The Efficacy of Adding Eicosapentaenoic Acid to Statin Monotherapy in the Prevention of Acute Coronary Syndrome in Patients with Coronary Artery Disease

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Abstract

Coronary artery disease (CAD) is a chronic medical condition caused by the buildup of plaque within the coronary artery endothelium. If left untreated it can progress to an acute coronary syndrome (ACS) which can lead to myocardial ischemia and death. Statins are lipid lowering agents used in clinical practice for the medical management of CAD. However, incidence of adverse cardiovascular (CV) events still occurs despite optimal therapy. Currently eicosapentaenoic acid (EPA) has been promoted to be effective when added to statins in lowering the incidence of CV events in patients with hypercholesterolemia. Through an analysis of several published research articles, this study found that adjunct EPA is a viable treatment option to statin therapy in preventing the progression of CAD to ACS in adults over 45, although further research is recommended before a change in clinical practice can be made.

Introduction

Coronary Artery Disease

Overview

- Consists of angina pectoris and acute coronary syndrome
- Leading cause of death in the United States (320,000/year)

Pathophysiology

- Chronic buildup of plaque in coronary artery endothelium leading to obstruction of blood flow, ischemia and infarction

Treatment

- Lifestyle modifications
- Medical Management: Cholesterol lowering agents, nitroglycerin, anti-platelets, and anti-hypertensives
- Surgical Management: Angioplasty vs. coronary artery bypass grafting
- EPA has shown to decrease levels of triglycerides, inflammatory markers and stabilize coronary artery plaques

Methods

- Literature Search: November 2018; PubMed and ClinicalKey
- Search Terms: **"myocardial infarction OR coronary artery disease AND eicosapentaenoic acid OR epa AND statin."**

Inclusion Criteria

- Randomized controlled trials (RCTs)
- Published 2008 or later
- Age: 45+

Exclusion Criteria

- Studies investigating other diseases
- Studies without a documented clinical trial
- Systematic reviews or meta-analyses
- Studies with no concomitant statin therapy

Results

Each study was a RCT designed to test the efficacy of adding EPA to statin therapy in patients with CAD to prevent progression of disease.

* Unless noted, all studies assessed for changes in lipid profiles and inflammatory markers via collected serum values.

1. Alfaddagh et al (2017) - Measured changes in coronary plaque volume via coronary computed tomographic angiography (CCTA).
2. Niki et al (2016) – Measured changes in lipid and fibrous plaque components via integrated backscatter intravascular ultrasound (IB-IVUS).
3. Nishio et al (2014) – Measured changes in fibrous-cap thickness via optical coherence tomography (OCT).
4 Nosaka et al (2017) – Measured changes in lipid profiles only, and incidence of adverse cardiac events via questionnaires at follow-up.
5. Takaki et al (2011) – Measured changes in arterial thickness via ultrasound of the carotid artery and ankle-brachial pulse wave velocity.
6. Toyama et al (2014) – Measured changes in endothelial dysfunction via ultrasonography of right brachial artery.
7. Watanabe et al (2017) – Measured changes in coronary plaque volume via IB-IVUS and incidence of CV events via questionnaires.

Study	LDL-C	EPA /AA	Inflammatory Markers	Plaque Stability	Reduction in CV Outcomes	Reduction in Progression of Baseline Disease
1.	NS	NA	NS	S	NS	S
2.	NS	S	S	S	NA	S
3.	NS	S	S	S	NS	S
4.	NS	S	NA	NA	S	S
5.	NS	S	NS	NA	NA	S
6.	NS	S	NS	NA	NA	S
7.	NS	S	NS	S	NS	S

Key: S = Significant; NS = Not Significant; NA= Results Not Available; LDL-C = Low-Density Lipoprotein Cholesterol; AA = Arachidonic Acid

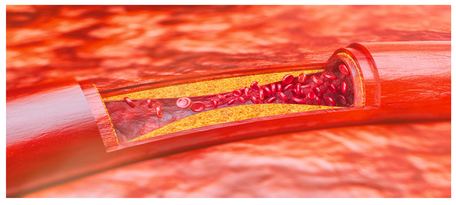
Discussion

Findings

- No significant changes in LDL-C in all 7 studies
- Significant increases in EPA/AA ratios in 6/7 studies
- Significant decreases in inflammatory markers in 2/2 studies that measured for PTX3, a marker more specific for cardiac inflammation
- Significant increases in coronary artery plaque stability in 4/4 studies measured through various imaging methods
- Significant decrease in CV outcomes found in 1 study
- Based on above findings, a reduction in progression of baseline CAD was found in all 7 studies.

Limitations

- Blinding: All studies were open-label RCTs
- Recruitment: 5/7 studies were single-center studies
- Bias: 6/7 studies were conducted exclusively in Japan
- Sample Size: 4/7 studies had marginal or inadequate sample sizes (N<100)



Conclusion

This study has shown enough **positive results** to warrant a **further investigation** for the potential use of EPA with statins in the reduction of disease progression in patients with CAD. Use of adjunct EPA is a relatively safe alternative with few side effects, and no significant changes to baseline LDL-C. However, further research focusing on improved study designs to limit biases, more representative samples, longer follow-ups, larger sample sizes, and better recruitments are needed to improve upon the limitations found in this study.

While the results of this study are positive, further research is necessary before a shift in clinical practice in the management and treatment of CAD can be recommended.

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