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The effect of artificial sweeteners on glycemic parameters of type 2 diabetes

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A B S T R A C T

Abstract
Development of instruments to measure habitual dietary intake in large epidemiological studies has been investigated extensively. The purpose of this study was to develop a computer-assisted personal interview system (CAPI) system for conducting dietary assessment. A 168-item food frequency questionnaire (FFQ), originally developed for the Tehran Lipid and Glucose Study, is used widely in food and nutrition studies in Iran. In addition to measurement errors at data recording and entry levels, the printed form is time-consuming and costly, both financially and environmentally. This technical report introduces a computer-assisted personal interviewing (CAPI) program to collect food and nutrition data using the Iranian 168-item FFQ. The U.S. Census Bureau's CSPro software was used to construct the CAPI application. The application runs on Android devices and computers with Microsoft Windows operating systems. The language of the CAPI is Farsi. This easy-to-use CAPI tool attempts to reduce time, cost, and human error in nationwide and local nutrition research.

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Introduction

Type 2 diabetes mellitus (T2DM) is the predominant form of diabetes worldwide which includes 90% of all diabetic patients in developed and developing countries. The International Diabetes federation has estimated 415 million diabetic patients in 2015 worldwide and it is estimated that this number will rise to 642 million until 2040 [1].

The most common complications of diabetes are end-stage of renal disease, non-traumatic lower extremity amputations, cardiovascular disease and blindness. Diabetes mellitus will also lead to morbidity and mortality of the suffering patients [2]. The 4.6 million subjects of diabetes were also reported in Iran in 2015 [3-5]. Medical nutritional therapy is an important approach in preventing, managing, and slowing the rate of development of diabetes complications. The most agreed-upon recommendation is the diet with low sugar and refined carbohydrates, and relatively high in soluble fibers [6]. Artificial sweeteners are synthetic compounds with 160 to 13,000 times sweeter than that of sucrose [7]. Natural sweeteners like sucrose and fructose contain calories which can be harmful for humans when taken in high quantities. So, these compounds are considered as attractive substitutes for sugar and

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are consumed for different purposes including weight loss, dental care, prevention of diabetes mellitus and hypoglycemia [8, 9].

Regarding to the increasing prevalence of diabetes in Iran, further intervention for treating and managing the diabetes seems to be critical. Thus, the medical nutrition therapy has the main role in treating and preventing diabetes [10]. The consumption of artificial sweeteners among diabetic patients is growing. Therefore this study aimed to evaluate the effects of artificial sweeteners on fasting blood glucose (FBG), 2 hours postprandial blood glucose (2hPP), Glycated Hemoglobin (HbA1c) and body mass index (BMI).

Subjects and methods
Patients

In this clinical trial thirty type 2 diabetic patients were randomly selected (10 males and 20 females) of those who referred to endocrine part of Baharestan clinics of Tabriz university of medical sciences. Inclusion criteria were age between 25-70 years, with at least six months of diabetic history, use of blood glucose lowering drugs without insulin therapy, 25<BMI<35, HbA1c in range of 6.5-7.5, with no significant weight changes and without consuming artificial sweeteners over the past three months before the trial. Before sampling, written informed consent was obtained from all patients. This clinical study was also approved by ethics committee of Tabriz University of medical sciences. Ethical code (93101) and IRCT registration number (IRCT2015091513612N6).

Diet intervention and sampling

A fasting and two hours postprandial blood samples were collected from all patients at baseline and the end of each phase of trial. Biochemical parameters including FBG, 2hPP and HbA1c were analyzed in both the first and the second trimester as control and case group, respectively. It was emphasized that all patients

have to avoid artificial sweeteners containing foods such as biscuits, chocolates, sugar,

Table 1. General characteristics of individuals

	Mean±SD (range)	Confidence interval 95%
Age (years)	51.6±15.6(25-70)	(45.75-57.42)
Height (cm)	161.91±11.99	(157.42-166.39)
Weight (kg)	82.40±14.35	(77-87.70)
Body mass index (Kg / m2)	31.6-5.5 (25-35)	(29.52-33.62)

Values are expressed as mean± SD (ranges in parenthesis).

beverages and use prescribed drugs for diabetes accompanying diabetic diet for the first trimester. For the second trimester, artificial sweeteners containing foods which included sugar, biscuits and chocolates were used under the supervision of a nutritionist. Candy, biscuits and sugar were contained Acesulfame potassium and saccharin, respectively. Dosage and type of medication were not changed during the trial. After the second trimester, final blood samples were collected.

Laboratory measurements

Serums were separated from whole blood by centrifuging at the end of every trimester and stored in -200C before analysis. The level of biochemical parameters including FBS, 2hPP were measured using enzymatic method by glucose kit (Pars Azmoon, 117500). HbA1c was also evaluated using diagnostic kit (Bionik, 304169). All measurements were performed by BT-3500 auto-analyzer system (Biotecnica instrument, Italy).

Statistics

Results were expressed as mean ± standard deviation (SD). SPSS 20 software was used for data analysis. The statistical significance of the results was determined using Kruskal-Wallis, paired t-test and non-parametric tests. $P < 0.05$ was considered as statistical significant.

