DIABETES TECHNOLOGY & THERAPEUTICS
Volume 16, Number 4, 2014

DOI: 10.1089/dia.2013.0178

DTT
Diabetes Technology & Therapeutics

*ORIGINAL ARTICLE*

# Effect of a 6-Month Intervention with Cooking Oils Containing a High Concentration of Monounsaturated Fatty Acids (Olive and Canola Oils) Compared with Control Oil in Male Asian Indians with Nonalcoholic Fatty Liver Disease

Priyanka Nigam, PhD,[1–4] Suryaprakash Bhatt, PhD,[5] Anoop Misra, MD,[1,2,6] Davinder S. Chadha, MD,[7] Meera Vaidya, PhD,[3] Jharna Dasgupta, MSc,[1] and Qadar M.A. Pasha, PhD[8]

## Abstract

***Objective:*** We investigated the effects of dietary intervention with canola or olive oil in comparison with commonly used refined oil in Asian Indians with nonalcoholic fatty liver disease (NAFLD).

***Subjects and Methods:*** This was a 6-month intervention study including 93 males with NAFLD, matched for age and body mass index (BMI). Subjects were randomized into three groups to receive olive oil ($n=30$), canola oil ($n=33$), and commonly used soyabean/safflower oil (control; $n=30$) as cooking medium (not exceeding 20 g/day) along with counseling for therapeutic lifestyle changes. The BMI, fasting blood glucose (FBG) and insulin levels, lipids, homeostasis model of assessment for insulin resistance (HOMA-IR), HOMA denoting $\beta$-cell function (HOMA-$\beta$CF), and disposition index (DI) were measured at pre- and post-intervention. Data were analyzed with one-way analysis of variance (ANOVA) and Tukey's Honestly Significant Difference multiple comparison test procedures.

***Results:*** Olive oil intervention led to a significant decrease in weight and BMI (ANOVA, $P=0.01$) compared with the control oil group. In a comparison of olive and canola oil, a significant decrease in fasting insulin level, HOMA-IR, HOMA-$\beta$CF, and DI ($P<0.001$) was observed in the olive oil group. Pre- and post-intervention analysis revealed a significant increase in high-density lipoprotein level ($P=0.004$) in the olive oil group and a significant decrease in FBG ($P=0.03$) and triglyceride ($P=0.02$) levels in the canola oil group. The pre- and post-intervention difference in liver span was significant only in the olive ($1.14\pm2$ cm; $P<0.05$) and canola ($0.66\pm0.33$ cm; $P<0.05$) oil groups. In the olive and canola oil groups, post-intervention grading of fatty liver was reduced significantly (grade I, from 73.3% to 23.3% and from 60.5% to 20%, respectively [$P<0.01$]; grade II, from 20% to 10% and from 33.4% to 3.3%, respectively [$P<0.01$]; and grade III, from 6.7% to none and from 6.1% to none, respectively). In contrast, in the control oil group no significant change was observed.

***Conclusions:*** Results suggest significant improvements in grading of fatty liver, liver span, measures of insulin resistance, and lipids with use of canola and olive oil compared with control oils in Asian Indians with NAFLD.

## Introduction

Nonalcoholic fatty liver disease (NAFLD) is believed to be an integral part of the metabolic syndrome, which comprises a cluster of abnormalities (abdominal obesity, dysglycemia, dyslipidemia, hypertension, procoagulant tendency, etc.) with insulin resistance as a central pathogenic factor. It is important that insulin resistance is independently correlated with NAFLD regardless of adiposity.[1–4] The prevalence of insulin resistance in Asian Indians residing in India ranges from approximately 7% to 55%.[5–7] Data show that about one-third of the urban population in large cities in

[1]National Diabetes, Obesity and Cholesterol Foundation, Safdarjung Development Area, New Delhi, India.
[2]Diabetes Foundation (India), New Delhi, India.
[3]Department of Food & Nutrition, Government M.H. College of Home Science and Science for Women, Jabalpur, India.
[4]Lavandoo Health India, Bangalore, India.
[5]Department of Medicine, All India Institute of Medical Sciences, New Delhi, India.
[6]Fortis-CDOC Center of Excellence for Diabetes, Metabolic Diseases and Endocrinology, B-16, Chirag Enclave, New Delhi, India.
[7]Department of Cardiology, Military Hospital (Cardio Thoracic Centre), Armed Forces Medical College, Pune, India.
[8]Institute of Genomics and Integrative Biology, New Delhi, India.

