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Original Article

The effects of glucose and fructose on body weight and some biochemical parameters in rats

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Summary. *Objective:* Dietary fructose from added sugar as high fructose corn syrup may causes major risks in obesity, hyperlipidemia, cardiovascular diseases, hyperuricemia and fatty liver. The aim of this study was to investigate and compare the effects of high fructose and high glucose intake on body weight and some biochemical parameters in rats. *Subject and methods:* The study was conducted on adult, 32 Wistar albino male rats (300-350 g weeks) which fed with standard laboratory chow. In each group, 8 rats was selected randomly and which was be composed four groups. The rats in each group, in addition to standard meal, different amount of glucose and fructose containing solutions (10% and 30% glucose-fed group, 10% and 30% fructose-fed group) was given by oral gavage for 6 weeks. At baseline and after 6 weeks total cholesterol, VLDL-cholesterol, triglycerides, uric acid, AST and ALT as biochemical parameters and liver histopathological examination of rats were determined. Body weight of the rats was evaluated every week. *Results:* The 30% fructose group caused higher AST levels according to 10% glucose group, 30% glucose group and 10% fructose group. At the end of 6 weeks, the mean body weight in the fructose-fed groups was higher than the glucose-fed groups ($p>0.05$). No statistically significant difference between rat groups' portal inflammation rates were found and the moderate and severe ballooning were observed in 30% fructose rats ($p<0.05$). *Conclusions:* As a result, dietary fructose from added sugar as high fructose corn syrup may causes major metabolic disorders.

Key words: fructose, glucose, body weight, biochemical parameters, portal inflammation

Introduction

Fructose, commonly known as fruit sugar, is also a major component of sweeteners such as table sugar, honey and high fructose corn syrup (HFCS) (1). Although fructose is a simple sugar that exists naturally in fruits and vegetables, the majority of dietary fructose comes from two sweeteners, sucrose and high-fructose corn syrup, which are commonly used in manufactured foods and beverages (2). Since the beginning of 20th century, fructose consumption has increased 4-fold by the introduction of HFCS (1). Especially, fructose consumption has increased as usage of HFCS in the Western diet. Based upon disappearance data, the annual per capita intake of HFCS from 1967 to 2006 increased from 0.03 to 58.2 lbs, whereas sucrose decreased from 98.5 to 62.3 lbs. Sucrose is a disaccharide and consists of 50% fructose and 50% glucose. The HFCS form used in soft drinks compose of 55% fructose, 42% glucose, and 3% oligosaccharides. Because of the higher fructose dose, soft drinks sweetened with HFCS would provide more fructose into the systemic circulation than soft drinks sweetened with sucrose. Furthermore, HFCS provides an immediate source of free fructose and glucose, whereas sucrose must first be broken down by sucrase (2,3). An increasing amount of fructose in the diet is suggested to play a causal role in the pathogenesis of the metabolic syndrome, insulin resistance, impaired glucose tolerance, type 2 diabetes, obesity, hyperlipidemia, cardiovascular diseases, hype-

ruricemia and fatty liver (4). Fructose does not increase the satiety signals of blood glucose and insulin to the same extent as does sucrose or glucose. Short-term food intake is inversely related to the glycemic and insulin responses to sugars, and it has been proposed that fructose does not suppress gastric appetite hormone and reduced insulin and leptin signaling in the brain. High fructose causes an increase in the synthesis of non-esterified fatty acids production. Fructose is lipogenic and stimulates triglyceride synthesis. Acute oral or intravenous administration of fructose results in a rapid increase in serum levels of uric acid through accentuated degradation of purine nucleotides and increased purine synthesis. The aim of this study was determined the effect of different amounts of fructose and glucose in rats to body weight and some biochemical parameters.

Material and Methods

Experimental design

This research conducted in Baskent University Production and Research Centre for Experimental Animal, Ankara, Turkey. This study was approved by Baskent University Ethical Committee for Experimental Resarch on Animals (Project no: DA14/14) and supported by Baskent University Research Fund.

Male rats were divided into four groups with each group comprising of eight animals. Male Wistar albino rats (32 weeks) weighing 300-350 g were randomly assigned to one of the four groups; 10% glucose-fed group, 30% glucose-fed group, 10% fructose-fed group and 30% fructose-fed group.

Group 1 n(8): Standart pellet+10% HFCS

Group 2 n(7): Standart pellet+30% HFCS

Group 3 n(8): Standart pellet+10% glucose solution

Group 4 n(7): Standart pellet+30% glucose solution

Sample size calculated on the basis of probability distribution of the measured values with a given significance level (e.g., 5%), medium effect size (e.g., 0.35) and the power of test (e.g., 85%). This analysis was performed using G*Power 3.1.3 software program.Thus, the total sample size was obtained in 32 rats. All animals were housed in cages and subjected to a 12 h light-dark cycle at 24 ± 2 oC and animals were fed on a standard pellet diet and water ad libitum. The solutions have been prepared by feeding to rats, at four concentrations, 10 and 30 g/ 100 milliliter glucose; 10 and 30 g/ 100 milliliter fructose. Solutions to be administered by gavage were stored at 4°C and warmed to room temperature. The follow-up terminated at the end of 6 weeks.

