009-0001-9345-6626 katarzynab508@gmail.com,

Kinga Filipek - Międzyleski Specialist Hospital in Warsaw, Poland, https://orcid.org/0009-0002-2758-4205 kiniafilipek@icloud.com

Jakub Kawka - Medical University Warsaw, ul. Żwirki i Wigury 61, 02-091 Warsaw, https://orcid.org/0009-0003-7046-8127, jakub.kawka00@gmail.com

Michał Muciek - Medical University Lublin, al. Racławickie 1, 20-059 Lublin, https://orcid.org/0009-0009-0657-0585 michalmuc99@gmail.com

Sebastian Mrugała – Medical University Białystok, Jana Kilińskiego 1, 15-089 Białystok
https://orcid.org/0009-0007-7307-4114 sebamrugala@gmail.com
Waldemar Mrugała - Medical University Lublin, al. Racławickie 1, 20-059 Lublin;
https://orcid.org/0009-0004-3853-0311 mrugalawaldek@gmail.com
Bartosz Skierkowski - Medical University Lublin, al. Racławickie 1, 20-059 Lublin
https://orcid.org/0009-0001-1353-4736 skierabartek@gmail.com
Natalia Zalewska – Bielanski Hospital, Warsaw https://orcid.org/0009-0009-9411-0887
natalia.zalewska2700@gmail.com

Abstract

Introduction: Metabolic syndrome is a wide-spread disease that affects even 30% of Polish population. The mentioned syndrome consists of: glucose intolerance, obesity, dyslipidaemia and high blood pressure. Change of lifestyle, particularly diet, is a crucial part of treatment of those issues. Artificial sweeteners are low-calorie or non-nutritive substances that are made for lowering sugar amounts in sweetened beverages. The use of artificial sweeteners rises among those, who want to lower their weight. Artificial sweeteners are well known substances, but their impact on health is still a matter of studies. We want to summarize the current knowledge about their impact on metabolic syndrome and its elements.

Objectives: The review and presentation of the current state of knowledge on impact of artificial sweeteners on metabolic syndrome and its components.

Material and methods: Review of the studies available on open access sources at PubMed, Google Scholar, National Library of Medicine and Coachrane.

Conclusions: Currently there is no evidence of positive impact of artificial sweeteners on the metabolic syndrome. Moreover, new studies prove a negative impact of those substances at obesity, glucose intolerance, dyslipidaemia and blood pressure. However there is a need of further studies about physiology of gut microbiota and current subject to strengthen current depth of evidence.

Keywords: Metabolic syndrome, artificial sweeteners, obesity, diabetes

Introduction and Purpose of the Study

Metabolic syndrome is a prevalent diagnosis in developed countries. According to estimates, approximately one billion people worldwide may have a diagnosed or are at risk of metabolic syndrome (1). The criteria for diagnosing metabolic syndrome according to the WHO in 1999 are listed below (1):

Fasting glucose concentration >110 mg/dl or >140 mg/dl after 2 hours in the OGTT test or treatment of diagnosed diabetes plus any two of the following:

1. HDL < 35 mg/dl in men and <40 mg/dl in women
2. Blood triglycerides >150 mg/dl or use of drugs lowering them
3. Waist/hip ratio > 0.9 in men and > 0.85 in women or BMI > 30 kg/m2
4. Blood pressure >140/90 mmHg

Type 2 diabetes is a civilization disease. Its incidence is increasing year by year in both developed and developing countries ((2)). In 1990, the number of people with diabetes was estimated at 3.9% in the male population and 3.5% in the female population. However, by 2019, this number had increased to 6.0% in the male population and 5.0% in the female population (2)Type 2 diabetes primarily affects adults. Its pathogenesis is based on insulin resistance, i.e., the resistance of GLUT receptors to the increase in blood glucose concentration. This results in a decreased glucose transport from the blood to cells and chronic high blood glucose levels. Over time, this leads to dysfunction of beta cells in the pancreas, their insufficiency, and their atrophy (3).