India has the metabolic syndrome.[3,7–9] Because insulin resistance and the metabolic syndrome are widely prevalent in Asian Indians, it is reasonable to assume that NAFLD would also be prevalent; however, data are scarce. Limited numbers of studies suggest prevalence of NAFLD in the range of approximately 6–32% in urban India.[10,11]

Selected dietary factors like high fats and sucrose have been shown to contribute to hepatic steatosis in experimental animals.[12] It is likely that an excess of the above-mentioned dietary factors may play an important part in the pathophysiology of NAFLD in humans as well. The contribution of intake of carbohydrates, saturated fatty acids, *trans* fatty acids, and *n*-6 polyunsaturated fatty acids (PUFAs), along with monounsaturated fatty acids (MUFAs) and fiber, in the development of fatty liver in Asian Indians has not been researched.

Many therapeutic agents have been tried for management of NAFLD; however, effective treatment is still unavailable. Furthermore, there is a paucity of data regarding dietary intervention in NAFLD.

We hypothesized that the dietary intervention with either canola oil (high MUFAs [61%], saturated fatty acid [7%], and balanced ratio [nearly 2:1] of *n*-6 [21%]/*n*-3 PUFAs [11%]) or olive pomace oil (high MUFAs [70%], saturated fatty acid [15%], and *n*-6 (9%)/*n*-3 PUFAs (1%)] would be effective in improving fatty liver in NAFLD subjects compared with other refined oils commonly used in India.

## Subjects and Methods

This study was conducted in New Delhi, India (North India) from May 2007 to December 2009 after approval from the institutional ethics committee. All subjects gave written informed consent. Subjects were recruited from the outpatient department of Fortis Hospital, New Delhi. Subjects with significant alcohol intake (>20 g/day), type 2 diabetes mellitus, cardiovascular disease, presence of other liver diseases (alcoholic liver disease, viral hepatitis, autoimmune hepatitis, primary biliary cirrhosis, biliary obstruction, drug-induced liver damage, etc.), severe end-stage organ damage, human immunodeficiency virus infection, and pregnancy or lactation were excluded from the study. A detailed history (demographic and social economic profiles, history of smoking, and alcohol intake and physical activity patterns) and family history (type 2 diabetes mellitus, overweight, hypertension, liver disease, and cardiovascular disease) were obtained.

### *Study design and intervention*

The study had a randomized, parallel, open-label design. The sample size has been calculated by using a previous animal study,[13] which showed the improvement of 37% in liver histology after taking olive oil. We assumed that intake of 20 mL/day of olive or canola oil will lead to a 20% improvement in human subjects. To determine the change in outcome with an $\alpha$ error of 5%, 90% power, and 10% dropouts, the effective sample size was 30 in each group. The duration of the intervention was 6 months after completion of a 1-month diet and exercise run-in period.

Subjects were matched for age (37.2 ± 6.2, 38.0 ± 6.4, and 36.2 ± 7.1 years, respectively; analysis of variance [ANOVA], $P = 0.84$) and body mass index (BMI) (27.2 ± 2.3, 27.4 ± 5.7, and 27.4 ± 2.7 kg/m$^2$, respectively; ANOVA, $P = 0.13$) to eliminate the confounding effect of age and BMI. In total, 93 subjects were enrolled who ranged in age from 20 to 50 years. Subjects were randomly allocated into one of three groups by computer-generated number to receive canola oil (from Canada; Hudson Canola Oil®; Dalmia Continental Pvt. Ltd., New Delhi), olive oil (Leonardo Olive Pomace Oil; Dalmia Continental Pvt. Ltd., New Delhi), or commonly used refined oil (composed of 12–16% saturated fatty acids, 15–24% MUFAs, and 50–60% PUFAs) such as soybean or safflower (control oil group) (*n*-6:*n*-3 ratio of 7:1 for soya oil and >100 for safflower oil) (other than canola oil/olive oil/other oils having a high content of MUFAs) as a cooking medium (not exceeding 20 g/day) for 6 months.

