# A Comparison of Fish Oil or Corn Oil Supplements in Hyperlipidemic Subjects with NIDDM

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**OBJECTIVE** — To examine the effects on blood lipids and glycemic control of fish oil and corn oil supplementation at two levels in subjects with hyperlipidemia and non-insulin-dependent diabetes mellitus (NIDDM).

**RESEARCH DESIGN AND METHODS** — Forty subjects (18 men and 22 women; aged 53.9 ± 7.0 years) with NIDDM and hyperlipidemia were randomly assigned to one of four treatment groups: 9 g of fish oil, 18 g of fish oil, 9 g of corn oil, or 18 g of corn oil daily supplementation for 12 weeks.

**RESULTS** — The level of oil supplements (9 g compared with 18 g) did not have a significant effect within each oil group on glycemic control and lipids. Significant differences ($P < 0.05$) in lipids were found when the 9-g and 18-g groups were combined. In subjects consuming fish oil, plasma very-low-density lipoprotein (VLDL) cholesterol ($P = 0.0001$), plasma triglyceride (TG) ($P = 0.0001$), and plasma VLDL TGs ($P = 0.02$ at 6 weeks and $P = 0.0001$ at 12 weeks) were significantly lowered compared with subjects consuming corn oil. Plasma VLDL cholesterol increased across time in the corn oil group ($P = 0.04$). Plasma low-density lipoprotein (LDL) cholesterol was temporarily increased ($P = 0.008$) in the fish oil group at 6 weeks, but the effect was no longer present at 12 weeks. No significant differences between fish oil– or corn oil–supplemented diets were found in total plasma cholesterol, high-density lipoprotein cholesterol, fasting plasma glucose, glycosylated $HbA_{1c}$, weight, and blood pressure.

**CONCLUSIONS** — In this study, fish oil supplementation improved plasma VLDL cholesterol, VLDL TGs, and total TGs while having a transient deterioration in LDL cholesterol in subjects with NIDDM. Furthermore, fish oil supplementation had no significant deleterious effect on glycemic control.

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NIDDM, non-insulin-dependent diabetes mellitus; LDL, low-density lipoprotein; TG, triglyceride; VLDL, very-low-density lipoprotein; HDL, high-density lipoprotein; FPG, fasting plasma glucose.

In recent years, several small clinical trials have examined the role of ω-3 fatty acids on various physiological parameters associated with coronary heart disease and diabetes control (1–12). The purpose of this study was to assess the effects of fish oil supplementation compared with corn oil supplementation on blood lipid profiles and glycemic control in hyperlipidemic individuals with non-insulin-dependent diabetes mellitus (NIDDM).

## RESEARCH DESIGN AND METHODS

— Forty subjects with NIDDM were recruited and informed consent was obtained. Study participants had to exhibit one or more of the following plasma lipid values: plasma cholesterol >5.17 mmol/l, plasma low-density lipoprotein (LDL) cholesterol >3.36 mmol/l, or plasma triglycerides (TGs) >6.47 mmol/l (13,14). Subjects came for 11 biweekly visits for a total of 21 weeks. Biweekly analysis was done to measure plasma total cholesterol, very-low-density lipoprotein (VLDL) cholesterol, high-density lipoprotein (HDL) cholesterol, LDL cholesterol, total TGs, and VLDL TGs (Impact 400E AutoAnalyzer, Gilford, Oberlin, OH). Also recorded biweekly were weight and blood pressure. Diabetes control was closely monitored with fasting plasma glucose (FPG) (model 23A glucose analyzer, YSI, Yellow Springs, OH) and glycosylated $HbA_{1c}$ ($GHbA_{1c}$) levels (model HA08100 Auto $A_{1c}$ Analyzer, Kyoto Dauchi, Kyoto, Japan).

After the baseline phase, subjects were randomly assigned at the 4th week of the study in a double-blind fashion for type of oil capsule to one of four treatment groups: daily doses of 9 g of fish oil, 18 g of fish oil, 9 g of corn oil, or 18 g of corn oil for 12 weeks. The fatty acid content of the capsules is found in Table 1. The last 4 weeks of the study were the postcapsule ingestion phase.

All parameters were tested across time using a three-factorial analysis of variance with a repeated measures factor.