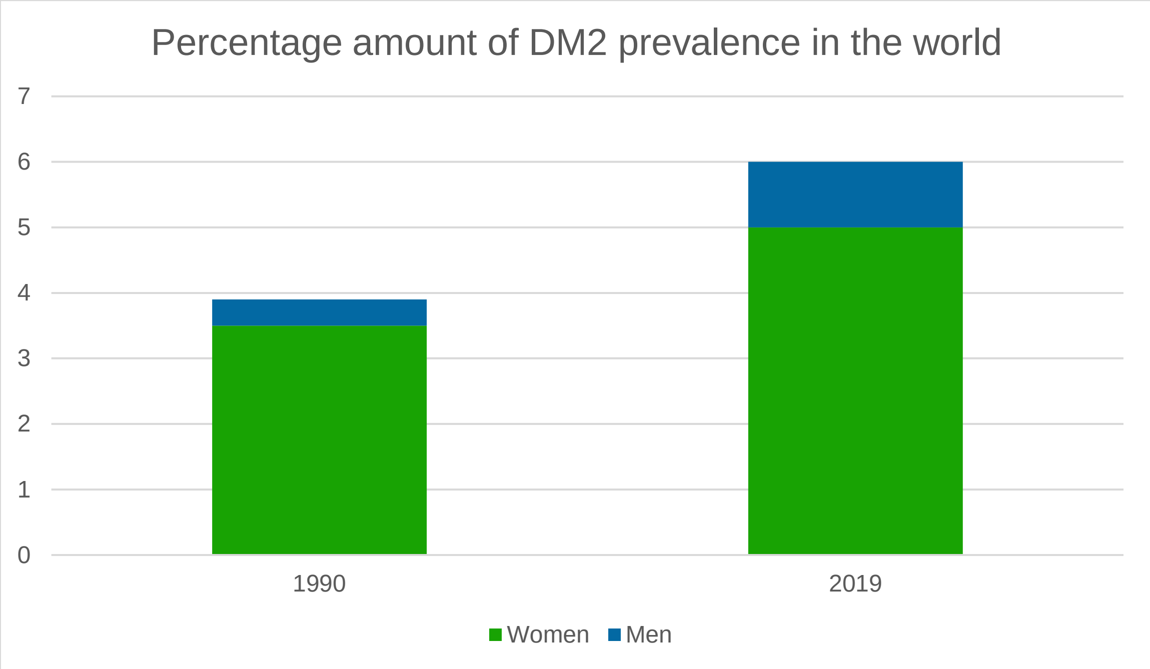

Chart 1. Comparison of the percentage of people with diabetes in 1990 and 2019 (2).

Type 2 diabetes can be diagnosed based on several diagnostic criteria:

Fasting blood glucose concentration:

Measurement of blood glucose concentration after an 8-hour fast. A concentration >126 mg/dL allows for the diagnosis of type 2 diabetes.

Oral glucose tolerance test (OGTT):

Measurement of blood glucose after 2 hours of orally ingesting 75 grams of glucose. Diabetes is diagnosed when the concentration is >200 mg/dL in the second hour of the test.

Hb A1C level in blood:

Patients with Hb A1C >6.5% in blood should be diagnosed with diabetes.

As seen, each criterion for diagnosing diabetes is based on blood glucose concentration or indirect indicators of this concentration (4). In every stage of type 2 diabetes, weight loss of approximately 10% is recommended, which reduces the risk of diabetes by up to 67% (5), improves glycemic control in those already affected, and may lead to disease remission (6). Lack of physical activity and an unhealthy diet are among the main risk factors for diabetes.

Obesity, which is a risk factor for diabetes, is also becoming increasingly prevalent worldwide (7). Between 1975 and 2014, the prevalence of obesity (BMI >30kg/m^2) increased from 3.2% to 10.8% in adult men and from 6.4% to 14.9% in adult women (7). Obesity is a multifactorial disease, but one of the main factors is caloric surplus in the diet. Switching from sugar-sweetened beverages to artificially sweetened ones is one of the proposed methods of dietary change by dietitians (8).

Artificial sweeteners (aspartame, acesulfame K, sucralose, stevia) are substances with no or negligible nutritional value. Their consumption, mainly in beverages, has been increasing for many years (9). They are about 200 times sweeter than sucrose and, in small doses, stimulate taste receptors without triggering insulin release dependent on these receptors (10).