Counseling for therapeutic lifestyle changes was given during the 1-month diet and exercise run-in period and the 6-month intervention, according to the subject's height, weight, and physical activity level. The daily energy intake advised was 15–21% protein (1–1.5 g/kg of desirable body weight), 55–70% carbohydrates, and 20% fats. A 40–45-min brisk walk daily was recommended for all participants. This was done to engage all the recruited subjects in the standard diet and exercise regimen before the start of the study. At this time, each patient's compliance was also ascertained. The baseline of anthropometry, biochemistry, and liver ultrasound was done after the 30-day run-in period and compared with post-intervention data. A standardized food frequency questionnaire and 24-h recall were used to gather the data on dietary intake.[14] The participants were provided with a diary to record 3 days of dietary intake (2 weekdays and 1 weekend day). The subject's spouse was also interviewed regarding participants' usual dietary intake pattern at home and when eating out. Particular care was taken to note consumption of dietary fats and alcohol. Biweekly telephone calls and monthly personal interviews were scheduled throughout the study to allow the opportunity to discuss any difficulties in preparation of diet and in compliance. To ensure compliance, an additional 500 mL of oil for the family and a measuring spoon were provided free of cost to all subjects, with advice about the similar amount of oil they should consume. On average, each subject was counseled for 30 min during each visit. It was ensured that all participants received standardized advice about diet, exercise, and other lifestyle factors; the only advice that was different was that for the type of oil.

One subject in the canola oil group was withdrawn owing to noncompliance with the prescribed diet and exercise for 2 weeks, and two participants from the same group were excluded because of their relocation to another city.

### *Measurements*

Weight, height, waist circumference, and blood pressure were evaluated as described previously.[10] BMI and waist–hip ratio were calculated. Estimations for fasting blood glucose (FBG), total cholesterol, serum triglycerides, high-density lipoprotein cholesterol, aspartate aminotransferase, alanine aminotransferase, and serum insulin were done as previously described.[10] The lower limit of detection of the insulin assay was 0.01 $\mu$U/mL, and the reference range was 2.1–22 $\mu$U/mL. The intra- and inter-assay percentage variations were 1.95% and 2.23%, respectively. Insulin resistance was measured by two surrogate measures: fasting insulin and homeostasis

model assessment for insulin resistance (HOMA-IR). The value of HOMA-IR was calculated by the following equation: (fasting insulin [in $\mu$U/mL] × fasting glucose [in mmol/L])/22.5. The value of HOMA denoting $\beta$-cell function was termed HOMA-$\beta$CF and was calculated as (20 × fasting plasma insulin [in mIU/mL])/(fasting plasma glucose [in mmol/L] – 3.5).[15] The disposition index (DI) provides a measure of $\beta$-cell function adjusted for insulin sensitivity and was calculated as insulin sensitivity (22.5/fasting insulin [in mU/mL] × fasting glucose [in mmol/L)] × HOMA-$\beta$CF.[16]

### *Ultrasound imaging of liver*

Liver ultrasound was carried out using a 3.5-MHz curvilinear probe (model G 60 S 2004; Siemens, Munich, Germany) by a trained radiologist with postgraduate qualifications, who followed the standardized procedure. A complete examination required both subcostal and intercostal scanning. The definition of fatty liver was based on a comparative assessment of image brightness relative to the kidneys, according to previously reported diagnostic criteria.[17–19] Severity of fatty liver was classified according to the brightness compared with the kidneys, blurring of the gallbladder wall, and attenuation of hepatic veins. Liver span was measured in the midclavicular line by marking the upper and lower limits of the liver using the ultrasonic probe. The radiologist performing the ultrasound was blinded to the clinical data.

### *Statistical analysis*

Results were presented as mean ± SD and median (minimum–maximum) values. The normality of distribution of each variable was tested, and transformed data were used when necessary. For intergroup comparison one-way ANOVA/Kruskal–Wallis test was applied, and post hoc or multiple comparison was done by paired $t$ test/Wilcoxon rank-sum (Mann–Whitney U) test and Wilcoxon signed-rank test as applicable. A value of $P < 0.05$ was considered statistically significant. Various statistical measures were evaluated using SPSS version 11 for Windows software (SPSS, Inc., Chicago, IL).

## Results

### *Baseline characteristics*

Participants (all males) in the olive oil ($n = 30$), canola oil ($n = 33$), and control oil ($n = 30$) groups were matched for age (37.2 ± 6.2, 38.0 ± 6.4, and 36.2 ± 7.1 years, respectively; ANOVA, $P = 0.84$) and BMI (27.2 ± 2.3, 27.4 ± 5.7, and 27.4 ± 2.7 kg/m$^2$, respectively; ANOVA, $P = 0.13$). One-way ANOVA performed on baseline (pre-intervention) anthropometric (BMI), clinical, biochemical (fasting insulin, HOMA for insulin resistance [HOMA-IR], and HOMA-$\beta$CF), and ultrasonographic (liver span) data of the participants revealed no significant differences among the groups (Table 1). Furthermore, the dietary intake and physical activity, both pre- and post-intervention, were similar in the three groups (Table 2). Participants in the three groups adhered to the prescribed therapeutic life changes.

