- Antihyperlipidemic drugs:

1- statins: inhibit HMG CoA reductase -> decrease intracellular cholesterol -> increase LDL receptors

◇ Decrease LDL + VLDL, increase HDL.

Atorvastatin, rosuvastatin -> the strongest

Lovastatin, pravastatin, simvastatin, fluvastatin-> intermediate

Cerivastatin -> weak

They all have the same efficacy, but they have different potencies of side effects at different doses.

S.E: myopathy Co Q10, rhabdomyolysis CK, nephrotoxicity, minor elevation of liver enzymes.

Don't use them with grapefruit or fibrates (except Pravastatin)

2- Fibrates: bind PPARs -> increase lipoprotein lipase -> decrease VLDL+LDL, increase HDL

Fenofibrate, Gemfibrozil (contraindicated in combined hyperlipidemia), **Bezafibrate.**

S.E: lithiasis, GI disturbances.

3- bile acid- binding resins: bind to bile acids and get excreted with feces -> increase LDLR-> decrease LDL

Cholestyramine and **colestipol**

Combine with **niacin**-> type IIa

Combine with **statins** too in case of extremely high hyperlipidemia.

S.E: GI disturbances, impair fat soluble drugs and vitamins absorption.

4- Niacin: inhibit lipolysis in adipose tissue -> decrease LDL+ VLDL, increase HDL / IIb+ IV

S.E: hyperuricemia, hyperglycemia, elevation of liver enzymes, increase prostaglandin-> flushing, GI irritation, peptic ulcer. (so contradicted in peptic ulcer patients)

* Scratching of the dose or using aspirin to decrease its side effects.

Withdrawn from market.

5- Ezetimibe: inhibits cholesterol absorption, mild effect but increased with statins -> synergistic activity

S.E: headache+ diarrhea

- New drugs of hyperlipidemia:

1- bempedoic acid: inhibition of ACYL -> decrease cholesterol -> increase LDLR + increase HDL

Selective to hepatic tissue bc it needs activation by very long chain acyl CoA synthase 1 which is mainly expressed in liver.

Use **ezetimibe** to inhibit duodenum cholesterol absorption.

S.E: hyperuricemia, gout, muscle pain, decrease hemoglobin-> anemia.

2- PCSK9 inhibitors: inhibition of this enzyme leads to increased liver LDLR and reduced cholesterol levels.

A- **monoclonal antibodies**: **Evolocumab, Alirocumab** / only flu- like symptoms

B- RNA silencing: **inclisiran**-> it's siRNA which needs GALNAc to carry it to the liver where it incorporates with RISC1-> can bind to PCSK9 mRNA.

S.E: injection site reaction

3- ApoC-III inhibitor: inhibition of this enzyme leads to more LPL-> decrease TG

Volanesoren: **ASO**-> siRNA, used in FCS, S.E: thrombocytopenia, injection site reaction.

4- ANGPTL3 inhibitors: inhibition of this enzyme leads to preserve LPL and EL-> decrease TG

A- **Evinacumab**: **monoclonal antibody** in serum

B- **Vupanorsen: ASO** in hepatocytes

- Antiarrhythmic drugs:

1- class I: bind to sodium channels and prevent sodium influx.

Supraventricular tachycardia

Ventricular tachycardia

Class Ia: moderate DT, reduce AP conduction velocity, increase ERP & APD

Quinidine (cinchonism), **procainamide, disopyramide**

S.E: Torsades de pointes with QT interval prolongation

class Ib: weak block, shortens ERP & APD, used in Ventricular tachyarrhythmias in case of prolong QT interval.

Lidocaine/ S.E: CNS effects

class Ic: marked block, only reduce AP conduction velocity, with normal ERP& APD

Used in atria, ventricles as a last choice.

CONTRAINDICATION: Ventricular tachycardia in presence of ischemic heart disease or old MI

Propafenone (slowed sinus rate), **flecainide** (vision problems+ teratogenic)

2- class II: in atria

Class IIa: β1 -adrenergic receptor inhibitors/ withdrawal/ Masks symptoms of hypoglycemia

Class IId: MuscarinicM2 receptor activators -> AV node inhibition/ positive ionotropic

Digoxin/ Sinus tachycardia or supraventricular tachyarrhythmias

Has cardiac adverse effects: Bradycardia, AV block, Paroxysmal atrial tachycardia, Sino atrial arrest, Ventricular tachycardia.

Class IIe: Adenosine A1 receptor activators/ negative chronotropic+ dromotropic -> (hyperpolarization).

Adenosine, ATP/ S.E: Sinus bradycardia, sinus arrest or AV block

3- class III: blocks potassium channels-> increases the duration of repolarization and the effective refractory period.

Amiodarone: oral, also activity in Na channel blocking/ supraventricular + ventricular tachycardia, except in QT interval elongation.

Sotalol: Also activity in Beta receptor blocking / in children

S.E: Torsades de pointes with QT prolongation

4- class IV: blocking Ca2+ entry through specific Ca2+ channels (CCB)

Class VIa: non-selective: **Bepridil**

- Selective: **Phenylalkylamines (verapamil)**, **benzothiazepines (diltiazem)**

prolonged ERP, increased AP recovery time, increased refractory period.

Done by: mariam qussay