Due to the trend of replacing sugar-sweetened beverages with beverages sweetened with the above-mentioned sweeteners, we will examine their impact on metabolic syndrome, and its elements as diabetes, obesity, blood-cholesterol level and blood pressure as these are the patients who potentially benefit the most from them.

Methods

The study contains data available in commonly accessible databases such as PubMed, the National Library of Medicine, Google Scholar, Cochrane, and Wiley. When searching for materials, we used keywords such as "artificial sweeteners," "diabetes," "metabolic syndrome," "glucose levels," "obesity," "hypertension," and "cholesterol." Articles were selected based on their title, abstract, and publication date. All articles were originally in English.

State of Knowledge

Impact of Sweeteners on Blood Glucose Levels

In most studies, artificially sweetened beverages were compared with sugar-sweetened beverages (11-14). The effects of artificial sweeteners on parameters such as fasting glucose concentration (mmol/L), insulin levels (mU/ml), and body weight (kg) were investigated. Studies including a diverse sample of participants (14, 15) showed no significant impact of artificial sweeteners on any of the above parameters compared to sucrose. However, there is evidence that patients already diagnosed with type 2 diabetes may benefit from replacing sugar-sweetened beverages with those sweetened with artificial sweeteners (11-13). In these studies, patients had better daily glucose profiles and less glucose variability during 24-hour monitoring. Interestingly, some newer studies suggest the opposite effect. According to them, patients with type 2 diabetes who consume artificially sweetened beverages have higher blood glucose levels, increased atherosclerosis, and overall mortality compared to those consuming beverages sweetened with sucrose (8). Some studies have also shown an increased risk of developing metabolic syndrome and type 2 diabetes in patients consuming artificially sweetened beverages compared to those who do not (16). In the diabetic population, beverages with artificial sweeteners have a negative impact on HbA1C values compared to natural sweeteners (sugar, low-calorie natural sweeteners, placebo). However, these differences were not significant for disease treatment and control (0.1% difference)(17). The authors cite the proven harmful effects of artificial sweeteners on gut microbiota, which contribute to sucrose intolerance, increased sweet taste threshold, and behavioral changes in individuals using artificial sweeteners excessively (8, 16, 18). Another issue with high doses of sweeteners is the stimulation of insulin secretion through sweet taste receptor activation (8, 19).

In light of conflicting facts, authors agree that further research in this field is needed to make a credible judgment about the impact of sweeteners on blood glucose levels.

Impact of Sweeteners on Body Weight

In studies observing patients over a short period, replacing sugar-sweetened beverages with artificially sweetened ones positively affected weight loss by reducing the energy load of meal(20-22) The beneficial effect of artificial sweeteners on weight loss is due to a general decrease in calorie intake, as beverages sweetened with them substituted for high-calorie sugary drinks (23). Weight gain or loss was assessed based on changes in BMI (kg/m^2). Larger systematic reviews and meta-analyses do not confirm this claim and at most suggest a neutral effect of these substances on weight loss(24, 25). Newer studies demonstrate a correlation between consumption of artificial sweeteners and weight gain (8, 16, 26). The proposed mechanism is increased consumption of sweet carbohydrates due to habituation to the sweet taste. Additionally, artificial sweeteners activate T1R2/T1R3 receptors in the oral cavity, triggering the cephalic phase of insulin secretion. These receptors are also found in the small intestine, where they are activated by artificial sweeteners, triggering the intestinal phase of insulin release. This leads to insulin resistance and glucose intolerance (27), and consequently to weight gain. However, a large meta-analysis examining the overall effect of a sweet taste in the diet on weight gain found no correlation between sweet taste and weight gain (28). Nevertheless, the study did not specifically examine artificial sweeteners, but rather all types of sweet products. Large studies also indicate the negative impact of artificial sweeteners on gut microbiota (18, 29).

As seen, the mechanisms leading to increased blood glucose levels are very similar to those affecting weight gain. However, weight gain depends on many behavioral factors. Patients using products sweetened with artificial sweeteners tend to consume a more processed and calorie-dense diet (16). Researchers have confirmed the relationship between sucralose consumption and high-fat diets (8), which have a higher caloric load. These conclusions do not include other artificial sweeteners (8).