### *Post-intervention Analysis*

a. Intergroup. Post-intervention weight and BMI (ANOVA, $P = 0.01$) of the olive oil group were significantly decreased from values for the control oil group, whereas there was no significant difference found between the other groups by Tukey's Highly Significant Difference test (Table 1). In the olive and canola oil groups, interventions lead to significant improvement in fasting insulin, HOMA-IR, HOMA-$\beta$CF, and DI values ($P < 0.001$) compared with the control oil group (Table 1). Between the olive and canola oil groups, a significant decrease in fasting insulin, HOMA-IR, HOMA-$\beta$CF, and DI ($P < 0.001$) was observed in the olive oil group (Table 1). Post-intervention, there was a nonsignificant reduction in alanine aminotransferase and aspartate aminotransferase enzyme activities in the three groups.

b. Intragroup. Intragroup analysis revealed significant changes in weight ($P = 0.01$), BMI ($P = 0.01$), fasting insulin ($P = 0.001$), HOMA-IR ($P = 0.001$), HOMA-$\beta$CF ($P = 0.03$), DI ($P = 0.004$), triglycerides ($P = 0.004$), and high-density lipoprotein cholesterol ($P = 0.03$) levels in the olive oil group. FBG ($P = 0.03$), fasting insulin ($P = 0.001$), HOMA-IR ($P = 0.001$), HOMA-$\beta$CF ($P = 0.03$), DI ($P = 0.004$), and triglycerides ($P = 0.004$) levels in the canola oil group also showed significant change (Table 1).

### *Liver span and grading of fatty liver*

The pre- and post-intervention difference in liver span was significant in the olive (1.14 ± 2 cm; $P < 0.006$) and canola (0.66 ± 0.33 cm; $P < 0.002$) oil groups. In these groups, post-intervention grading of fatty liver was reduced significantly: grade I, from 73.3% to 23.3% and 60.5% to 20%, respectively ($P < 0.01$); grade II, from 20% to 10% and 33.4% to 3.3%, respectively ($P < 0.01$); and grade III, from 6.7% to none and 6.1% to none, respectively. In contrast, in the control oil group no significant change was observed. Most important is that 66.7% and 76.7% of the participants in the olive and canola oil groups, respectively, reverted to normal liver grading after intervention (Table 3).

## Discussion

The effect of consumption of cooking oil having a high concentration of MUFAs and a balanced ratio of $n$-6/$n$-3 PUFAs on NAFLD has not been previously investigated in Asian Indians. In the current study we showed that intervention with olive and canola oils as a cooking medium was effective in reducing the liver span and grade of fatty infiltration in addition to improving insulin sensitivity.

Previously, Folsom et al.[20] showed that a MUFA-rich diet improved insulin sensitivity, as indicated by lower HOMA-IR values post-intervention, compared with carbohydrate-rich and high-saturated fat diets. The present study has also shown improvement in insulin sensitivity in NAFLD participants using high-MUFA oil compared with the control oil group. The mechanism could be improvement of postprandial triglycerides and glucagon-like peptide-1 responses in insulin-resistant participants and up-regulation of glucose transporter-2 expression in the liver.[21]

Furthermore, Garg[22] showed that MUFA-rich diets compared with high-carbohydrate diets lowered levels of plasma triacylglycerol (19%), total cholesterol (3%), and very low-density lipoprotein cholesterol (22%) and increased the

Table 1. Comparison of Anthropometric, Biochemical, and Hepatic Profiles, Pre- and Post-Intervention, Among the Three Intervention Groups