Results

General characteristics of individuals are shown in table 1. The average age and BMI of

Table2. Comparison of biochemical parameters between groups

Parameters	Number	The beginning of first trimester (The usual diabetic diet)	The end of first trimester	The end of second trimester (Artificial sweeteners)	P-value
FBS(mg/dl)	30	124±21	121±25	152±42	*0.040
HbA1C (%)	30	7.1±1	6.8±0.9	7.40±1.2	*0.040
2hpp (mg/dl)	30	162±38	164±24	222±7.2	*<0.001
BMI(kg/m²)	30	31.6±5.5	31.4±48.5	31.5±5.75	0.596

Values are expressed as mean± SD. p< 0.05 was considered as statistically significant.

the participants were 51.60±15.67 and 31.62±5.53, respectively.

As shown in table 2, a significant increase in FBS (p=0.04), HbA1c (p=0.04) and BS 2hpp (p<0.001) parameters was observed at the end of the second trimester in comparison with the beginning of the first trimester (the usual diabetic diet). No significant differences were observed in BMI parameter between groups (p=0.596).

Discussion

About thirty million diabetic people were estimated in 2014 in the United States, in which over 25% of this population remained undiagnosed. Since 2007, the prevalence of this disease has increased from 7.8% to 9.3%. The increasing burden of diabetes may be because of population aging, obesity, sedentary lifestyles, consumption of simple sugars and calorie-dense foods, particularly among ethnic groups with greater susceptibility to the disease [11].

Because of the associated microvascular and macrovascular disease, diabetes accounts for almost 14 percent of United States health care expenditures. So that, one-half of them are related to complications including myocardial infarction, stroke, end stage of renal disease, retinopathy and foot ulcers [6, 11].

The goals of therapy for diabetes mellitus are to eliminate symptoms related to hyperglycemia, reduce or eliminate the long-term microvascular and macrovascular complications and allow the patient to achieve normal lifestyle standards [6]. Medical nutrition therapy is a term used by the American diabetes association to describe the optimal coordination of caloric intake with other aspects of diabetes therapy including insulin, exercise and weight loss. Primary prevention measures of medical nutrition therapy are directed at preventing or delaying the onset of type 2 diabetes in high-risk individuals (obese or prediabetes) by weight reduction [5, 6].

A 2013 review reported that there are insufficient evidences to suggest that replacing dietary sugar with non-caloric sweeteners alone is beneficial for energy balance, weight loss, or diabetes risk factors. This review clarified that restriction of calorie input is more important than sugar avoidance for weight management. However, replacing dietary sugar with non-caloric sweeteners was useful for managing blood sugar in diabetes patients with the recommendation of moderate usage of sweeteners [12].

Vermunt et al [13] also have shown that no short-term weight loss differences were observed after aspartame use as compared to sugar in obese subjects following a controlled energy-restricted diet. However, consumption of aspartame was associated with improved weight maintenance after a year.

Furthermore, Lawrence et al [14] reported that sugar-sweetened beverage consumption was associated with significantly elevated risk of type 2 diabetes, whereas the association between artificially sweetened beverages and type 2 diabetes was largely explained by health status, pre-enrollment weight change, dieting, and body mass index. A positive association between artificially sweetened beverages and fruit juice consumption and incidence of type 2 diabetes has also reported in Imamura et al study [15]. Other studies have revealed that sweeteners affect increase of blood sugar in a shorter time period (less than one year) than BMI [16].

On the other hand, Raben et al [17] have shown increased energy intake, body weight, fat mass and blood pressure after 10 week consuming large amounts of sucrose (28% of energy). These effects were not observed in individuals who consumed artificial sweeteners. There is also evidences that sugar-sweetened beverages may increase the risk of metabolic syndrome and type 2 diabetes not only through obesity but also by increasing dietary glycemic load, leading to insulin resistance, β-cell dysfunction, and inflammation, according to a 2010 meta-analysis [18]. The effects of artificial sweeteners and the risk of cancer remain unclear since 2015 [19]. It is while, the United State Food and Drug Administration regulates artificial sweeteners as food additives [20].

According to a controversial study artificial sweeteners may contribute to increase diabetic complications. Researchers in Israel found that artificial sweeteners used in diet drinks and other foods can disrupt healthy microbes that live in the gut, leading to higher blood sugar levels which is an early sign of diabetes [21].

Some studies have shown benefits of artificial sweeteners consumption and little induction of a glycemic response [22,23]. Whereas, others demonstrated association between artificial sweeteners consumption and weight gain and increased risk of type 2 diabetes [24, 25]. However, the use of artificial sweeteners by individuals suffering from metabolic syndrome make it difficult to interpret different findings.

Most Artificial sweeteners pass through the human gastrointestinal tract without being

digested by the host and thus directly encounter the intestinal microbiota, which play central roles in regulating multiple physiological processes [26-28]. Composition and function of microbiota are affected different metabolic states such as obesity and diabetes mellitus [29-32]. It has been proven that microbiota alterations have been associated with metabolic syndrome tendency [33].

In this study we compared artificial sweetener with frequent diabetic diet at 6 months. HbA1C, FBS and 2hpp increased significantly after artificial sweetener diet compered to frequent diabetic diet. No significant differences were observed in BMI between groups. As described previously, body mass index did not change in short time duration of artificial sweeteners and long term use of it, which may lead to weight gain.

Acknowledgments

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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