Impact on Lipid Profile

Animal studies have shown a decrease in the anti-atherosclerotic effect of HDL in animals fed with artificial sweeteners (30). The proposed mechanism involves modifying apo-A-1 production by artificial sweeteners in the body, thereby altering the structure of HDL. Studies examining this topic have reached conflicting conclusions. A large meta-analysis from 2023 examining this issue showed a slight increase in LDL in healthy individuals (31). A higher LDL level is associated with an increased risk of obesity and, consequently, metabolic syndrome (32). WHO also confirms the decrease in HDL fraction, increase in LDL, and total triglyceride levels in their meta-analysis from 2022 (33). The reasons why artificial sweeteners would contribute to dyslipidemia are not clear. Molecular mechanisms have only been studied in animal cells so far (30).

Impact on Blood Pressure

Patients consuming artificially sweetened beverages had increased blood pressure compared to those who did not drink them (34-36). Moreover, there is evidence that individuals consuming artificially sweetened beverages are more likely to develop hypertension than those consuming beverages sweetened with sucrose (37). The impact on gut microbiota and behavioral changes are proposed mechanisms for the increase in blood pressure. Dysbiosis of gut microbiota leads to oxidative stress, increased inflammatory markers, and impaired nitric oxide production (8, 36, 38). Additionally, the synergistic effect of consuming artificially sweetened beverages along with salt-rich foods significantly contributes to this phenomenon (16, 36, 38). Another mechanism leading to the development of hypertension may be the influence of other components of sweetened beverages. This was demonstrated by a study confirming that cola-type beverages have a greater impact on the development of hypertension than beverages sweetened with other types of artificial sweeteners (39). Phosphorus compounds or dyes in these beverages are suspected to be responsible for this effect (39).

Discussion

Both the number of people with metabolic syndrome and the consumption of artificial sweeteners are increasing every year. Replacing sugar-sweetened beverages with those sweetened with artificial sweeteners was supposed to sound like one of the reasonable approaches to gradually change the lifestyle of these patients. However, new knowledge about gut microbiota and a longer familiarity with artificial sweeteners show that this is not necessarily the optimal approach. Dietary habits of patients, which are difficult to isolate from the influence of sweeteners themselves, also significantly affect the interpretation of study results. The discrepancy between older studies (showing positive effects of artificial sweeteners) and newer ones (indicating their neutrality or harmfulness) is why further work will be needed to draw correct conclusions. Further development of knowledge about gut microbiota and its importance to human health will certainly be important in understanding the mechanisms of artificial sweeteners' impact on parameters covered in this study. Nevertheless, there is potential in beverages sweetened with artificial sweeteners for individuals closely monitoring their diet as a substitute for sugar-sweetened beverages when they want to lose weight.

Summary

Currently, there is no evidence for the beneficial effects of artificial sweeteners on the development of metabolic syndrome and/or its components. On the contrary, recent studies indicate a negative impact of consuming artificial sweeteners on blood glucose levels, body weight, lipid profile, and blood pressure. When comparing artificial sweeteners with sucrose, the differences between them are only visible in the amount of consumed calories, which positively affects weight loss only in the population controlling the rest of the diet. Significant limitations of studies regarding dietary habits make the interpretation of results difficult. Further research in this field is necessary.

Author's Contribution

Conceptualization: F. Czyżewski; methodology:J. Kawka; software:N. Zalewska; check: F. Czyżewski, A. Baranowska; formal analysis: S. Mrugała; investigation: F. Czyżewski, W. Mrugała, K. Filipek, M. Muciek, B. Skierkowski; resources: F. Czyżewski, W. Mrugała, k. Filipek, M. Muciek, B. Skierkowski; data curation: K. Baranowska, N. Zalewska; writing – rough preparation: F. Czyżewski, N. Zalewska, K. Baranowska, A. Baranowska, M. Muciek; writing – review and editing: F. Czyżewski, J.Kawka, S. Mrugała, W. Mrugała, K. Filipek, B. Skierkowski; visualization: K. Baranowska, B.Skierkowski; supervision: F. Czyżewski, N. Zalewska; project administration: F. Czyżewski;

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Conflict of Interest

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