MEDIBEATS
The Medical Bulletin

In Lipidology

- In ASCVD risk factor, low HDL cholesterol makes a place over ↑LDLC, ↑Non-HDLC.
- LDL has a linear relationship with ASCVD whereas Hypertension, HDL has an U-shaped relationship.(LDLC- lower the better).
- Statin reduces cholesterol by ↑LDLR activity. HMGCoA reductase inhibition - decrease cholesterol in cell–cell ↑LDLR in order to↑ cholesterol in cell-LDLR takes cholesterol from blood-decrease cholesterol in blood.
- Statin, Ezetimibe (Improve-IT) ,PCSK-9 inhibitors (Fourier and Odyssey), Bempedoic Acid(Cleartrial),Bile acid sequestrant (Colesevelam), Inclisiran (orion 10, orion11) are available to treat LDLC.
    - Ezetimibe prevent absorption of intestinal cholesterol (interferes with NPC-1L1 protein of intestinal epithelial cell).
    - PCSK 9 inhibitors- inhibit PCSK 9 activity (activity increased due to gain of function mutation of PCSK 9 gene). Inclisiran (siRNA) prevent production of PCSK9 (due to loss of function mutation)by degradation of it smRna.
    - Bempedoic acid (ACL enzyme inhibitor), works upstream of statin target.
    - Colesevelam prevent cholesterol reabsorption in ileum- LDLR upregulation-LDLC by 15-25%.
- Atorvastatin and Rosuvastatin are commonly used Statin. Atorvastatin 40-80mg/ Rosuvastatin 20-40 mg- High Intensity statin, Atorvastatin 10-20 mg/Rosuvastatin 5-10 mg are moderate intensity statin.
    - Moderate intensity statin High intensity statin =30
    - High intensity statin =50
    - High intensity statin+Ezetemibe =65
    - PCSK9inhibitor =60
    - PCSK9I+highintensitystatin =75
    - PCSK9I+highintensitystatin+Ezetemibe =85
    - Mod. Intensity statin+Bempedoicacid+Ezetemibe =63.6
- ***Shift in Lipid lowering treatment Paradigm:-***

✓ ***Current paradigm:-*** Statin 1st line, then Non-Statin therapy to reach target LDLC

✓ ***Potential future paradigm:-***

✓ siRNA 1st line, then statin and non-statin therapies for each target LDLC.

Statin	PCSK9I	PCSK9siRNA
365doses/yr	26doses/yr	2doses/yr

✓ Beyond LDLC, Key secondary end points:-Non HDLC, ApoB, hsCRP

- Besides LDLC reduction, lifestyle modification (physical exercise – 20% cholesterol reduction, wt. and healthy diet), control of conventional risk factors (smoking, HTN, DM, alcohol intake), lipoprotein apheresis are the different goal bars for the management of dyslipidemia to reduce ASCVD.
- ***Darker side of the moon:-*** increase Coronary Ca2+, LP(a) – neutral, DM (except Pitorvastatin), hemorrhagic stroke, mypoathy, statin resistance, SGLT2+Rosuvastatin =Rhabdomyolysis.
- ***When lipid profile normal, but pt. has a risk factor for ASCVD?*** –Test coronary intimal thickness, CAC score, LP(a) measurement.
- ***Lipid testing :-*** before starting treatment- 2 measurement with an interval of 1-12wks (except ACS and very high risk) after starting treatment every8 +/-4 wk still target is reached, then annually.
- In High risk pt. with increase TG, despite statin (135-499 mg%), Icosapentethyl2x 2 gm/day may be considered along with statin.
- USPSTF (US Preventive services Task Force)- primary prevention (3 must be present)–40-75yrs, 1or more CVD risk factor(lipid, DM, HTN, smoking), 10yrs CVD risk(10% or more).
- LDL- Bad Cholesterol, HDL-Good Cholesterol, TG- Ugly cholesterol, ApoA– deadly cholesterol.
- ***How much LDL can be reduced?*** – upto30mg%
- Familial hypercholesterolemia – 1 baby/min, premature CAD and calcific AV stenosis, gene mutation- LDLR gene (most common cause among Indians, 85-90%), Apo B gene, PCSK 9 gene, DLCN Criteria (Dutch Lipid Clinic Network)- gold standard for diagnosing FH, Simon Broome Diagnostic Criteria-simpleand used for clinical purpose.

Dr. Samirkantadatta
MBBS, MD (Medicine)