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Pearls in Lipidology and CVD

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1. **LDL-C:** Atherosclerosis is a preventable disorder. LDL-c plays a central role in Atherosclerosis, Epidemiological, Observational studies, Genetic studies, and randomized control trials have shown the impact of LDL as the Culprit. The more the reduction of LDL-c seen in the primary and secondary prevention trials by using statins, either moderate dose or high dose more benefit that was witnessed in CV reduction both in morbidity and mortality. Hence, our prime focus should be lowering LDL-c and keeping it low throughout our life. **LDL-C: Lower the better, Earlier the better & Longer, the better.**
2. **Statins** are safe and efficacious in reducing LDL-c with the least side effects. Pleiotropic actions of statins are added advantage which saved millions of lives.
3. **Residual risk** is seen in all primary and secondary prevention trials ranging from 55 to 70%. Hence, we need to reduce LDL –c further with high-dose statins or the maximally tolerated dose of statins with non-statin drugs like Ezetimibe or PCSK9 inhibitors. RCTs of adding non-statin drugs with statins have shown remarkable benefits in reducing the risk of ASCVD, including mortality. Lower levels of LDL –c such as 30 mg to 50 mg, are safe with no significant side effects.
4. **Triglycerides:** Atherosclerosis is aggravated by TG-rich Lipoprotein particles [TGRLP]. 75% of the pathogenesis of atherosclerosisis contributed LDL-c, whereas the remaining is by the TGRLP. A recent study has emphasized and advised therapy for reducing TG. Icosopent Ethylesters [EPA] 4 gms/ day in the REDUCE-IT trial has reduced primary endpoints by 25% and CV death by 20%. This molecule is eagerly awaited for its use in Indian patients.
5. **Fibrates:** Reduction of TG by fibrates were seen in 5 landmark trials. However, subgroup meta-analysis revealed 35% CV risk reduction in patients with TG > 204 mgs% compared to patients with TG <204 mgs%. There is no mortality benefit seen with fibrates. Fibrates are indicated in patients with TG levels exceeding 500 mgs% to prevent Pancreatitis. The role of fibrates for ASCVD risk reduction in people with TG between 200 – 500 mgs% is not encouraging. Ongoing studies with Pemafibrate will reveal the safety and efficacy of fibrates with statins.
6. **NON–HDL -c** becomes secondary targets in patients with TG levels > 200 mgs% after reaching the goal of LDL cholesterol. Non-HDL-c is considered an important parameter that covers LDL–c and IDL, VLDL, VLDL Remnants, Chylomicron remnants, and LP (a). Non –HDL –c does not require any laboratory technique. It is simply the value we get after subtracting HDL-C from Total Cholesterol. i.e TC-HDL-C = Non –HDL-c . Infact, Non-HDL-c covers all atherogenic lipoproteins with apo-B content. Hence, it is recommended as a co-primary target. Treatment of Non-HDL does not differ much. A high dose of statin will bring down the Non-HDL –c. If the residual risk is identified, we need to use Triglyceride lowering therapy. Non-HDL-c subsumes the impact created by TGRLP. Non- HDL-c goal

should be 30 mgs% more than the LDL-c goal for various risk categories.

7. **Apo B** is considered the most important risk factor for atherosclerosis. All atherogenic lipoproteins contain apo-B 100 except chylomicron remnants attached with apo-B 40. Routine assessment of apo-B is not recommended because of its cost and lack of global standardization. Non –HDL-c is considered the poor man's apo –B, which requires only simple calculation.

8. **LP(a)** is genetically determined, and the structure simulates plasminogen. It has proinflammatory and prothrombotic features responsible for increased ASCVD risk and mortality. Recent studies have shown that LP (a) is the Culprit for premature CAD, Stroke events, Peripheral arterial disease & recurrence of ASCVD events. It is recommended to screen for LP(a) even at the first visit for lipid profile testing. Values above 50 mgs% are considered to potentiate the risk for ASCVD. No drug is effective in controlling this other than Niacin. However, Niacin has a lot of side effects and precipitates stroke events. All studies which used Niacin did not show any CV benefit. The promising molecule is only PCSK9 inhibitor – Evolocumab.

9. **FH: HoFH, HeFH:** Familial Hypercholesterolemia is a forgotten entity. It is undiagnosed undertreated. The diagnosis of familial hypercholesterolemia is based on many criteria, including Simon-broom criteria. Clinical signs including Xanthomas, Tendon Xanthomas are striking features. Homozygous FH occurs in children with markedly elevated LDL cholesterol. Premature coronary artery disease and death occur before the age of 20 years. Heterozygous FH patients will get premature coronary artery disease and death between 20 & 50 years of age. Genetic testing is rarely required. Cascade screening is essential to identify affected individuals in the family. Aggressive control of LDL –c and other modifiable risk factors will prolong their lives.

10. **Therapeutic Lifestyle Changes,** which include Diet, Exercise, Smoking cessation, and reducing stress levels, will help all patients with lipid disorders. Clinicians need to emphasize the role of therapeutic lifestyle changes during every visit by the patient.

11. **Newer drugs** like PCSK9 inhibitor, Icosopent-Ethylester, and Bempedoic acid will help us reduce CV risk both morbidity and mortality over and above high dose statin and ezetimibe.