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High corn oil dietary intake improves health and longevity of aging mice

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ABSTRACT

Corn oil has been recommended as a replacement for saturated fats because of its high levels of poly- and monounsaturated fatty acids. In the present study, we tested whether very high levels of corn oil (58.6% fat-derived calories, FDC) intake improve health and longevity of aging mice. Twelve month old male C57BL/6 mice were fed a normal diet (10% FDC of corn oil, N) or a high fat diet (58.6% FDC of corn oil, HF) for 13–15 months. Our results show that a HF diet significantly increased the longevity of the aged mice (at 25 months of age, 53.8% of mice died in the N group, whereas the mortality rate was only 23.2% in the HF group). High corn oil also reversed aging-increased blood lipids including triglyceride, total cholesterol and LDL. Similarly, high corn oil intake overturned aging-raised pro-inflammatory markers including IL-1β, IL-6, and monocyte chemotactic protein-1 (MCP-1) in the blood. In addition, corn oil intake reversed aging-damaged rotarod performance and liver function. Interestingly, the HF group was significantly heavier than the N group (53.6 g/mouse vs. 41.3 g/mouse); however, both HF and N groups had the same calorie intake (12.48 kcal/d/mouse vs. 12.24 kcal/d/mouse). Although, the HF group's food consumption was lower than that of the N group (2.4 g/d/mouse vs. 3.4 g/d/mouse). These results suggest that if total calorie consumption stays in the normal range, very high levels of corn oil intake improve health and longevity of aging mice.

1. Introduction

High saturated fat diets are well associated with obesity prevalence and the increased risk of cardiovascular disease, diabetes and cancer. Reducing saturated fats from the diet is recommended to eliminate Western diet-induced health problems. The common alternatives of animal (saturated) fats for humans are plant oil, including soybean oil, peanut oil and corn oil because of the high percentage of unsaturated fat acids.

Corn oil is composed mainly (99% of the refined or 96% of the crude oil) of acylglycerols (mono-, di- and primarily tri-), and has 59% polyunsaturated (PUFA), 24% monounsaturated (MUFA) and 13% saturated fatty acid (SFA). The PUFA to SFA ratio (P/S) is about 4.6. Corn oil has one of the highest PUFA levels after sunflower, safflower, walnut and wheat germ oil (Landers and Rathmann, 1981). The primary PUFA is linoleic acid (C18:2n−6), with a small amount of linolenic acid (C18:3n−3) giving a n−6/n−3 ratio of 83. Corn oil contains a significant amount of ubiquinone and high amounts of gamma-tocopherols (vitamin E) (Dupont et al., 1990). These high contents of PUFA and vitamin E may contribute to the health benefits of corn oil consumption.

The beneficial effects of PUFA have been extensively investigated, however, there are very few studies investigating the effects on human health with long-term corn oil consumption, particularly on the older population. This is very important because corn oil is the second leading vegetable oil consumed in the United States (USDA, 2014). Since U.S. adults age 65 and older heavily consume this high fat oil, their population is rapidly increasing and is projected to reach 71 million by 2030. The objectives of the present study are to investigate the long-term health effect of high volume of corn oil consumption in aging mice and to understand the relevant mechanisms.

2. Methods and Materials

2.1. Experimental Animals and Diets

Twelve-month old male C57BL/6 mice were purchased from the National Cancer Institute (Bethesda, MD). Mice were housed in an environmentally-controlled (23 ± 2 °C; 12-h light: dark cycle) animal facility and they were given ad libitum access to food and water. To test the health effect of high corn oil intake, mice were randomly divided into two groups (n = 31) and given either a normal diet (N) or a high

Abbreviations: BW, body weight; EFAs, essential fatty acids; FDC, fat-derived calories; GSR, glutathione-disulfide reductase; GSH, glutathione; H&E, hematoxylin and eosin; HDL, high-density lipoprotein; HF, high corn oil diet; IFN-γ, interferon gamma; IL, interleukin; KC, keratinocyte chemoattractant; LDL, low-density lipoprotein; MCP-1, macrophage chemoattractant protein-1; MUFA, monounsaturated fatty acid; N, normal diet; PUFA, polyunsaturated fatty acid; ROS, reactive oxygen species; SFA, saturated fatty acid; SOD, superoxide dismutase; TNFα, tumor necrosis factor-α; YC, youth control.

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corn oil diet (HF). Both diets are based on the AIN-93 produced by Dyets Inc. (Bethlehem, PA) with two exceptions: 1) soybean oil was replaced with corn oil and 2) the percentage of corn oil in each diet. The normal diet has 10% fat derived calories (FDC) and the HF diet has 58% fat derived calories (FDC) (Reeves et al., 1993). This dose of corn oil (58% FDC) was calculated based on previous studies using high fat diet (60% FDC, 6% from soybean oil and 54% from lard) (Sung et al., 2014). Detailed compositions of the diets are listed in Table 1. To ensure the stability of the corn oil, diets were stored at 4 °C and were kept away from light. The diets were replaced every week. Body weight (BW) and food consumption were monitored weekly. The general health and well-being of the mice were monitored daily. If a mouse was reported as or marked as sick, the criteria for euthanizing mice were independently assessed by a veterinarian adhering to the Institutional Animal Care and Use Committee guidelines. Mice with a BW less than 30% of their original BW and other critical conditions including severe ulcerative dermatitis, urinary obstruction and abdominal masses were euthanized by inhalation of CO_2 and censored. When the median for the control group was reached, the remaining 14 mice from the control group and 12 mice from the HF group were fasted overnight and euthanized using CO_2, and their blood and tissues were collected for biochemical and physiological analysis. The HF group continued until the median was reached. We also collected blood and tissues from youth control mice (12-month old, 12 mice, YC) to compare the changes of biochemical and physiological analysis with the other two groups. The animal protocol was approved by the Institutional Animal Care and Use Committee at Meharry Medical College.