**Table 1—*Fatty acid composition of capsules***

| Carbon chain | Common name | % of corn oil capsules | % of fish oil capsules |
|---|---|---|---|
| 16:0 | Palmitic acid | 10.1 | 1.7 |
| 16:1 | Palmitolic acid | | 0.5 |
| 18:0 | Stearic acid | 1.8 | 4.4 |
| 18:1 | Oleic acid | 25.7 | 7.9 |
| 18:2 | Linoleic acid | 57.2 | 3.0 |
| 18:3 | Linolenic acid | 1.0 | 2.5 |
| 18:4 | | | 3.7 |
| 20:1 | | | 2.0 |
| 20:4 | Arachidonic acid | | 2.0 |
| 20:5 | Eicosapentaenoic acid | | 28.8 |
| 22.5 | Docosapentaenoic acid | | 5.1 |
| 22.6 | Docosahexaenoic acid | | 27.3 |
| Unknown | | 4.2 | 11.1 |
| Total | | 100.0 | 100.0 |

Carbon chain length and number of double bonds.

A Newman-Kuels multiple comparison test was used to identify significant interactions at the $P < 0.05$ level.

**RESULTS** — Demographic data on the subjects are found in Table 2. Overall capsule ingestion compliance rate for all study subjects was 97.1%. The level of oil supplements (9 g/day compared with 18 g/day) did not have significant effects on glycemic control and blood lipids within the fish oil and corn oil groups. When the 9-g and 18-g groups were combined, significant differences ($P < 0.05$) in lipids were found.

No significant differences were found among weight, FPG, and $GHbA_{1c}$ between the treatment groups or across time (Table 3). Although differences were observed in $GHbA_{1c}$, these were not at the $P < 0.05$ level of significance.

The results of the plasma lipid analysis can be found in Table 4. Plasma VLDL cholesterol level was significantly lower ($P = 0.0001$) in fish oil subjects compared with corn oil subjects at 12 weeks of supplementation. There was a significant rise in plasma VLDL cholesterol ($P = 0.04$) in the corn oil subjects from week 6 to week 12 of supplementation. Total plasma TG was significantly lower ($P = 0.0001$) in the fish oil subjects compared with the corn oil subjects at 6 and 12 weeks of supplementation. Plasma VLDL-TG was significantly lower in the fish oil subjects compared with the corn oil subjects at 6 weeks ($P = 0.02$) and at 12 weeks of supplementation ($P = 0.0001$). LDL cholesterol was significantly higher in the fish oil subjects ($P = 0.008$) at 6 weeks, but this difference disappeared at 12 weeks of supplementation. No significant differences were found in total plasma cholesterol or HDL cholesterol.

**CONCLUSIONS** — The results of this study confirm the lipid-lowering effect of fish oil supplementation with regard to total plasma TGs, VLDL TGs, and VLDL cholesterol reported by other investigators (1–3,5,8,9). Previous small studies have reported similar increases in LDL cholesterol (3,5,9).

Some previously reported studies have indicated a deterioration in glycemic control during fish oil supplementation (2–5,15). Our study carefully monitored diabetes control in a larger group of individuals for a longer period of time, and there were no significant changes in FPG or $GHbA_{1c}$ in any treatment group.

The question of whether to use fish oil supplements in treating hyperlipidemia in individuals remains a topic of debate within the diabetes community (15–19). Long-term compliance with large daily doses of fish oil capsules and the associated cost are concerns for this method of treating hyperlipidemia. Based

**Table 2—*Demographic data on subjects with NIDDM by treatment group***

| Descriptor | All subjects | Fish oil subjects | | Corn oil subjects | |
|---|---|---|---|---|---|
| | | 9 g | 18 g | 9 g | 18 g |
| Age (years) | 53.9 ± 7.0 | 55.2 ± 6.2 | 53.4 ± 8.8 | 52.2 ± 6.2 | 54.6 ± 7.1 |
| Sex (*n*) | | | | | |
| M | 18 | 4 | 6 | 4 | 4 |
| W | 22 | 6 | 4 | 6 | 6 |
| Duration of NIDDM (years) | 8.5 ± 5.9 | 11.1 ± 6.1 | 8.5 ± 7.6 | 7.2 ± 3.8 | 7.0 ± 4.2 |
| Age at onset of NIDDM (years) | 45.4 ± 6.4 | 47.4 ± 5.5 | 44.9 ± 8.4 | 44.3 ± 4.6 | 47.6 ± 6.7 |
| NIDDM therapy (*n*) | | | | | |
| Insulin | 22 | 9 | 7 | 3 | 3 |
| Oral agents | 14 | 1 | 1 | 6 | 6 |
| Diet only | 4 | 0 | 2 | 1 | 1 |
| Race (*n*) | | | | | |
| White | 24 | 5 | 8 | 4 | 7 |
| Black | 8 | 1 | 1 | 5 | 1 |
| Hispanic | 8 | 4 | 1 | 1 | 2 |

Data are means ± SD. No values were significantly different at $P < 0.05$. Daily oil supplementation was given for 12 weeks. $n = 40$ for all subjects; $n = 10$ for each group.