| *Variable* | *Group* | | | *ANOVA P value* |
|---|---|---|---|---|
| | *Olive oil* | *Canola oil* | *Control oil* | |
| Weight (kg) | | | | |
| Pre-intervention | 77.8 ± 7.9 | 81.5 ± 9.2 | 79.8 ± 9.1 | 0.23 |
| Post-intervention | 72.8 ± 7.5[a] | 77.3 ± 8.9 | 78.2 ± 8.3[a] | 0.02 |
| *P* value* | 0.01 | NS | NS | |
| Body mass index (kg/m$^2$) | | | | |
| Pre-intervention | 27.3 ± 2.4 | 27.4 ± 5.7 | 27.4 ± 2.7 | 0.13 |
| Post-intervention | 25.6 ± 2.3[a] | 26.9 ± 2.8 | 27.4 ± 2.5[a] | 0.03 |
| *P* value* | 0.01 | NS | NS | |
| Waist circumference (cm) | | | | |
| Pre-intervention | 93.6 ± 6.0 | 95.2 ± 8.6 | 93.9 ± 7.6 | 0.45 |
| Post-intervention | 90.7 ± 5.1 | 92.9 ± 8.1 | 91.9 ± 6.7 | 0.29 |
| *P* value* | NS | NS | NS | |
| Fasting blood glucose (mg/dL) | | | | |
| Pre-intervention | 93.5 ± 12.6 | 91.9 ± 13.7 | 88.6 ± 11.9 | 0.24 |
| Post-intervention | 89.6 ± 12.2 | 84.0 ± 11.9 | 88.5 ± 10.6 | 0.13 |
| *P* value* | NS | 0.03 | NS | |
| Fasting insulin ($\mu$U/mL) | | | | |
| Pre-intervention | 8.1 ± 2 | 9.9 ± 1.8 | 12.1 ± 1.8 | 0.25 |
| Post-intervention | 3.0 ± 1.8[ac] | 4.9 ± 2.0[ab] | 11.0 ± 1.8[bc] | 0.004 |
| *P* value* | 0.001 | 0.001 | NS | |
| HOMA-IR | | | | |
| Pre-intervention | 2.2 ± 2.2 | 2.4 ± 2.0 | 2.4 ± 1.8 | 0.21 |
| Post-intervention | 0.7 ± 1.8[bc] | 1.1 ± 2.0[ab] | 2.2 ± 1.8[bc] | 0.004 |
| *P* value* | 0.001 | 0.001 | NS | |
| HOMA-$\beta$CF | | | | |
| Pre-intervention | 29.9 ± 2.7 | 36.5 ± 0.7 | 49. ± 2 | 0.21 |
| Post-intervention | 7.3 ± 2.4[ac] | 18.1 ± 0.8 | 36.5 ± 1.8[bc] | 0.003 |
| *P* value* | 0.03 | 0.03[ab] | NS | |
| Disposition index | | | | |
| Pre-intervention | 5.9 ± 0.18 | 5.9 ± 0.08 | 5.9 ± 0.11 | 0.23 |
| Post-intervention | 3.1 ± 1.9[ac] | 5.2 ± 1.9[ab] | 6.8 ± 1.2[bc] | 0.003 |
| *P* value* | 0.004 | 0.004 | NS | |
| HDL-C (mg/dL) | | | | |
| Pre-intervention | 37.9 ± 4.4 | 39.6 ± 5.5 | 39.3 ± 5.12 | 0.39 |
| Post-intervention | 41.2 ± 4.6 | 40.5 ± 5.8 | 35.0 ± 5.5 | 0.61 |
| *P* value* | 0.03 | NS | NS | |
| Triglycerides (mg/dL) | | | | |
| Pre-intervention | 181.1 ± 82.4 | 186.6 ± 82 | 183.8 ± 100 | 0.97 |
| Post-intervention | 170.3 ± 58.3 | 154.6 ± 48.7 | 182.1 ± 105 | 0.50 |
| *P* value* | 0.004 | 0.004 | NS | |
| Liver span (cm) | | | | |
| Pre-intervention | 14.3 ± 1.3 | 14.3 ± 1.4 | 15.0 ± 1.9 | 0.14 |
| Post-intervention | 13.8 ± 1.2[b] | 13.3 ± 1. 5[a] | 1.8 ± 1.9[ab] | 0.001 |
| *P* value* | 0.006 | 0.002 | NS | |
| AST (U/L) | | | | |
| Pre-intervention | 35.8 ± 21.8 | 33.1 ± 13.8 | 31.7 ± 8.9 | 0.14 |
| Post-intervention | 33.2 ± 4.6 | 29 ± 6.2 | 31.2 ± 13.3 | 0.18 |
| *P* value* | NS | NS | NS | |
| ALT (U/L) | | | | |
| Pre-intervention | 39.8 ± 19.9 | 33.9 ± 3.2 | 34.7 ± 8.9 | 0.20 |
| Post-intervention | 38.1 ± 11.3 | 31.5 ± 6.2 | 34 ± 18.1 | 0.11 |
| *P* value* | NS | NS | NS | |

Data are mean ± SD values. The control oil group included commonly used refined oils such as soybean or safflower.

[ab]Means sharing a common superscript letter are significantly different at $P < 0.05$ based on Tukey's Highly Significant Difference multiple comparison tests following a significant one-way analysis of variance (ANOVA).

*$P$ value for the results of a paired $t$ test between pre- and post-intervention.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL-C, high-density lipoprotein cholesterol; HOMA-$\beta$CF, homeostasis model assessment for $\beta$-cell function; HOMA-IR, homeostasis model assessment for insulin resistance; NS, not significant.