2.2. Measurements of Serum Biological Markers and Hepatic Antioxidants

Serum total cholesterol, HDL-cholesterol, and triglycerides in mice were measured using a PTS CardioChek Blood Analysis Meter (Maria Stein, OH) according to the manufacturer's instructions and our previous report (Si et al., 2011). LDL-cholesterol was calculated using the formula from the manual of the analysis meter: LDL-cholesterol = total cholesterol − HDL-cholesterol − triglyceride / 5. Serum cytokines and chemokines including interleukin (IL)-6, IL-1β, IL-10, tumor necrosis factor-α (TNFα), keratinocyte chemoattractant (KC), monocyte chemotactic protein 1(MCP-1) and interferon gamma (IFN-γ) were tested by a Luminex mouse cytokine array assay (Capital Biosciences, MD) as previously described (Si et al., 2011; Veenbergen et al., 2010). The activity of glutathione-disulfide reductase (GSR) in the liver was measured as we previously described (Si et al., 2011).

2.3. Pathological Analysis

Fresh livers were fixed in 10% phosphate buffered neutral formalin, embedded in paraffin, cut at thicknesses of 5 μm, and then stained with hematoxylin and eosin (H&E) for histological examination of hepatic lesions. Three sections from each mouse were examined. The pathological alterations in the liver were scored according to the levels of vacuolar changes (hydropic degeneration or lipidosis) in hepatocytes (1 = 0–10%, 2 = 10–30%, 3 = 30–50%, and 4 ≥ 50% of hepatocytes affected).

Table 1
Diet composition and energy distribution.

Ingredient	Normal diet (N)		High fat diet (HF)	
	g/kg	kcal/kg	g/kg	kcal/kg
Casein	140	501.2	226.8	811.9
L-Cystine	1.8	7.2	3	12.0
Sucrose	100	400	100	400
Corn starch	465.7	1676.52	75.7	272.52
Dyetrose	155	589	155	589
Corn oil	40	360	340	3060
Cellulose	50	0	50	0
Mineral mix #210050	35	29.4	35	30.8
Vitamin mix #310025	10	38.7	10	38.7
Choline bitartrate	2.5	0	2.5	0
Total	1000.00	3602.02	1000.00	5214.96

2.4. Rotarod Test

Rotarod assay, a simple and accurate approach to examining age-related changes in balance and motor coordination (Baur et al., 2006), was performed using the rotarod apparatus (Med Associates, St. Albans VT) at 14 and 25 month old mice to examine their ability to remain on an revolving rod (Coyle et al., 2008). Briefly, a mouse was briefly placed in a separate lane of a rotarod with an accelerating speed (2–20 rpm) until the mouse fell off the rod. The length of time and speed of the mouse which stayed on the rod were recorded.

2.5. Statistical Analysis

The longevity curves were plotted using the Kaplan–Meier method including all available mice at each time point (Baur et al., 2006), and the Logrank test was applied to compare the distributions of the different groups. The results from the pathological analysis of the liver were analyzed using the Kruskal–Wallis test, and significant differences between treatment groups were further analyzed using the Mann–Whitney-U test. All other data were analyzed with one-way ANOVA and significant differences between treatment groups were further analyzed using the t-test. P-values less than 0.05 were considered to be statistically significant (*, $P < 0.05$; **, $P < 0.01$).

3. Results

3.1. Longevity

At 25 months of age, 53.8% of mice had died in the N group, whereas the mortality rate was only 23.2% in the HF group ($P = 0.02$, Fig. 1). The median for the HF group was reached two months later at 27 months of age. While the sample size (n = 31/group) was relatively small for a typical longevity study, we think that the observed effects of high corn oil on the longevity of aging mice is a real action of this compound because such a large difference between the two groups was unlikely due to random variation.

3.2. Similar Energy Intake

Although the average BW in the HF group was significantly higher than that in the N group as shown in Fig. 2A, the food consumption in the HF group was significantly lower than that in the N group

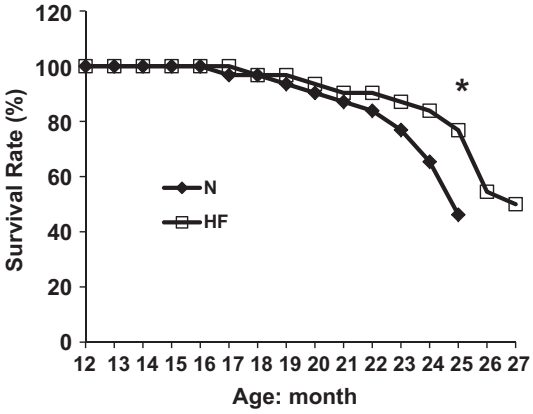

Fig. 1. Longevity curve in normal diet (N) and high corn oil diet (HF) mice for 13–15 months. There was an initial 31 mice/group. *$P < 0.05$.