**Table 3—*Weight, $GHbA_{1c}$, and FPG of subjects with NIDDM***

| | Weeks of Supplementation | | |
|---|---|---|---|
| | 0 | 6 | 12 |
| Weight (kg) | | | |
| Fish oil ($n$ = 20) | 93 ± 16.2 | 93 ± 16.5 | 93 ± 16.6 |
| Corn oil ($n$ = 20) | 86 ± 11.3 | 86 ± 11.4 | 85 ± 11.0 |
| $GHbA_{1c}$(%) | | | |
| Fish oil ($n$ = 20) | 7.3 ± 1.5 | 7.6 ± 1.5 | 7.7 ± 1.7 |
| Corn oil ($n$ = 20) | 7.6 ± 1.7 | 7.7 ± 1.9 | 7.8 ± 2.0 |
| FPG (mmol/l) | | | |
| Fish oil ($n$ = 20) | 10.4 ± 3.4 | 12.2 ± 3.5 | 11.6 ± 3.4 |
| Corn oil ($n$ = 20) | 11.6 ± 3.5 | 12.1 ± 3.3 | 12.4 ± 3.5 |

Data are means ± SD. No values were significantly different at $P < 0.05$.

on our data, there appears to be no deleterious effect on diabetic control in individuals with NIDDM in conjunction with fish oil supplementation. Thus, this form of therapy may be considered in severe hypertriglyceridemic diabetic subjects unresponsive to conventional lipid-lowering strategies.

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**Table 4—*Plasma lipid values of subjects with NIDDM***

| Plasma lipid values (mmol/l) | Weeks of Supplementation | | |
|---|---|---|---|
| | 0 | 6 | 12 |
| Total cholesterol | | | |
| Fish oil ($n$ = 20) | 6.35 ± 0.87 | 6.31 ± 0.95 | 6.49 ± 0.98 |
| Corn oil ($n$ = 20) | 6.51 ± 1.28 | 6.80 ± 1.54 | 6.83 ± 1.05 |
| HDL cholesterol | | | |
| Fish oil ($n$ = 20) | 1.05 ± 0.37 | 1.02 ± 0.35 | 1.00 ± 0.45 |
| Corn oil ($n$ = 20) | 0.94 ± 0.26 | 0.95 ± 0.31 | 0.93 ± 0.27 |
| LDL cholesterol | | | |
| Fish oil ($n$ = 20) | 3.71 ± 0.78 | 4.04 ± 0.92* | 4.08 ± 0.78 |
| Corn oil ($n$ = 20) | 3.87 ± 1.30 | 3.62 ± 1.30* | 3.87 ± 1.43 |
| VLDL cholesterol | | | |
| Fish oil ($n$ = 20) | 1.01 ± 0.68 | 0.71 ± 0.59† | 0.71 ± 0.56 |
| Corn oil ($n$ = 20) | 1.06 ± 0.66 | 0.94 ± 0.66†‡ | 1.28 ± 1.15‡ |
| Total TGs | | | |
| Fish oil ($n$ = 20) | 6.13 ± 3.13 | 4.86 ± 2.76§ | 4.67 ± 2.61‖ |
| Corn oil ($n$ = 20) | 7.80 ± 4.83 | 9.26 ± 11.42§ | 8.59 ± 7.53‖ |
| VLDL TGs | | | |
| Fish oil ($n$ = 20) | 4.16 ± 2.76 | 2.82 ± 2.21¶ | 2.63 ± 1.87# |
| Corn oil ($n$ = 20) | 4.75 ± 3.35 | 4.38 ± 3.60¶ | 5.84 ± 6.19# |

Data are means ± SD. *$P$ = 0.008, LDL cholesterol, fish oil vs. corn oil at 6 weeks; †$P$ = 0.0001, VLDL cholesterol, fish oil vs. corn oil at 6 weeks; ‡$P$ = 0.04, VLDL cholesterol, corn oil at 6 weeks vs. corn oil at 12 weeks; §$P$ = 0.0001, Total TGs, fish oil vs. corn oil at 6 weeks; ‖$P$ = 0.0001, Total TGs, fish oil vs. corn oil at 12 weeks; ¶$P$ = 0.02, VLDL, fish oil vs. corn oil at 6 weeks; #$P$ = 0.0001, VLDL, fish oil vs. corn oil at 12 weeks.

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