Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): a randomised open-label, blinded endpoint analysis

Dr Mitsuhiro Yokoyama MD a, Hideki Origasa PhD b, Masunori Matsuzaki MD c, Yuji Matsuzawa MD d, Yasushi Saito MD e, Yuichi Ishikawa MD f, Shinichi Oikawa MD g, Jun Sasaki MD h, Hitoshi Hishida MD i, Hiroshige Itakura MD j, Toru Kita MD k, Akira Kitabatake MD l, Noriaki Nakaya MD m, Toshiie Sakata MD n, Kazuyuki Shimada MD o and Kunio Shirato MD p, for the Japan EPA lipid intervention study (JELIS) Investigators

Summary

Background

Epidemiological and clinical evidence suggests that an increased intake of long-chain n-3 fatty acids protects against mortality from coronary artery disease. We aimed to test the hypothesis that long-term use of eicosapentaenoic acid (EPA) is effective for prevention of major coronary events in hypercholesterolaemic patients in Japan who consume a large amount of fish.

Methods

18 645 patients with a total cholesterol of 6.5 mmol/L or greater were recruited from local physicians throughout Japan between 1996 and 1999. Patients were randomly assigned to receive either 1800 mg of EPA daily with statin (EPA group; n=9326) or statin only (controls; n=9319) with a 5-year follow-up. The primary endpoint was any major coronary event, including sudden cardiac death, fatal and non-fatal myocardial infarction, and other non-fatal events including unstable angina pectoris, angioplasty, stenting, or coronary artery bypass grafting. Analysis was by intention-to-treat. The study was registered at ClinicalTrials.gov, number NCT00231738.

Findings
At mean follow-up of 4.6 years, we detected the primary endpoint in 262 (2.8%) patients in the EPA group and 324 (3.5%) in controls—a 19% relative reduction in major coronary events (p=0.011). Post-treatment LDL cholesterol concentrations decreased 25%, from 4.7 mmol/L in both groups. Serum LDL cholesterol was not a significant factor in a reduction of risk for major coronary events. Unstable angina and non-fatal coronary events were also significantly reduced in the EPA group. Sudden cardiac death and coronary death did not differ between groups. In patients with a history of coronary artery disease who were given EPA treatment, major coronary events were reduced by 19% (secondary prevention subgroup: 158 [8.7%] in the EPA group vs 197 [10.7%] in the control group; p=0.048). In patients with no history of coronary artery disease, EPA treatment reduced major coronary events by 18%, but this finding was not significant (104 [1.4%] in the EPA group vs 127 [1.7%] in the control group; p=0.132).

Interpretation

EPA is a promising treatment for prevention of major coronary events, and especially non-fatal coronary events, in Japanese hypercholesterolaemic patients.

Affiliations

a. Kobe University, Kobe, Japan
b. Division of Clinical Epidemiology and Biostatistics, Toyama University, Toyama, Japan
c. Yamaguchi University, Yamaguchi, Japan
d. Sumitomo Hospital, Osaka, Japan
e. Chiba University, Chiba, Japan
f. Kobe University, Kobe, Japan
g. Nippon Medical School, Tokyo, Japan
h. International University of Health and Welfare Graduate School of Public Health Medicine, Fukuoka, Japan
i. Fujita Health University School of Medicine, Aichi, Japan
j. Ibaraki Christian University, Ibaraki, Japan
k. Kyoto University, Kyoto, Japan
l. Showa Hospital, Hyogo, Japan
m. Nakaya Clinic, Tokyo, Japan
n. Nakamura Gakuen University, Fukuoka, Japan
o. Jichi Medical School, Tochigi, Japan
p. Saito Hospital, Miyagi, Japan

Correspondence to: Dr Mitsuhiro Yokoyama, Cardiovascular Medicine Division, Department of Internal Medicine, Kobe University Graduate School of Medicine, 7-5-2, Kusunoki-cho, Chuo-ku, Kobe, 650-0017 Japan