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Editorial Open Access

Treating to Target – The LDL Conundrum!

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Editorial

Lipid-lowering therapy is one of the most effective and cost-efficient means of saving patients from mortal cardiovascular events. Up to ten percent, absolute benefit and the accrued benefits of reduction in CV events with continued statin therapy make it one of the most wonderful pharmacotherapies in modern medicine. The linear association of LDL to the incidence of cardiovascular disease is well documented. Treating LDL levels to target is of prime importance to reduce MACE events in these patients. Targets for primary and secondary prevention, have been well-defined in several guidelines across the world, based on a very large body of evidence. Lipidologists have been criticized for making LDL – a moving target, but that is necessary because of cumulative strong "NEW" evidence of cardiovascular benefits, when LDL is treated to very low levels – 30 to 50 mg per decilitre. Recent trials with aggressive LDL-lowering targets have shown very significant benefits. In addition, reducing residual risk – addressing hyper triglyceridemia, and high lipoprotein seems to provide additional benefits in terms of reduced MACE events. It is important for us clinicians to be convinced about the benefits of intensive lipid-lowering and not slack off once lipid targets are achieved. Sustained clinical benefits are seen with continued treatment to target approach, indefinitely. Physicians should realize that these patients have a sustained risk of MACE events, stroke, and peripheral vascular disease.

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Important roadblocks to lipid-lowering therapies – may be listed as patient-driven – statin intolerance, cost factors, medication noncompliance, and sheer ignorance. Physician reluctance to sustain high-dose lipid-lowering seems to arise from a lack of and deficit in conviction about the benefits. We need to overcome both by continued patient education and awareness programs and evidence-based therapy approaches for physicians. The line between aggressive lipid lowering in primary versus secondary prevention is gradually getting blurred and hit

hard and hit fast is becoming standard to reduce the time of exposure of vasculature to high LDL levels!

The dilemma in the mind of the treating physicians is – whether the intensity of lipid-lowering should be de-escalated once the storm of ACS or acute cerebrovascular event has passed, and the patient is clinically stable for about 6 weeks to 3 months. When a "topped off" dose of a drug is reached, and the patient's lipid profile still hovers at borderline target levels – whether to escalate to a costlier regimen and tip the balance of cost versus benefits or stay on with the same doses and wait. The recent availability of high-dose statin and aspirin, clopidogrel combinations, is a boon to the Indian population, as therapy becomes very cost-effective. There are patient examples of LDL and Lipoprotein levels rebinding after completing an expensive course of Evolocumab for six months – which sow the seeds of doubt in the minds of physicians.

In the second volume of ERWEJ journal – 2022, 2(2), Mudit Sabharwal and colleagues, have attempted to elegantly address this issue and have highlighted the role of Ezetimibe as an add-on therapy to high-dose statins to achieve and maintain target-based therapy. Ezetimibe is a definite value addition to high-dose statin therapy. Almost placebo-like adverse event profile and low cost – make it an attractive option.

Recent research has moved forward, from the work on blocking enzymatic processes (Statins, Ezetimibe, Bempedoic acid), to cellular receptors (PCSK9i) and messenger RNA (Inclisaran) levels. With the new evidence-based resurgence of Ezetimibe, approval of Bempedoic acid for clinical use, and availability of PCSK9 inhibitors and potent molecules like Inclisaran, our armament against dyslipidemia appears very potent and complete.

There are, of course, patients, who continue to suffer CV events despite maximum lipid lowering. Research should continue to focus on these patients for whom we have no answers to why atherosclerosis continues to relentlessly progress, producing high MACE rates and mortality.

In a majority of patients, especially around the time of an acute event, high-intensity lipid-lowering therapy runs smoothly and is accepted by the patient. Subsequently, patients and their treating clinicians, naturally let their guard drop, and compliance rates of therapy fall. A constant vigil is necessary to overcome this laxity and we should reinforce the importance of lifestyle modification, strict diet, and medication compliance at every patient visit.

Future directions

In addition to treating to target, we should look towards the high-risk vulnerable patient with a holistic approach towards addressing all other risk factors. The special group of patients who continue to suffer events despite very low lipid levels, patients who rebound after a course of Evolocumab, where life-long therapy is not an option due to cost reasons, need special attention. Will Inclisaran and its cousin molecules become the new anti-atheroma vaccines in the next century and help us stem the cardiovascular disease epidemic?

Only treating to target and maintaining it – will give us the true picture!