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LETTER TO THE EDITOR

The Response to Fish Oil in Patients with Heart Disease Depends on the Predominant Arrhythmia Mechanism

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Dear sir,

We have read with interest the paper by Nodari et al [1] and the editorial by Dr. Raitt [2] on fish oil fatty acids and arrhythmic risk in heart failure patients caused by idiopathic dilated cardiomyopathy. In both publications, the mechanism by which fish oils may be both pro- and antiarrhythmic are mentioned but remain un-clarified. The heterogeneous response to fish oil in patients with heart disease may be explained by the arrhythmia mechanism.

The GISSI Trial showed that long-term supplementation with fish oil reduced cardiovascular mortality following a myocardial infarction [3]. This could be attributed to a 45% reduction in sudden death, suggesting a direct antiarrhythmic effect of fish oil in these patients [4]. Subsequently, the effect of fish oil on arrhythmias was studied in patients with implanted cardiac defibrillators that suffered from a variety of cardiac pathologies [5–7]. The results were controversial; proarrhythmic and antiarrhythmic effects as well as absence of effects were documented. The recent meta-analysis by Jenkins and co-workers [8] confirmed heterogeneous outcomes in fish oil trials and concludes that fish oils need to be prescribed with caution. The question remains: Why is the response to fish oil heterogeneous? One possibility is that the diverse patient populations have different arrhythmogenic substrates (heart failure, acute ischemia, infarcted myocardium).

Circulating and membrane-bound fish oils shorten the cardiac action potential duration by modulating several ion channels (for review see [9]). Shortening of the action potential, as seen in fish oil fed pigs [10], is proarrhythmic during acute myocardial ischemia [11]. Blockade of the cardiac sodium channel by fish oil may slow conduction, and favor reentrant activation. In contrast, the cardiac action potential is prolonged during heart failure, leading to triggered arrhythmias [12]. Action potential or repolarization time shortening in this setting is antiarrhythmic. In the patients with idiopathic dilated cardiomyopathy that were studied by Nodari and coworkers [1], the predominant arrhythmia mechanism likely is triggered activity. These triggered arrhythmias are inhibited by fish oil in isolated myocytes of patients with end-stage heart failure as a result of cardiac action potential shortening in combination with lower diastolic calcium levels and a reduced response to β-adrenergic stimulation [13].

Fish oils also affect heart rate, lipoprotein levels, inflammatory pathways and hypertrophy and thus also indirectly may determine whether the heart develops arrhythmia.

Altogether this leads to a complex situation; fish oil is antiarrhythmic under conditions of heart failure, and proarrhythmic under condition of acute myocardial ischemia. Patients, especially those with heart disease, may have both types of arrhythmia mechanisms. This makes the outcome of dietary supplementation with fish oil difficult to predict.

The paper of Nodari [1] nicely demonstrates that the effect of fish oil can be best studied in a well defined patient population. We are of the opinion that fish oil supplementation can be safely administered in these patients with idiopathic dilated cardiomyopathy. Whether or not this is the case for other heart disease patients depends on the main arrhythmia mechanism.

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