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Editorial

Intensive statin therapy in India: Demonstrating efficacy and safety

India presently leads the world in the prevalence of coronary heart disease (CHD).[1] There are several unique features about the Asian Indian lipid profile that not only increases the risk of CHD but also results in the severe prematurity of major adverse cardiovascular events (MACE) compared to the rest of the world. Twenty-five percent of myocardial infarctions' (MI) in India occur in patients younger than 40 years of age and two-thirds occur before age 55.[2] Asian Indians have on average lower low-density lipoprotein cholesterol (LDL-C) levels, higher levels of small dense LDL-C, LDL particles, non-high-density lipoprotein cholesterol (HDL-C), apolipoprotein B (ApoB), lipoprotein(a) and triglycerides and the associated lower HDL-C levels, compared with Western countries.[3] There is often the misleading clinical impression due to lower baseline LDL-C levels in India, that less intensive statin therapy is required. There is also the concern that due to lower body mass indexes and common polymorphisms of the statin metabolic pathways (i.e., CYP 3A4 and C19) in Asian Indians that lower doses of statins should be utilized to avoid potential adverse side effects. These issues combined with a lack of clinical trial safety data in Asian Indians explains the dearth of high dose statin utilization in India despite large cardiovascular outcome trials (CVOT) demonstrating the superiority of high over low intensity statin therapy. In fact, the AHA/ACC 2013 guidelines advocate either atorvastatin 80 mg or rosuvastatin 40 mg for all patients with clinical atherosclerotic cardiovascular disease,[4] but yet these doses are under utilized throughout India.

This is why the ROSUVEES-2 trial (Efficacy and Safety of the Intensive Dose of Rosuvastatin 40 mg/day in Patients with Acute Coronary Syndrome and at High Risk of Cardiovascular Disease),[5] is a welcome addition to the medical literature to support the safety and efficacy of the rosuvastatin 40 mg dose specifically in an Asian Indian population with a recent acute coronary syndrome (ACS). Shah and his co-investigators have documented that rosuvastatin 40 mg can be given to Asian Indian patients during the hospitalization for an ACS with excellent LDL-C lowering efficacy, and a very low rate of adverse side effects. Comparing the ROSUVEES-2 baseline data to the recently completed IMPROVE-IT trial,[6] which was also conducted in an ACS population; validates the differences in the risk profiles for Asian Indians compared to the rest of the world. Compared to the IMPROVE-IT patients, the ROSUVEES-2 population was 10 years younger (64 vs. 54 years old), HDL-C was 10 mg/dl lower (48 mg/dl vs. 38 mg/dl), triglycerides 31 mg/dl higher (137 mg/dl vs. 168 mg/dl) and the inflammatory marker hs-CRP was also higher (6.9 mg/L vs. 3.8 mg/L). Since most of the residual risk for recurrent events occurs in patients with high triglycerides combined with low HDL-C,[7] the ROSUVEES-2 trial emphasizes the need to maximize the statin for all patients presenting with an ACS, especially in India. Higher intensity compared to lower dose statin treatment is associated with greater reductions in LDL-particles, small LDL-C, apoB and non-HDL-C in which elevations likely explains much of the higher residual risk in the Asian Indian population.[8–10] Perhaps a good target of therapy for Asian Indian CHD patients should be the total cholesterol to HDL-C ratio (TC/HDL-C). In the ROSUVEES-2 trial the baseline TC/HDL-C decreased from 5.1 to 3.7 ($p < .001$). Most reassuring from the ROSUVEES-2 trial data was the safety profile of the rosuvastatin 40 mg dose. There were no adverse effects on CPK, SGOT, SGPT and eGFR. Only 3.5% of patients ($n = 8$) had a dose reduction due to myalgias. These results compare very favorably with the safety and tolerability of rosuvastatin 40 mg in clinical trials conducted outside of India. Therefore there appears to be very little need for additional concerns for utilizing rosuvastatin 40 mg in Asian Indians compared to patients in the rest of the world.

Hopefully, this new data will reassure clinicians in India to initiate rosuvastatin 40 mg in their patients during the hospitalization for an ACS. The potential pleotropic effects of statin therapy in addition to the greater modification of atherogenic lipoproteins by utilizing the higher intensity doses provides an unprecedented opportunity to maximize residual risk factor modification. The ROSUVEES-2 trial provides the evidence needed to document both the efficacy and safety of this more aggressive lipid modifying as well as anti-inflammatory approach.

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