Evaluation of Measurements

At baseline and at the end of the 6 weeks, total cholesterol (TC), VLDL-cholesterol (VLDL-C), triglyceride (TG), uric acid (UA), alanine aminotransferase (ALT), aspartate transaminase (AST) measurements were sampled. For the experiment; the animals were starved overnight for 12 h before the blood collection process and approximetly 1mL blood sample was collected from each rat by snipping the tail using heparin anti-coagulant under diethyl ether anaesthesia. Then, plasma was obtained from the blood using a centrifuge at 4 °C for 15 min. Serum total cholesterol, triglyceride and uric acid levels were assayed by enzymatic tests, using an AbbottÒ Architect C8000 Analyzer according to the manufacturers specifications. (Abbott Park, IL, USA). VLDL cholesterol was calculated from measurements obtained for triglyceride using the following formula: VLDL = Triglyceride/5 (mg/dL). Serum ALT and AST levels were assayed by an UV test according to standardized method, using an Abbott© Architect C8000 Analyzer according to the manufacturers specifications. (Abbott Park, IL, USA). Body weight was measured weekly during the follow-up.

Liver histopathology

Histopathologic examination was carried out at the end of 6 weeks. Steatohepatitis was evaluated using the grading and staging system of Brunt et al. (5). The grades were classified as grades 0-4, which were based on the percent of hepatocytes involved in the biopsy (0: none, 1: 10%, 2: 10–33%, 3: 33–66%, 4: 66%).

Statistical analysis

The results were expressed as mean±SD or mean (95% CI). Paired t-tests were used to estimate the presence of changes in study parameters for each experiment group (e.g., Group 1: 10% HFCS; Group 2: 30% HFCS; Group 3: 10% glucose solution; Group

Table 1. Effect of fructose and glucose feeding on biochemical parameters and systolic blood pressure for 6 weeks

	10% Glucose		p[1]	30% Glucose		p[2]	10%Fructose		p[3]	30% Fructose		p[4]
	Baseline	After 6 Weeks		Baseline	After 6 Weeks		Baseline	After 6 Weeks		Baseline	After 6 Weeks	
Cholesterol	75.6±14.95	110.8±64.19	0.184	92.6±36.88	93.8±57.32	0.879	69.5±10.83	72.7±11.10	0.554	69.8±8.11	74.1±16.11	0.249
VLDL-C	14.0±3.52	37.2±37.43	0.177	17.9±9.25	20.3±15.49	0.418	16.0±5.14	17.1±4.67	0.596	14.0±2.94	16.9±5.55	0,242
Triglycerid	70.0±17.60	186.0±187.34	0.179	89.5±46.25	101.5±77.47	0.418	80.0±25.71	85.3±23.36	0.596	70.0±14.71	84.7±27.77	0.242
Uric asid	1.46±0.51	2.0±0.36	0.061	1.33±0.19	1.53±0.60	0.359	1.3±0.26	1.3±0.34	0.547	1.4±0.29	2.0±0.36	0.006*
ALT	74.8±64.19	65.4±20.05	0.620	54.2±17.81	53.5±10.23	0.907	65.6±16.68	74.6±31.05	0.544	69.6±24.64	89.0±19.44	0.015*
AST	124.8±71.36	177.7±50.6	0.010*	116.3±7.53	119.1±24.13	0.754	97.3±11.85	134.8±48.34	0.067	106.0±27.39	206.3±47.23	0.002*

p^{1-4}:The significance test of differences between baseline and after six weeks values for each group.
VLDL-C:VLDL-Cholesterol

4: 30% glucose solution), In addition, the absolute changes (the difference between baseline values and after six weeks values) were tested between groups using one-way ANOVA. The distribution of changes was evaluated for normality assumptions using One Sample Kolmogorov–Smirnov test. The Fisher exact test was used for proportions. SPSS version 21.0 was used to analyze the recorded data. Significant values of p<0.05 were considered to be statistically significant.

Results

The mean of plasma UA, TG, TC, VLDL-C, ALT and AST at baseline and after the six weeks were shown in Table 1. It was found that the significant differences in mean values of AST in 10% glucose-fed group (p=0.010); uric acid, ALT and AST in 30% fructose fed group (p=0.011, p=0.015, p=0.002, respectively). The 30% fructose group caused the difference in AST levels according to 10% glucose group, 30% glucose group and 10% fructose group.

The difference of the initial and final body weight were shown in Figure 1. After a 6 week trial, the mean body weight in the fructose-fed groups was higher than the glucose-fed groups, but there were no significant differences in body weight gain among groups (p>0.05) (Figure 1).

