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Original Article

Statin therapy/lipid lowering therapy among Indian adults with first acute coronary event: The dyslipidemia Residual and Mixed Abnormalities IN spite of Statin therapy (REMAINS) study

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ABSTRACT

Objective: The primary objective was to evaluate the effect of statin therapy/lipid lowering therapy (LLT) on lipid profile, in adults presenting with first acute coronary event.
Methods and material: A multicentre, observational, prospective cohort study of lipid profiles pre- and post-statin therapy/LLT, among adult patients with confirmed diagnosis of first acute coronary event. The primary outcome measures were low-density lipoprotein cholesterol (LDL-C) in mg/dl, high-density lipoprotein cholesterol (HDL-C) in mg/dl and triglycerides (TG) in mg/dl at baseline and end of study (EOS, 12 weeks [mean: 13.5 weeks]).
Results: Totally 474 patients completed the study. Number of patients with any LDL-C abnormality (LDL-C [all; LDL was abnormal, either alone or along with other lipid parameter(s)]) decreased from 118 (24.9%) to 27 (5.7%), and for LDL-C (only; only the LDL was abnormal), from 46 (9.7%) to 13 (2.7%), both from baseline to EOS. Of 118 patients with high LDL-C (all) at baseline, 91 (77.1%) had reduction in LDL-C to <100 mg/dl, of which 54 (45.8%) had LDL-C <70 mg/dl at EOS. The patients with LDL-C fraction abnormalities decreased, while HDL-C abnormalities increased at EOS from baseline. No major difference was observed at baseline and EOS in levels of TG (all [TG was abnormal, either alone or along with other lipid parameter(s)]) and TG (only [only the TG was abnormal]). Six (1.3%) had seven serious adverse events.
Conclusions: Though statin therapy is effective in lowering LDL-C, there still remains residual dyslipidemia, which probably should be tackled with therapeutic and non-therapeutic options.

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1. Introduction

Several large trials have demonstrated the efficacy of statins in the primary prevention of cardiovascular events, including first acute major coronary event in adults with average triglycerides (TG) and low-density lipoprotein-cholesterol (LDL-C) and below average high-density lipoprotein-cholesterol (HDL-C) levels.[1–4] Further, trials on statin therapy such as Scandinavian Simvastatin Survival Study (4S)[5] and Cholesterol and Recurrent Events Trial (CARE)[6] also established their role in reducing coronary events such as stroke risk, fatal coronary artery disease (CAD) and nonfatal myocardial infarction (MI). For secondary prevention of acute coronary events, high levels of LDL-C, carotid artery remodeling, morbid obesity and low levels of HDL-C are important prognostic indicators to evaluate the efficacy of aggressive lipid therapy strategies.[7]

The prevalence of dyslipidemia is increased in diabetic patients, which contributes to the higher incidence of cardiovascular diseases (CVDs), resulting in higher morbidity and mortality.[8] The American Diabetes Association recommends the use of statins by diabetic patients with overt CVD and by patients without CVD who are older than 40 years of age and have one or more CVD risk factors, regardless of baseline lipid levels.[9]

At present, statins are the gold-standard treatment options for lowering LDL-C. Additionally statins are also known for their ability to reduce the risk of cardiovascular events and their excellent safety profile.[10–12] Besides LDL-C, other lipid parameters, such as high TG[13,14] and low HDL-C levels[15,16] also play a role in the causation and progression of coronary heart disease (CHD).

One of the Cholesterol Treatment Trialists' Collaboration (CCT) meta-analyses states that statin therapy can safely reduce the 5-year incidence of major coronary events, coronary revascularization, and stroke by about one fifth per mmol/L reduction in LDL cholesterol, largely irrespective of the initial lipid profile or other presenting characteristics.[17]

Management of lipid parameters beyond LDL-C may require additional therapeutic or non-therapeutic options to statin therapy, to likely benefit the patients with residual risks.[18,19] In clinical practice, there is scarce information about the extent to which CHD patients on lipid therapy achieve control of HDL-C, LDL-C, and TG. Further, there is paucity of data regarding occurrence of cardiovascular events among patients with mixed dyslipidemia (at least 2 lipid abnormalities) compared to patients with LDL-C abnormalities alone. There is also a lack of understanding in the use of comprehensive lipid management therapies to target dyslipidemia beyond LDL-C as a secondary prevention measure subsequent to a CHD event.

In India, there is a wide gap in translation of evidence to practice. Though there is evidence[20] to suggest that in patients with diabetes, low HDL-C levels are stronger predictor of mortality from CHD than LDL-C, further quantification of protocol based treatment regimen as well as residual abnormality and risk has never been studied.

The primary objective of our observational study was to evaluate the effect of statin therapy/LLT on lipid profile, in Indian adults presenting with first acute coronary event. The prevalence of mixed dyslipidemia, the need to address low HDL-C and/or high TG in addition to, or in the absence of high LDL-C post statin therapy/LLT, and the various risk subgroups (including individuals with prevalent diabetes mellitus) were also assessed.

2. Materials and methods

2.1. Study design

We conducted a multicenter, observational, prospective cohort study in 19 tertiary care centers of India in patients with first acute coronary event. The study was planned for 12 weeks from the onset of first acute coronary event. However, all patients who were on statin therapy/LLT (as per the discretion of their respective investigators) for an average of 13.5 weeks were analyzed in this study. This was taken as the end of study (EOS) period.

2.2. Setting

The study was initiated on 23rd April 2010 and was completed at all the centers by 15th December 2012. The patients were enrolled at the time of their first acute coronary event presentation (Index Date), information about demographics; current medical treatment, family history and acute coronary event were collected by interviewing the patients. Physical examination was conducted of all the patients prior to discharge. At baseline and EOS visits, investigations and lipid assessments were performed. The study flow chart is presented in Fig. 1. The required study data was collected and entered into a case record form (CRF). The final protocol and informed consent form (ICF) were reviewed and approved by the Institutional Ethics Committees/Institutional Review Boards, at each trial sites, participating in the study. Prior to initiation of the study, a written informed consent was obtained from the patients, who participated in this study. Each participating tertiary care center with dedicated cardiac/coronary care facility was responsible for recording and maintaining the data in source documents in compliance with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) – Good Clinical Practice (GCP) and institutional requirements for the protection of confidentiality of patients.

2.3. Study population

Men and women aged ≥35 years with a confirmed diagnosis of first acute coronary event (STEMI [ST elevation myocardial infarction]/NSTEMI [non-ST elevation myocardial infarction]/unstable angina) were included in the study. Other inclusion criteria were: access to medical records covering the entire study period, potential to collect (8 h) fasting blood sample within 24 h of onset for symptoms; considered for initiation/maintenance/modification of statin therapy before discharge from hospital; availability of core data set and willing to comply with the study requirements. Patients who were already participating in a clinical trial or any other type of

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