Table 2. Comparison of Macronutrient Intake, Pre- and Post-Intervention, Among the Three Intervention Groups

| | Group | | | |
|---|---|---|---|---|
| *Variable* | *Olive oil* | *Canola oil* | *Control oil* | *ANOVA P value* |
| Carbohydrate (ln) (g) | | | | |
| Pre-intervention | 5.2 ± 0.3 | 5.2 ± 0.4 | 5.2 ± 0.4 | 0.90 |
| Post-intervention | 5.0 ± 0.3 | 5.0 ± 0.2 | 5.1 ± 0.3 | 0.20 |
| *P* value* | NS | NS | NS | |
| Protein (ln) (g) | | | | |
| Pre-intervention | 3.9 ± 0.4 | 3.8 ± 0.4 | 3.9 ± 0.5 | 0.50 |
| Post-intervention | 3.7 ± 0.2 | 3.7 ± 0.2 | 3.8 ± 0.3 | 0.36 |
| *P* value* | NS | NS | NS | |
| Total fat (ln) (g) | | | | |
| Pre-intervention | 4.7 ± 0.7 | 4.6 ± 0.3 | 4.7 ± 0.3 | 0.18 |
| Post-intervention | 4.3 ± 0.3 | 4.4 ± 0.3 | 4.3 ± 0.3 | 0.53 |
| *P* value* | NS | NS | NS | |
| Total energy (ln) (Kcal) | | | | |
| Pre-intervention | 7.6 ± 0.2 | 7.5 ± 0.2 | 7.6 ± 0.26 | 0.32 |
| Post-intervention | 7.3 ± 0.2 | 7.3 ± 0.2 | 7.3 ± 0.2 | 0.64 |
| *P* value* | NS | NS | NS | |

Data are mean ± SD values. The control oil group included commonly used refined oils such as soybean or safflower.
*$P$ value for the results of a paired $t$ test between pre- and post-intervention.
ln, log natural; NS, not significant.

high-density lipoprotein cholesterol level (4%), although low-density lipoprotein cholesterol did not differ significantly. The findings of present study are in line with the only other study that has shown the role of MUFAs in reduction of triglyceride accumulation in the liver in experimental animals.[13] Our observations are important in light of the information that intake of *n*-PUFAs also has been shown to reduce hepatic triglyceride levels in experimental human studies.[23–25] Mechanisms of action of MUFAs and *n*-3 PUFA in amelioration of hepatic triglyceride accumulation is not clearly known. MUFAs decrease insulin resistance, triglyceride by increasing fatty acid oxidation through activation of peroxisome proliferator-activated receptor alpha or by reducing the activation of sterol regulatory element binding protein and inhibiting lipogenesis.[26] On the other hand, *n*-3 PUFAs suppress lipogenic enzymes such as fatty acid synthase and stearoyl-coenzyme A desaturase 1 mediated by reduction of the level of mature sterol regulatory element binding protein-1 protein in the liver, thus may reduce hepatic triglyceride storage.[27]

As previously stated, the effect of MUFAs on NAFLD has been investigated only in animals,[13] whereas the effect of *n*-3 PUFAs on NAFLD has been investigated in two uncontrolled trials in humans.[23,24] However, in our study, the change in liver span was small after the intervention, and a larger change would have been more clinically significant. Furthermore, it is possible that values of hepatic transaminases and liver span could be significantly better after a longer duration of intervention.

We acknowledge the limitations of allowing participants to make their own food choices and our use of patient-reported data to analyze dietary intake. Our study was modeled on the idea of practicality and feasibility when implementing treatments that impact lifestyle modification. Another limitation of this study was that the diagnosis of NAFLD was based on liver ultrasonography. It has been argued that other methods (magnetic resonance spectroscopy and liver biopsy) are better tools for defining NAFLD and could be considered as "gold standards." Conversely, ultrasonography is by far the most common method of diagnosing NAFLD in clinical practice and has a fair sensitivity (87%) and specificity (94%) in detecting hepatic steatosis.[28] It is simple to perform, noninvasive, and cost-effective and does not entail any radiation hazard and could also be used in epidemiological studies.

