Fish Oil Supplementation and the Risk of Ventricular Tachycardia and Ventricular Fibrillation in Patients with Implantable Defibrillators: a meta-analysis

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Background --- Sudden cardiac death (SCD) is a very common, and often the first, manifestation of coronary heart disease. Increased attention has been given to the reduced incidence of SCD among people taking omega-3 polyunsaturated fatty acids (omega-3 PUFAs). The protective effect of seems to be due to an anti-arrhythmic effect.

Methods and Results --- This meta-analysis reviewed three journals on the beneficial anti-arrhythmic effect of omega-3 PUFAs in patients with a history of ventricular tachycardia (VT) or ventricular fibrillation (VF) and an implantable cardioverter defibrillator. Three trials involving 1148 patients were included in this review. The population was homogenous. Results of the three studies showed no significant reduction in the number of VF/VT events needing intervention and all-cause mortality. However, there is a trend toward benefit, particularly in the reduction of the mortality rate.

Conclusion --- This meta-analysis supports the provides evidence that a supplement containing long-chain n-3 fatty acids has anti-arrhythmic actions in humans and may reduce the risk of potentially life-threatening arrhythmias in those at risk. ***Phil Heart Center J 2007;13(2):171-173.***

Key Words: Fish oil ■ ventricular arrhythmia ■ sudden cardiac death ■ defibrillator ■ meta-analysis

Sudden cardiac death (SCD) is a very common, and often the first, manifestation of coronary heart disease. The majority are caused by acute ventricular arrhythmias (Brouwer, 2006). A search for preventive measures is needed. During the past years, increased attention has been given to the reduced incidence of SCD among people eating fish or taking supplements of fish oils or very-long-chain n-3 polyunsaturated fatty acids (omega-3 PUFAs). The protective effect of marine omega-3 PUFA on SCD seems to be due to an anti-arrhythmic effect of omega-3 PUFA, an effect mainly demonstrated in in-vitro experiments and in animal studies (Christensen, 2005). In the results of the secondary prevention trial, the Diet And Reinfarction Trial (DART), it showed a significant reduction in total and cardiovascular mortality (both by about 30%) in patients who consumed at least two servings of fatty fish per week after suffering from myocardial infarction. These encouraging reports led us to hypothesize that omega-3 PUFAs might prevent ventricular arrhythmias in high-risk patients.

Objective

The purpose of this meta-analysis was to review whether omega-3 PUFAs has a beneficial anti-arrhythmic effect in patients with a history of ventricular tachycardia (VT) or ventricular fibrillation (VF) and an implantable cardioverter defibrillator, as manifested in decreased need for ICD intervention and decreased mortality.

Criteria For Considering Studies For This Review

Types of studies

Randomized controlled trials (RCTs) in which patients with a history of ventricular tachycardia or ventricular fibrillation were randomized to treatment with fish oil or placebo for the prevention of VF/VT.

Search Methods For Identification Of Studies

We searched the MEDLINE for all articles, journals, and publication from 1985 up to the present, with the search terms "omega-3 fatty acids," "fish oil," "PUFA," "ventricular tachycardia," and "ventricular fibrillation."

Selection Criteria

We have three clinical trials which met the criteria for inclusion. They used omega-3 PUFAs for the prevention of ventricular tachyarrhythmias in patients with a history of ventricular tachycardia or ventricular fibrillation and ICD implantation. All the clinical trials were prospective, randomized, double blind, and placebo-controlled

Data Collection And Analysis

Data was extracted from the studies and recorded. Data included: number of patients enrolled in every group,

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baseline characteristics, inclusion/exclusion criteria, treatment schema and doses, length of follow-up, and the incidence of endpoints. Statistical analyses were performed by statistical package Review Manager 4.2.9,

Data Collection And Analysis

Data was extracted from the studies and recorded. Data included: number of patients enrolled in every group, baseline characteristics, inclusion/exclusion criteria, treatment schema and doses, length of follow-up, and the incidence of endpoints. Statistical analyses were performed by statistical package Review Manager 4.2.9, version 2006. We analyzed dichotomous outcomes using odds ratios with a random effects model.

Results

Three trials involving 1148 patients were included in this review. The population was homogenous. The study by Leaf et al (2005) had the largest proportion of patients noncompliant to the treatment regimen among the three trials. Individually, all three studies showed no significant benefit in either mortality or frequency of ICD intervention. In the study by Leaf et al (2005), those who took fish oil supplement had higher RBC content of EPA plus DHA. There was no significant difference in the number of deaths, but there was a non-significant trend toward a longer time to first ICD event for VT/VF and reduction in total number of confirmed VF/VT events among patients randomized to fish oil compared to placebo. This is also similar to the findings from Brouwer et al (2006) and Raitt et al (2005). Results of the three studies showed no significant reduction in the number of VF/VT events needing intervention and all-cause mortality. However, there is a trend toward benefit, particularly in the reduction of the

