We conclude that, in the age range studied, a single maintenance dose of digoxin is equivalent to a twice-daily dosage regimen in maintaining therapeutic serum concentrations of digoxin.

REFERENCES


Increased incidence of epistaxis in adolescents with familial hypercholesterolemia treated with fish oil

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The results of nutritional and epidemiologic studies of Greenland Eskimos, in whom the incidence of coronary atherosclerosis and myocardial infarction is very low, led some years ago to the suggestion that the nature of dietary fat may be important in the prevention of these conditions.1,2 Subsequent studies confirmed an association between the ingestion of fish oil and decreased mortality rates for coronary artery disease and favorable changes in plasma lipids, notably decreases in levels of triglycerides and very low density lipoprotein.3 The results of these studies suggested that the beneficial effect of diets containing fish was likely due to the presence of a high proportion of polyunsaturated fatty acids of the omega-3 series, principally eicosapentaenoic acid, in fish oil. This conclusion led to extensive use of commercially developed preparations of refined marine oils as dietary supplements.

The mechanism of the beneficial effect of dietary omega-3 fatty acids is still unclear. The most consistent and positive effect has been the observation that plasma levels of triglycerides and very low density lipoprotein are lowered. Potentially hazardous side effects of diets enriched in omega-3 polyunsaturated fatty acids include problems related to the effect on platelet function. High dietary omega-3 fatty acid intake causes changes in the fatty acid composition of platelet membranes and a reduction of platelet aggregation and thrombogenesis in vivo.4-6 These side effects may limit the usefulness of currently available fish oil preparations in the treatment of hyperlipidemia.

The purpose of the study reported here was to evaluate the potentially beneficial effect of dietary fish oil supplementation on plasma lipid levels in a small group of adolescent patients with familial hyperlipoproteinemia type II, and to note possible undesirable side effects.

METHODS

We studied seven female and four male adolescents, 11 to 21 years of age, with FHL type II. The diagnosis of each case was based on a positive family history, typical abnormalities of plasma lipid levels, and absence of evidence of any other condition to account for the lipid abnormalities. All subjects were apparently heterozygous for FHL type II; five were classified as having FHL type IIa and six, type IIb, on the basis of plasma triglyceride levels. All subjects were maintained on their usual modified low cholesterol–low saturated fat diet throughout the study; two also received...
The subject had been receiving 5 gm offish oil per day for the fifth and sixth months of therapy. The subject had asymptomatic occult blood in the stool one occasion; the bleeding time was normal. None of the subjects had any evidence of liver dysfunction; all prothrombin and partial thromboplastin times and platelet counts were normal.

### DISCUSSION

Among our patients, fish oil treatment, in the dosages used, had no overall statistically significant effect on any class of plasma lipids during the relatively short period of the study. Decreased triglyceride levels in response to dietary fish oil supplementation are one of the most consistent findings reported from studies on adults, particularly subjects with hypertriglyceridemia.3 The difference may be due to the lower dosages of fish oil we employed in our patients. In contrast to the apparent lack of effect on plasma lipids, fish oil treatment was associated with an unexpectedly high incidence of bleeding problems.

Of our 11 subjects, three had prolongation of bleeding time during fish oil supplementation. In one case, the abnormality and associated bleeding were considered to be serious enough to discontinue treatment. Dyerberg and Bang4 noted prolonged bleeding times in Eskimos who consumed diets high in marine fish. The results of subsequent investigations showed that persons who consumed diets high in fish oils had increased levels of eicosapentaenoic acid, and lower levels of arachidonic acid, in their plasma lipids and platelet membranes. Sanders et al.9,10 noted that bleeding times were increased in every one of 12 healthy male subjects aged 19 to 31 years who consumed 20 ml of cod liver oil daily for 6 weeks. Although only three of the subjects in our study had abnormal bleeding times, a surprising eight of the total reported an increased incidence of nosebleeds. Whether this was due to an effect on platelet function that was too subtle to affect the bleeding time as measured clinically, but sufficient nonetheless to cause an increased incidence of epistaxis, is unknown.

### REFERENCES


### Table. Effect of fish oil treatment on plasma lipid levels

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Type of FHL</th>
<th>Before treatment (mmol/L)</th>
<th>After treatment (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>Ia</td>
<td>1.12 ± 0.30 (15)</td>
<td>0.96 ± 0.34 (27)</td>
</tr>
<tr>
<td></td>
<td>Ib</td>
<td>2.91 ± 1.29 (18)</td>
<td>2.14 ± 1.08 (35)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Ia</td>
<td>8.55 ± 1.61 (15)</td>
<td>9.03 ± 2.40 (27)</td>
</tr>
<tr>
<td></td>
<td>Ib</td>
<td>7.67 ± 1.77 (18)</td>
<td>7.63 ± 2.06 (35)</td>
</tr>
<tr>
<td>LDL-C</td>
<td>Ia</td>
<td>6.80 ± 1.31 (15)</td>
<td>7.47 ± 2.36 (27)</td>
</tr>
<tr>
<td></td>
<td>Ib</td>
<td>5.39 ± 1.93 (18)</td>
<td>5.68 ± 2.01 (34)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>Ia</td>
<td>1.19 ± 0.28 (15)</td>
<td>1.15 ± 0.29 (27)</td>
</tr>
<tr>
<td></td>
<td>Ib</td>
<td>2.91 ± 1.29 (18)</td>
<td>2.14 ± 1.08 (35)</td>
</tr>
</tbody>
</table>

Values represent the means ± SD, with the number of observations in parentheses.

LDL-C, Low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.
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Benefit of intravenously administered immune serum globulin in patients with Guillain-Barré syndrome

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The pathologic features of Guillain-Barré syndrome and of experimental allergic neuritis induced in animals are similar; they consist of inflammatory lesions scattered throughout the peripheral nervous system. These lesions are characterized by lymphocytic infiltration of the myelin sheath, which may lead to segmental demyelination. The association of anti-peripheral-nerve myelin antibodies with damage to myelin, and the induction of demyelination in animals injected with serum obtained from patients with GB syndrome, suggest that this syndrome has an immunologic basis. Plasmapheresis has been critically studied and shortens the duration of severe weakness and assisted ventilation; it has been successfully applied in the treatment of children with severe GB syndrome. However, the requirement for sophisticated equipment and experienced personnel to perform the procedure hinders the routine application of this modality of therapy.

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As an alternative therapy to plasmapheresis, we have treated three patients who had severe GB syndrome with intravenously administered immune serum globulin. We report the rapid improvement of muscle strength in all three patients.

METHODS

Patients. In two girls and one boy, whose ages were 12 and 13 years, progressive muscle weakness began 3 to 8 days before hospital admission. Two of the three patients had sensory symptoms, including numbness, paresthesias, and transient muscle pain (Table). Muscle stretch reflexes were diminished or absent in all three patients. Lumbar puncture performed 3 to 8 days after the onset of symptoms revealed increased protein levels in all patients (Table), and electromyographic studies revealed decreased motor nerve conduction velocities associated with an absent F response, suggesting demyelination. All three patients had evidence of antecedent or concomitant infections. The clinical presentation, electromyographic changes, and evidence of increased levels of protein in cerebrospinal fluid led to the diagnosis of GB syndrome in these patients.