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Review

Secondary cvd prevention—Lipid modification strategies: A critical analysis

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ABSTRACT

Lipid modification holds the key to effective secondary prevention of cardiovascular disease (CVD). However there is a controversy on whether it's all about targeting specific lipid sub fractions to a particular level or a direct effect of the agent(s) used or both. This review intends to look into these important issues from an evidence-based perspective. What is the appropriate timing of testing for lipid profile after a cardiovascular event? What is the rationale behind initiating with a high dose statin after an acute coronary event? What is the role of targeting lipid sub fractions beside LDL cholesterol? Is there any role for non-statin based therapy after an acute cardiovascular event? What constitutes a long-term lipid modification strategy in patients post CVD? These are very important questions, which needs to be addressed adequately as well as scientifically. The secondary CVD preventive strategies form a lipid perspective, which requires a thorough review.

Contents

Abbreviations: CVD, cardio vascular disease; NCD, non-nommunicable disease; MONICA, multinational MONItoring of trends and determinants in CArdiovascular disease; CHD, coronary heart disease; ACS, acute coronary syndrome; TG, triglyceride; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; Hs-CRP, highly sensitive C-Reactive protein; IL-6, interleukin-6; FFA, free fatty acid; VLDL-C, very low density-cholesterol; cTnT, cardiac Troponin T; AMI, acute myocardial infarction; STEMI, ST elevation myocardial infarction; NSTEMI, non ST elevation myocardial infarction; DAPT, dual antiplatelet therapy; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; NICE, national institute for health and care excellence; ACC, american college of cardiology; AHA, american heart association; RCT, randomized controlled trial; AIM HIGH, athero- thrombosis intervention in metabolic syndrome with low HDL/High triglycerides: impact on global health out- comes; PROVE IT-TIMI 22, pravastatin or atorvastatin evaluation and infection therapy–thrombolysis in myocardial infarction; MACE, major adverse cardiac events; PCI, percutaneous coronary intervention; TNF-α, tumor necrosis factor- α; SPARCL, stroke prevention by aggressive reduction in cholesterol levels; CKD, chronic kidney disease; BMI, body mass index; IMPROVE-IT, improved reduction of outcomes: vytorin efficacy international trial.

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1. Introduction

- It was estimated that in the year 2008 there were nearly 17 million deaths attributed to cardiovascular diseases (CVD) worldwide [1]. However there were regional discrepancies ranging from 4% in high-income countries to 80% in the middle to low-income groups [2].
- There are two important developments driving policy makers to take note of increasing CV mortality & morbidity. The first was related to a sharp increase in non-communicable diseases (NCDs) due to increasing urbanization and secondly a shift in CVD in the younger age groups.
- According to the Global estimates those younger than 60 years are the ones most affected by CVD. These statistical measures point at the scope of formulating an effective preventive strategy to reduce the CVD burden.
- According to the MONICA study, improved healthcare facilities accounted for nearly one-third reduction in coronary heart disease (CHD) mortality and the remaining two thirds were attributed to modification of established risk factors [3]. The delivery of health care facility is one of the most prominent factors responsible for the discrepant CVD outcomes in different parts of the World. Since this is related to Government policy it is beyond the scope of this review.
- Modification of risk factors (modifiable) as a result is the best possible way an individual physician can make a difference in reducing the CVD burden. Lipids hold a very important place as far as modifying CVD risk factors is concerned (Table 1) In countries where there has been a significant reduction in CVD over the last 4 decades; reduction in blood pressure, lipids and smoking rates were the principal contributors [4].
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Table 1
Modifiable risk factors for CHD (Ref. [4]).

- Smoking
- Dietary factors
- Physical activity
- Obesity
- Diabetes Mellitus
- Blood Lipids
- Blood Pressure

Another observation, which resulted in shifting the focus on preventable strategies, was that it was possible to impact the CVD burden in a short span of time. Traditionally CVD progression was conceived as a very slowly evolving event leading to clinical outcomes. Hence success of a preventive strategy would practically remain invisible. However recent understanding points at the fact that modifying risk factors in a large section of society can rapidly alter the adverse outcomes associated with CVD. Geoffrey Rose's Prevention Paradox suggests targeting the moderate risk groups with a preventive strategy instead of the high risk ones. With this strategy, a smaller shift in the disease risk in the whole population can bring about large changes in the outcome burden [5].

- Thus lipid modification takes the center stage along with blood pressure and lifestyle modification as far as making this significant difference is concerned.

2. Definitions: primary, secondary & tertiary CVD prevention (Table 2)

- The definition of secondary prevention suggests that it deals with reducing recurrent CV events. It encompasses a multifactorial approach including lifestyle modification and pharmacological intervention. Lipid modification is a very important pharmacological component of secondary CVD prevention .

3. Lipids and CVD: pathophysiology post ACS

There are two different windows of opportunity as far as modifying lipids are concerned as a part of secondary CVD preventive strategy:

- Post ACS: Immediate phase.
- Post ASC: Long-term phase.

3.1. Post ACS: immediate phase

The lipid sub fractions are affected in a phasic manner immediately after acute coronary syndrome (ACS). There is a reduction in TC, LDL-C, HDL-C as well as elevation of TG within 24 h of an acute CV event [7]. This data points at not only at an impact on the pre-ACS lipid status but also its association with inflammation. The acute myocardial tissue damage and necrosis induces an inflammatory response identified by elevation of hs-CRP & IL-6.

Table 2
Definitions (Ref. [6]).

PRIMARY CVD PREVENTION	SECONDARY CVD PREVENTION	TERTIARY CVD PREVENTION
• Strategies formulated prior to CVD onset.	• Strategies formulated after CVD has already occurred.	• Aim is to soften the brunt of ongoing disease.
• Population-based target of risk factors.	• Pharmacological treatments with structured follow up.	• Aggressive pharmacological treatment, cardiac rehabilitation and stress on quality of life.

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