The effect of fructose and glucose feeding on portal inflamation and hepatocyte ballooning in rats' livers for 6 weeks were shown in Table 2. No statistically significant difference between rat groups' portal inflammation rates were found. Both 10% fructose and 30% fructose groups, 2 of the 8 rats were observed mild inflammation. There were statistically significant differences between the rat groups in terms of hepatocyte ballooning (p=0.025). Mostly, the moderate and severe ballooning were observed in 30% fructose rats (Table 2).

Discussion

When we analyzed the difference of body weight during a 6 week treatment, the mean body weight in

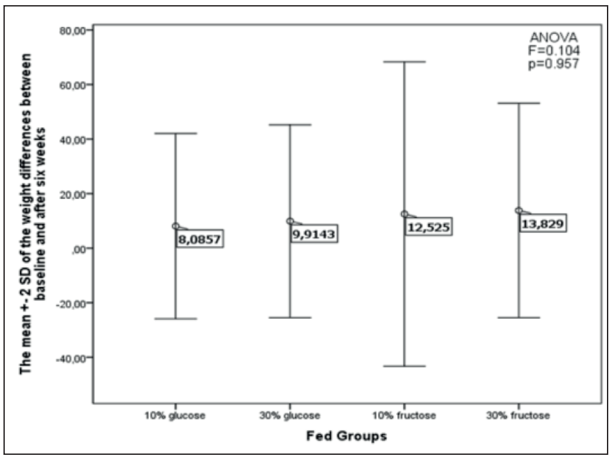

Figure 1. Effect of fructose and glucose feeding on body weight in rats for 6 weeks

Table 2. Effect of fructose and glucose feeding on portal inflamation and hepatocyte ballooning in rats' livers for 6 weeks

	10% Glucose		30% Glucose		10% Fructose		30% Fructose		
	n	%	n	%	n	%	n	%	
Portal Inflamation									
No	7	26.9	7	26.9	6	23.1	6	23.1	p=0.886
Mild	1	25.0	-	-	2	50.0	1	25.0	
Hepatocyte Ballooning									
No	3	25.0	5	41.7	-	-	4	33.3	p=0.021*
Yes	5	27.8	2	11.1	8	44.4	3	16.7	

the fructose-fed groups has shown higher than the glucose-fed groups (p>0.05) (Figure 1). This study was suggested that the weight gain by fructose feeding as previous studies.Over the past several years, the reasons for the increase in obesity prevalence have shown that increased the sugar added to food and it has taken the place of the sucrose to HFCS by researchers (6-8). HFCS caused an increase in body weight greater than sucrose in both male and female rats. This increase in body weight was accompanied by an increase in fat cumulation and circulating levels of TG (9).

In recent studies having drawn attention to fructose has emphasized the absence of satiety such as other sugars. Plasma glucose and insülin levels effected the state of satiety after food consumption. Although fructose does not contribute to the feeling of fullness, has the same energy load with the blood sugar glucose. Therefore, as long as the amount of glucose decreases and the amount of fructose increases, the feeling of fullness occurs later and it is consist of more eating behavior (10,11). The excessive consumption of HFCS may contribute to the incidence of obesity by reducing insulin and leptin levels (12). The intake of HFCS would not lead to insulin or leptin-induced satiety. Because fructose leads to increased plasma free fatty acids, leptin, adiponectin, abdominal adipose tissue and impaired insulin sensitivity (13,14). The recent studies demonstrate that compared to pure glucose, chronic fructose feeding does not suppress the appetite hormone ghrelin and does not provide enough insulin and leptin secretion (15,16). In a study which was analyzed the long-term effects of HFCS on body weight, the rats with access to HFCS gained significantly more body weight than sucrose groups (9). Fructose (or sucrose) administration to humans and rats also induces attributes of liver diseases and may have a role in the pathogenesis of fatty liver diseases (17,18). The fatty liver disease includes a broad spectrum of manifestations of fatty liver, ranging from steatosis alone, steatosis with inflammation, steatosis with hepatocyte injury, or steatosis with sinusoidal fibrosis in relation to the progress of the pathological state (19,20). In this study we investigated whether fructose could play a role metabolic disorders in liver.

Administration of high doses fructose can also cause elevation of portal inflamation rates hepatocyte ballooning. The moderate and severe ballooning were observed in most 30% fructose rats. But there were no statistically significant difference between rat groups' portal inflammation rates were found. If only both 10% fructose and 30% fructose groups, 2 of the 8 rats were observed mild inflammation. Ackerman et al., demonstrated that implementation of fructose to rats results in hepatic steatosis with a 198% increase in hepatic triglycerides and an 89% increase in hepatic cholesterol concentration and Davail et al., evidenced high fructose diets also develop fatty liver (21,22)

Conclusion

As a conclusion, dietary fructose from added sugar as high fructose corn syrup may causes major risks in obesity, fatty liver disease, insulin resistance, hyperlipidemia, impaired glucose tolerance, Type 2 diabetes, cardiovascular diseases, hyperuricemia, gout and meta-

bolic syndrome. So, the healthy preference of fructose source in diets is fruit and the amount of safe dietary intake of fructose may accept as 10% of total energy.

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