Antihyperlipidemic drugs

Notes

•Chylomicrons released from intestine take lipids absorbed from intestine to tissues (ex; adipose)—≥ lipids are then broken into circulating free fatty acids —≥liver secretes vldl which goes to blood and carries free fatty acids (now called ldl)to liver—≥ liver synthesizes cholesterol

•Too much cholesterol in tissues—≥ atherosclerosis—≥angina—≥mi—≥heart failure.

•Hdl takes cholesterol from blood to liver and liver breaks it to bile salts and then expelles it out of the body

Hyperlipidemia is caused by

1- Lifestyle (fat consumption+ lack of exercise)
2- Single inherited gene in lipoprotein metabolism
3- Mixture of both

Incidence of heart failure is correlated with :

1- High : ldl, vldl and triglycerides
2- Low: hdl

•antihyperlipidemic drugs should be taken indefinitely

Antihyperlipidemic drugs targets:

1-decrease production of lipoprotien carriers of cholesterol and triglycerides (ldl and vldl)

2- increase degradation of lipoprotiens

3-decrease cholesterol absorption and increase its removal from body.

Antihyperlipidemic drugs:

1- Statin 2- niacin 3-fibrates 4-bile acid binding resins 5-cholesterol absorption inhibitors

statins

(false pride) mnemonic

1-highest efficacy: atorvastatin, rosuvastatin

2-medium: lovastatin , fluvastatin, pravastatin , simvastatin

3-not used anymore: cerivastatin

Mechanism of action:

1-HMGCoA inhibitors (3-hydroxy-3-methylglutaryl coenzyme A) they inhibit the rate limiting step of cholesterol synthesis

2-increase ldl receptors : no cholesterol synthesis= more ldl receptors on liver=decrease in ldl and more hdl is released to bring cholesterol from tissues to liver

Side effects:

1-biochemical abnormalities in liver function

2-myopathy and rhabdomyolysis

Contraindicated with:

1-pregnant and nursing mothers

2- children and teenagers

(some children with familial hyperlipidemia can use it but they have to be older than 8)

catabolism :

1- Lovastatin, simvastatin, and atorvastatin = through CYP3A4
2- Fluvastatin and rosuvastatin=CYP2C9
3- pravastatin= sulfation

• anything that increases the efficacy of statins will increase the risk of myopathy

Statins efficacy affecting drug- drug interactions:

1-drugs that inhibit CYP45 like verapamil and amiodarone (increase efficacy)

2-drugs that increase expression of CYP3A4 (like: rifampin) decrease 3A4 dependent reductase inhibitors efficacy.

3-inhibitors of CYP2C9 like(metronidazole) increase efficacy (plasma levels) of fluvastatin and rosuvastatin

4- ≥ 1 liter of grapefruit juice daily can increase the efficacy of lovastatin , simvastatin and atorvastatin

Niacin (vitamin b3)

Mechanism of action:

1- Inhibits lipolysis in adipose tissue : no lipolysis=no free fatty acids=less production of cholesterol (inhibits hormone sensitive lipase)
2- Lowers ldl and vldl
3- Inhibits all types of hdl catabolism

•it is the most effective agent in hdl increase, but no longer used as much

Uses:

1-Type IIb and iv hyperlipoproteinemia (both ldl and vldl are increased)

2-Hypercholesterolemia

Adverse effects

1- Cutaneous flushing, burning and itching
2- Gi irritation , nausea , vomiting and peptic ulcer activation
3- Elevation of liver enzymes, hyperglycemia, and hyperuricemia

Fibrates

- They are derived from fibric acid

Types:

1-fenofibrate 2-gemfibrozil 3-bezafibrate

Effect:

1- Lower :Ldl , cholesterol and triglyceride
2- Increase: hdl

Mechanism of action:

They bind to peroxisome proliferator activated receptors (ppars) that regulate lipid metabolism and as a result they increase the expression of lipoprotein lipase.(breaks triglycerides so we get rid of them)

•they are used in treatment of hypertriglyceridemia

Adverse effects:

1-mild gi disturbances (most common)

2-lithiasis: gallstones (cuz they increase biliary cholesterol excretion)

3-myositis (voluntary muscle inflammation)

Note: they compete with coumarin anticoagulants for binding sites on plasma proteins (increase warfarin's effect)

Cholesterol absorption inhibitors:

ezetimibe

•Inhibit intestinal absorption of dietary cholesterol

•Can cause headache and diarrhea

Bile acid binding resins

Types:

1-cholestyramine 2-colestipol

Effect: lower Ldl (benefits less than statins)

•they are either given with statins or niacin or given to ppl with statins allergy

Moa:

Bind to bile acids in intestine= forms insoluble complexes excreted in bile= low bile in intestine = more formation of bile from cholesterol

•because it lowers cholesterol it increases ldl receptors therefor decreasing ldl and vldl and increasing hdl.

•these are rugs of choice, used for type 2a hyperlipidemia

Side effects:

1-gi disturbances: constipation and nausea

2-impair absorption of fat soluble vitamins (A D E K)

3-interact with absorption of (tetracycline, warfarin, digoxin and aspirin)

Should be taken 1-6hrs after medications

	statins	niacin	fibrates	Bile acid resins
effect	More hdl Lower ldl and vldl	More hdl Lower ldl and vldl	More hdl Lower: ldl, cholesterol , triglycerides	More hdl Lower ldl and vldl
moa	Hmgcoa inhibitors	Inhibits lipolysis and hdl catabolism	Bind to ppars Increase lipoprotien lipase	Bind to bile acids in intestine
Side effects	Liver function Myopathy	Cutaneous Gi High liver enzymes, hyperglycemia and hyperuricemia	Gi Gallstones myopathy	Gi Vitamins and medication absorption
Type of hyperglycemia	----------	2B and Iv hypercholesterolemia	hypertriglycemia	2A