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Fructose and Oxidized LDL in Pediatric Nonalcoholic Fatty Liver Disease: A Pilot Study

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Introduction

Diet changes are a primary lifestyle change recommended in the treatment of pediatric nonalcoholic fatty liver disease (NAFLD), however, it is not clear which diet components are the most important to target. In the U.S., the consumption of fructose has increased nearly 50% and, on average, adolescents have a high intake (12% of total daily calories).¹ Diets high in fructose are known to increase plasma lipids and oxidative stress², both areas suspected in NAFLD pathogenesis. Recently, NAFLD patients were found to consume more fructose compared to matched controls.³ Given this and our previous animal studies⁴, we designed a pilot study evaluating a low-fructose diet in children with nonalcoholic fatty liver disease.

Methods

This was a randomized, controlled, 6-month pilot study of 10 children with NAFLD using diet education; low-fructose versus low-fat. Seven children had a confirmatory liver biopsy demonstrating nonalcoholic steatohepatitis (NASH), and the remainder were diagnosed using serology and ultrasound. Written informed consent/ assent was obtained and the study

The authors have no conflicts of interest with regard to this study.

was approved by the Children's Memorial Hospital Institutional Review Board and the Northwestern University General Clinical Research Center (GCRC), Chicago.

The low-fructose diet consisted of eliminating: 1) sugar containing beverages; 2) fruit juice and 3) food items with high-fructose corn syrup (HFCS) as one of the top 5 ingredients on the label. The low-fat diet was based on the American Heart Association recommendations. All subjects were given standard activity advice. Diet was assessed using a multiple-pass 24-hour dietary recall at 0, 1, 5 and 6 months⁵ and analyzed using the Nutrition Coordinating Center's Food and Nutrient Database at the University of Minnesota.

Morning blood and urine samples were obtained after an overnight fast. Oxidized low density lipoprotein (oxLDL) was measured using ELISA (Alpco Diagnostics, Uppsala, Sweden) and urinary isoprostanes by commercially available kit (Oxford Biomedical Research, Rochester Hills, MI). The association between oxLDL and fructose was compared using Pearson's correlation. Data analysis was done using SPSS version 16.0 (Chicago, IL).

RESULTS

Mean age was 13.3 ± 0.65 years for the low-fructose group compared to 12.5 ± 1.0 years for low-fat, $p = \text{ns}$. At baseline, subjects in the low-fructose group reported lower total energy intake ($p = 0.03$, Table 1), however energy intake controlling for weight was not significantly different (29.6 ± 3.3 kcal/kg/day compared to 22.5 ± 2.7 , $p = 0.14$).

For all 10 subjects, at baseline, oxLDL significantly correlated with both total fructose ($r=0.66$, $p = 0.04$) and percent energy from fructose. After six months, oxLDL was significantly decreased in the low-fructose group ($p = .03$) but unchanged in the low-fat group. Change in ALT was not significant in either group.

Comment

In animal studies, a high fructose diet induces a "metabolic syndrome", including insulin resistance, hypertriglyceridemia, abdominal obesity, hypertension and hepatic steatosis as well as oxidative stress.⁶ In this study, we show that oxidized LDL correlates with fructose intake and a low-fructose diet education was associated with improved oxidized LDL in 6 children with NAFLD. Because over 75% of fructose in a typical U.S. diet is from added sources (processed foods) and only ~25% is from fruits and vegetables,¹ it is practical to consider education in low-fructose diet as a possible means to improve management of NAFLD. Our study was limited by the small sample size and the challenges of attempting to alter a single nutrient in the diet.

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Table 1

Variables at baseline and after 6 months of dietary intervention

	Low Fructose Group n=6 Mean $\pm$ se		Low Fat Group n=4 Mean $\pm$ se	
	baseline	follow-up	baseline	follow-up
Energy(kcal/day) *	1729 $\pm$ 166	1766 $\pm$ 91	2412 $\pm$ 229	1593 $\pm$ 82
Carbohydrate(% total calories)	59 $\pm$ 3	49 $\pm$ 3	52 $\pm$ 3	51 $\pm$ 4
Fructose(g)	53 $\pm$ 15	31 $\pm$ 4	43 $\pm$ 16	23 $\pm$ 4
Fat(% total calories)	31 $\pm$ 2	37 $\pm$ 2	35 $\pm$ 3	31 $\pm$ 3
Protein(% total calories)	12 $\pm$ 1	16 $\pm$ 1	14 $\pm$ 1	19 $\pm$ 2
BMI(z-score)	20 $\pm$ 0.2	1.9 $\pm$ 0.3	2.3 $\pm$ 0.2	2.3 $\pm$ 0.2
Systolic BP(mm Hg)	122.5 $\pm$ 4.0	112.3 $\pm$ 5.8	118.0 $\pm$ 3.6	127.5 $\pm$ 4.3
Diastolic BP(mm Hg)	60.7 $\pm$ 3.6	67.0 $\pm$ 3.7	66.8 $\pm$ 1.4	64.8 $\pm$ 6.4
AST(IU/L)	71.2 $\pm$ 12.2	51.0 $\pm$ 13.0	65.3 $\pm$ 25.6	51.3 $\pm$ 20.9
ALT(IU/L)	125.5 $\pm$ 22.0	83.6 $\pm$ 25.4	103.3 $\pm$ 55.6	92.5 $\pm$ 49.6
Cholesterol(mg/dL)	183.5 $\pm$ 12.5	176.3 $\pm$ 14.7	153.5 $\pm$ 7.5	160.5 $\pm$ 11.3
HDL(mg/dL)	42.8 $\pm$ 2.1	37.5 $\pm$ 3.0	45.8 $\pm$ 3.4	46.0 $\pm$ 1.7
LDL(mg/dL)	118.2 $\pm$ 10.3	115.0 $\pm$ 13.0	93.0 $\pm$ 4.5	92.8 $\pm$ 5.0
Triglycerides(mg/dL)	113.0 $\pm$ 23.2	119.8 $\pm$ 20.4	96.8 $\pm$ 13.8	108.0 $\pm$ 25.5
Oxidized LDL(U/L) **	69.2 $\pm$ 5.7	61.2 $\pm$ 5.6	59.5 $\pm$ 1.8	60.1 $\pm$ 6.3
Urinary Isoprostanes ng/ml)	5.2 $\pm$ 0.9	4.5 $\pm$ 0.5	5.5 $\pm$ 1.1	5.7 $\pm$ 0.9

* Significant difference ($p < 0.05$) between baseline low fructose and low fat groups (by Mann-Whitney U).

** Significant difference ($p < 0.05$) between baseline and 6 month follow-up (sign test).

¹ Follow up diet variables represent average of reported diet at 1, 5 and 6 months.