Table 3. Pre- and Post-Intervention Grading of Fatty Liver

| | *Pre-intervention* | | | *Post-intervention* | | |
|---|---|---|---|---|---|---|
| *Variable* | *Olive oil* (n = *30*) | *Canola oil* (n = *33*) | *Control oil* (n = *30*) | *Olive oil* (n = *30*) | *Canola oil* (n = *30*) | *Control oil* (n = *30*) |
| Grade I | 22 (73.3) | 20 (60.5) | 17 (58.62) | 7 (23.3) | 9 (20) | 19 (63.3) |
| Grade II | 6 (20) | 11 (33.4) | 9 (31.3) | 3 (10)[a] | 1 (3.3)[a] | 8 (26.7) |
| Grade III | 2 (6.7) | 2 (6.1) | 4 (10.3) | — | — | — |
| Normal | — | — | — | 20 (66.7)[a] | 20 (76.7)[a] | 3 (10) |

Data are number (%). No significant differences were observed among the groups at the pre-intervention stage. The control oil group received for cooking commonly used refined oils such as soybean or safflower.
[a]Significant difference ($P < 0.01$) compared with the control oil group using $t$ test.

This is the first oil-based dietary intervention study done on Asian Indians with NAFLD.

In conclusion, the results of this 6-month randomized intervention trial provide evidence that use of olive and canola oils (rich in MUFAs and having a balanced *n*-6/*n*-3 PUFAs ratio) as a cooking medium resulted in a significant reduction in fatty liver severity and liver span in NAFLD. Improvement of fatty liver was accompanied by amelioration in insulin resistance and dyslipidemia. All together, these beneficial changes may also decrease the risk for developing type 2 diabetes mellitus and cardiovascular disease in Asian Indians predisposed to develop these diseases.

### Acknowledgments

We thank Dalmia Continental Pvt. Ltd. for funding the project.

### Author Disclosure Statement

No competing financial interests exist.
All authors have read and approved the final manuscript.

### References

1. Mohan V, Farooq S, Deepa M, , Ravikumar R, Pitchumoni CS: Prevalence of non-alcoholic fatty liver disease in urban south Indians in relation to different grades of glucose intolerance and metabolic syndrome. Diabetes Res Clin Pract 2009;84:84–91.
2. Meigs JB: Invited commentary: insulin resistance syndrome? Syndrome X? Multiple metabolic syndrome? A syndrome at all? Factor analysis reveals patterns in the fabric of correlated metabolic risk factors. Am J Epidemiol 2000;152:908–911; discussion 912.
3. Fabbrini E, Magkos F, Mohammed BS, Pietka T, Abumrad NA, Patterson BW, Okunade A, Klein S: Intrahepatic fat, not visceral fat, is linked with metabolic complications of obesity. Proc Natl Acad Sci U S A 2009;106:15430–15435.
4. Marchesini G, Bugianesi E, Forlani G, Cerrelli F, Lenzi M, Manini R, Natale S, Vanni E, Villanova N, Melchionda N, Rizzetto M: Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. Hepatology 2003;37:917–923.
5. Misra A: Insulin resistance syndrome: current perspective and its relevance in Indians. Indian Heart J 1998;50: 385–395.
6. Wasir JS, Misra A: The metabolic syndrome in Asian Indians: impact of nutritional and socio-economic transition in India. Metab Syndr Relat Disord 2004;2:14–23.
7. Misra A, Khurana L: Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab 2008;93(11 Suppl 1):S9–S30.
8. Mohan V, Deepa R, Rani SS, Premalatha G; Chennai Urban Population Study (CUPS No.5): Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India: the Chennai Urban Population Study (CUPS No. 5). J Am Coll Cardiol 2001;38:682–687.
9. Misra A, Misra R, Wijesuriya M, Banerjee D: The metabolic syndrome in South Asians: continuing escalation & possible solutions. Indian J Med Res 2007;125:345–354.
10. Bajaj S, Nigam P, Luthra A, Pandey RM, Kondal D, Bhatt SP, Wasir JS, Misra A: A case-control study on insulin resistance, metabolic co-variates & prediction score in non-alcoholic fatty liver disease. Indian J Med Res 2009;129:285–292.
11. Amarapurkar DN, Amarapurkar AD: Nonalcoholic steatohepatitis: clinicopathological profile. J Assoc Physicians India 2000;48:311–313.
12. Li Z, Soloski MJ, Diehl AM: Dietary factors alter hepatic innate immune system in mice with nonalcoholic fatty liver disease. Hepatology 2005;42:880–885.
13. Hussein O, Grosovski M, Lasri E, Svalb S, Ravid U, Assy N: Monounsaturated fat decreases hepatic lipid content in nonalcoholic fatty liver disease in rats. World J Gastroenterol 200;13:361–368.
14. Thimmayamma BVS, Rau P: Diet survey methods. In: Thimmayamma BVS, ed. A Handbook of Schedule and Guidelines in Socio-Economic and Diet Survey. New Delhi: National Institute of Nutrition, Indian Council of Medical Research, 1987:1–8.
15. Caumo APG, Brunani A, Luzi L: New insights on the simultaneous assessment of insulin sensitivity and beta cell function with the HOMA2 method. Diabetes Care 2006; 29:2733–2734.
16. Kahn SE, Prigeon RL, McCulloch DK, Boyko EJ, Bergman RN, Schwartz MW, Neifing JL, Ward WK, Beard JC, Palmer JP: Quantification of the relationship between insulin sensitivity and beta-cell function in human subjects. Evidence for a hyperbolic function. Diabetes 1993;42:1663–1672.
17. Hsiao PJ, Yang YH, Lin WY, Yang JF, Chiu CC, Chuang WL, Tsai TR, Yu ML: Significant correlations between severe fatty liver and risk factors for metabolic syndrome. J Gastroenterol Hepatol 2007;22:2118–2123.
18. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, Mullen KD, Cooper JN, Sheridan MJ: The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology 2002;123:745–750.
19. Hamer OW, Aguirre DA, Casola G, Lavine JE, Woenckhaus M, Sirlin CB: Fatty liver: imaging patterns and pitfalls. Radiographics 2006;26:1637–1653.
20. Folsom AR, Ma J, McGovern PG, Eckfeldt H: Relation between plasma phospholipid saturated fatty acids and hyperinsulinemia. Metabolism 1996;45:223–228.
21. Assy N, Nassar F, Nasser G, Grosovski M: Olive oil consumption and non-alcoholic fatty liver disease. World J Gastroenterol 2009;15:1809–1815.
22. Garg A: High-monounsaturated-fat diets for patients with diabetes mellitus: a meta-analysis. Am J Clin Nutr 1998;67: 577S–582S.
23. Spadaro L, Magliocco O, Spampinato D, Piro S, Oliveri C, Alagona C, Papa G, Rabuazzo AM, Purrello F: Effects of n-3 polyunsaturated fatty acids in subjects with nonalcoholic fatty liver disease. Dig Liver Dis 2008;40: 194–199.
24. Capanni M, Calella F, Biagini MR, Genise S, Raimondi L, Bedogni G, Svegliati-Baroni G, Sofi F, Milani S, Abbate R, Surrenti C, Casini A: Prolonged n-3 polyunsaturated fatty acid supplementation ameliorates hepatic steatosis in patients with non-alcoholic fatty liver disease: a pilot study. Aliment Pharmacol Ther 2006;23:1143–1151.
25. Sofi F, Giangrandi I, Cesari F, Corsani I, Abbate R, Gensini GF, Casini A: Effects of a 1-year dietary intervention with n-3 polyunsaturated fatty acid-enriched olive oil on nonalcoholic fatty liver disease patients: a preliminary study. Int J Food Sci Nutr 2010;61:792–802.
26. Soriguer F, Morcillo S, Cardona F, Rojo-Martínez G, de la Cruz Almaráz M, Ruiz de Adana Mde L, Olveira G, Tinahones F, Esteva I: Pro12Ala polymorphism of the PPARG2