Discussion

The result of the three studies did not show a reduction in all-cause mortality and frequency of ICD intervention in high-risk patients for VF/VT, but showed a trend toward benefit. There is evidence that omega-3 PUFAs reduce cardiovascular mortality via an anti-arrhythmic effect. Studies in rats show that a diet high in omega-3 PUFAs reduced the risk of VF during acute ischemia compared with control animals (McLennan, 1993). It changes the spontaneous beating rate of cultured myocardial cells, prevent and terminate drug-induced arrhythmias, and can bind to and inactivate myocardial sodium channels, a class I anti-arrhythmic effect (Kang, 1994). There are four human prospective randomized trials that have shown that supplementation with fish oil is associated with a decreased risk of sudden death without a consistent change in risk of myocardial infarction, the largest of which is the GISSI-Prevenzione trial, which showed significant differences within 4 months in those who were receiving fish oil.

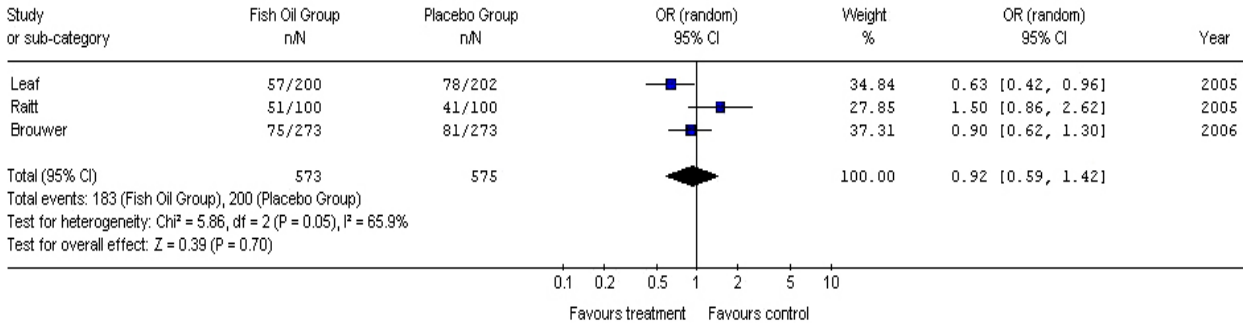

Figure 1. Forrest Plot of Hazard Ratios of Fish Oil Treatment for Frequency of ICD Therapy for VF/VT.

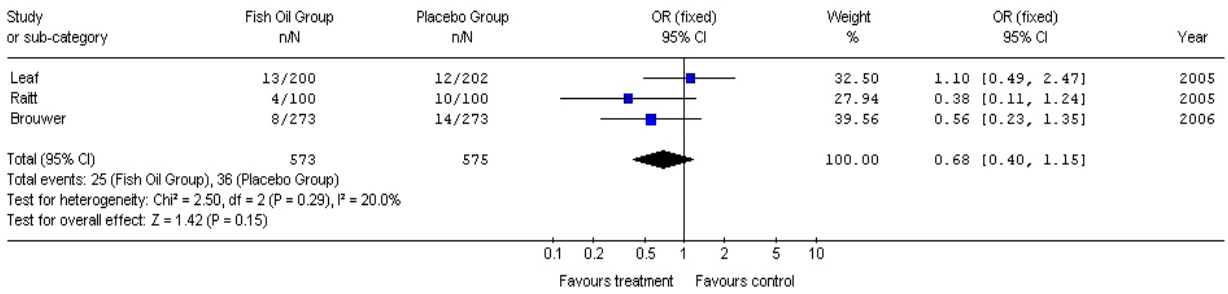

Figure 2. Forrest Plot of Hazard Ratios of Fish Oil Treatment for All-Cause Mortality.

The discordance between these three trials and those of previous studies may lie in the fact that experimental models used ischemic VF as an endpoint, and the cohort and clinical trials used sudden death as an end point. These studies used ICD therapy for VT or VF as the primary end point, and this may not be an ideal surrogate for the risk of sudden death. In addition, prior clinical studies were performed in patients with recent myocardial infarction and relatively well-preserved ventricular function, in whom ischemic VF might be the expected primary cause of sudden death. In contrast, the patients in our study were substantially different in that they had not had a recent myocardial infarction, had significantly reduced left ventricular function, and, perhaps, had a history of sustained ventricular arrhythmia. A hypothesis suggested by Leaf et al. suggests that fish oil may have its most profound anti-arrhythmic effects in the setting of acute ischemia and VF. Although the majority of patients in the study had coronary artery disease, they all had experienced episodes of sustained VT or VF outside of the setting of acute myocardial infarction. The mechanism of arrhythmia in such patients, is unlikely to be ischemic but, instead, was probably myocardial scar-based reentry (Leaf 2005).

Limitations

This meta-analysis is limited by the small number of studies and patients, including the large noncompliant rate.

Conclusion

This meta-analysis supports the evidence that a supplement containing long-chain n-3 fatty acids has anti-arrhythmic actions in humans and may reduce the risk of potentially life-threatening arrhythmias in those at risk.

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