Early Protection Against Sudden Death by n-3 Polyunsaturated Fatty Acids After Myocardial Infarction

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Roberto Marchioli, MD; Federica Barzi, MS; Elena Bomba, MD; Carmine Chieffo, MD; Domenico Di Gregorio, MD; Rocco Di Mascio, MD; Maria Grazia Franzosi, MD; Enrico Geraci, MD; Giacomo Levantesi, MD; Aldo Pietro Maggioni, MD; Loredana Mantini, MD; Rosa Maria Marfisi, MS; G. Mastrogiuseppe, MD; Nicola Mininni, MD; Gian Luigi Nicolosi, MD; Massimo Santini, MD; Carlo Schweiger, MD; Luigi Tavazzi, MD; Gianni Tognoni, MD; Corrado Tucci, MD; Franco Valagussa, MD; on behalf of the GISSI-Prevenzione Investigators

Background
Our purpose was to assess the time course of the benefit of n-3 polyunsaturated fatty acids (PUFAs) on mortality documented by the GISSI-Prevenzione trial in patients surviving a recent (<3 months) myocardial infarction.

Methods and Results
In this study, 11,323 patients were randomly assigned to supplements of n-3 PUFAs, vitamin E (300 mg/d), both, or no treatment (control) on top of optimal pharmacological treatment and lifestyle advice.

Early efficacy of n-3 PUFA treatment for total, cardiovascular, cardiac, coronary, and sudden death; nonfatal myocardial infarction; total coronary heart disease; and cerebrovascular events was assessed by right-censoring follow-up data 12 times from the first month after randomization up to 12 months.

Survival curves for n-3 PUFA treatment diverged early after randomization, and total mortality was significantly lowered after 3 months of treatment (relative risk [RR] 0.59). **[41% reduced risk]**

The reduction in risk of sudden death was specifically relevant and statistically significant already at 4 months (RR 0.47). **[53% reduced risk]**

A similarly significant, although delayed, pattern after 6 to 8 months of treatment was observed for cardiovascular, cardiac, and coronary deaths.

Conclusions
The early effect of low-dose (1 g/d) n-3 PUFAs on total mortality and sudden death supports the hypothesis of an antiarrhythmic effect of this drug.

Such a result is consistent with the wealth of evidence coming from laboratory experiments on isolated myocytes, animal models, and epidemiological and clinical studies.

THESE AUTHORS ALSO NOTE:

"A growing consensus for a direct relationship between increased intake of n-3 polyunsaturated fatty acids (PUFAs) either from dietary sources or as a pharmacological supplementation and decreasing risk of coronary heart disease has become apparent over the years." (15 references)

Large-scale clinical trials of patients surviving recent myocardial infarction have provided solid evidence of the efficacy of low-dose (1 g/d) n-3 PUFAs in reducing overall and cardiovascular mortality.

This study involved 11,323 patients with recent (<3 months) myocardial infarction. They were followed for 3.5 years on the efficacy of n-3 PUFAs 1 g/d, vitamin E 300 mg/d, a combination of the two, and control. The follow-up represented 38,418 person years.

RESULTS

"Patients allocated to n-3 PUFA treatment had a significantly lower mortality even after only 3 months of treatment."

This benefit on reduced mortality was highly statistically significant at 42 months.

The n-3 PUFA group had a small but significant reduction in triglyceride concentrations that was not observed in controls.

As compared with controls, n-3 PUFA treatment did not change glycemia or blood fibrinogen levels.

DISCUSSION

"The analysis of the time course of the appearance of the effects of n-3 PUFAs showed an early and highly significant reduction of sudden cardiac death."

The results point to an antiarrhythmic / antifibrillatory effect of n-3 PUFAs.

"The antiarrhythmic and antifibrillatory effects of n-3 PUFAs have been reported in animal studies on marmosets, rats, and dogs, as well as in laboratory experiments on isolated myocytes."

"According to the results of electrophysiological studies, n-3 PUFAs seem to modulate ion currents (primarily of Na^+ and Ca^{++}) in the myocyte sarcolemma, shifting the steady-state inactivation potential to more negative values, increasing the depolarizing current necessary to elicit an action potential by approximately 50% and prolong the refractory period by about 3-fold."
[Lowers the resting threshold so that the heart is more stable against trivial excitation depolarization or arrhythmic dysfunction].

There was a 41% relative risk reduction of total mortality observed after 3 months of treatment with n-3 PUFAs.
At the end of the study (3.5 years) the relative risk reduction was 21%.
The authors explained this in part as expected as numbers of patients stopped taking their n-3 PUFAs after the active trial period of 12 months.

CONCLUSIONS

The significant reduction of mortality documented in this trial with a low dose (1 g/d) of n-3 PUFAs appears very early in the course of the treatment and is explained mainly by the decrease of sudden death.

"The findings provide an important support to the hypothesis of an antiarrhythmic and/or antifibrillatory role of n-3 PUFAs, which should be formally tested with adequately sized trials on well-defined candidate clinical conditions."

This article has 35 supportive references.

KEY POINTS FROM DAN MURPHY

(1) In the patients who had already suffered myocardial infarction, supplementation with 1 g/d of n-3 PUFA's significantly lowered sudden mortality after 3 months of treatment.

(2) This study considered 1 g/d of n-3 PUFA to be "low dose."

(3) The n-3 PUFAs supplementation group also showed significant reduction in cardiovascular, cardiac, and coronary deaths with 6 to 8 months of treatment.

(4) Numerous studies support the cardiovascular protective effect of n-3 PUFAs, but this article death supports the hypothesis of an antiarrhythmic and antifibrillatory effect**.**
[At a time when public officials want every agency from airplanes to schools to carry and have staff trained in the use of defibrillators].

(5) The n-3 PUFA supplementation also reduced triglyceride levels without adversely affecting blood sugar levels.

(6) The evidence presented is that n-3 PUFAs stabilized cardiac electrical depolarization by lowering the resting electrical threshold.
[A similar explanation is used with respects to the nociceptive afferent system and the reduction of pain perception].

COMMENTS FROM DAN MURPHY

These patients had already suffered myocardial infarction.

This article adds to the evidence of the cardiovascular protective benefits of n-3 PUFAs.

This study used supplementation of n-3PUFAs rather than consumption of fish.

This is important because some patients / chiropractors will not eat fish.

The article did not indicate if the n-3 PUFA supplemented was alpha-linolenic acid (18 carbons, plant based), eicosapentaenoic acid (20 carbons, fish based), or docosahexaenoic acid (22 carbons, fish based).

I believe that it is important to know.

In any case, this article continues to support that n-3 PUFAs in the diet is an important aspect of the INNATE DIET.

PUFAs protect the cardiovascular system, reduce cancer, improve immune system function, reduce pain, and build a better brain.