gene is associated with type 2 diabetes mellitus and peripheral insulin sensitivity in a population with a high intake of oleic acid. J Nutr 2006;136:2325–2330.
27. Clarke SD: Nonalcoholic steatosis and steatohepatitis. I. Molecular mechanism for polyunsaturated fatty acid regulation of gene transcription. Am J Physiol Gastrointest Liver Physiol 2001;281:G865–G869.
28. Mathiesen U L, Franzen L E, Aselius H, Resjö M, Jacobsson L, Foberg U, Frydén A, Bodemar G: Increased liver echogenicity at ultrasound examination reflects degree of steatosis but not of fibrosis in asymptomatic patients with mild/moderate abnormalities of liver transaminases. Dig Liver Dis 2002;34:516–522.

Address correspondence to:
*Anoop Misra, MD*
*Fortis-CDOC Center of Excellence for Diabetes*
*Metabolic Diseases and Endocrinology*
*B-16, Chirag Enclave*
*New Delhi, India*

*E-mail:* anoopmisra@metabolicresearchindia.com

**This article has been cited by:**


1. Shrivastava Usha, Misra Anoop. 2015. Need for Ethnic-Specific Guidelines for Prevention, Diagnosis, and Management of Type 2 Diabetes in South Asians. *Diabetes Technology & Therapeutics* **17**:6, 435-439. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
2. Shrivastava Usha, Misra Anoop. 2014. Intervention Trials for Prevention of Metabolic Syndrome and Type 2 Diabetes: Focus on Asian Indians. *Diabetes Technology & Therapeutics* **16**:8, 531-541. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]