Differences between Statins and Their Use in Different Patient Population

Background

Statins are hydroxymethylglutaryl-coenzyme A reductase inhibitors (HMG-CoA reductase inhibitors), used in the treatment of dyslipidemia.

Hydrophilic Versus Lipophilic Statins

Categories	Statins	Comments
Hydrophilics	• Rosuvastatin (synthetics) • Fluvastatin (synthetics) • Pravastatin (derived from fungi)	Exhibit greater hepatoselectivity and less influence on smooth muscle proliferation
Lipophilics	• Atorvastatin (synthetics) • Lovastatin (derived from fungi) • Simvastatin (derived from fungi)	Cross the blood-brain barrier more readily, which may lead to central nervous system complaints such as insomnia (rare)

Different Patient Population

Multiple co-morbidities with multiple medications

- In clinical situations where patients must receive multiple medications (eg, patients with HIV/AIDS), pravastatin is least likely to interact because it is not metabolized by CYP450.
- Atorvastatin, lovastatin, and simvastatin are metabolized by the 3A4 isoform, while fluvastatin is metabolized by 2C9.

Possible drug interactions include:

- CYP450 3A4 inhibitors (azole antifungals, macrolides, calcium channel blockers, cyclosporine, cimetidine, and grapefruit juice)
- CYP450 2C9 inhibitors (omeprazole, ritonavir, azole antifungals)
- Inducers of both CYP450 3A4 and CYP450 2C9 (phenobarbital, rifampin, phenytoin, and carbamazepine).

Renal Impairment:

- Moderate-to-severe renal impairment: pravastatin dose should be modified
- Severe renal impairment: lovastatin, rosuvastatin, and simvastatin dose should be modified
- No change in dose is needed: atorvastatin and fluvastatin (not affected by renal impairment)

Hepatic Impairment:

- Hepatotoxicity from statins typically leads to an elevation in aminotransferase levels, reflecting hepatocellular injury as opposed to cholestatic injury.

Samah El Salem
PharmD Candidate

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- The benefits of statins in lowering cholesterol and preventing heart disease outweigh the potential risks of hepatotoxicity, even in patients with chronic liver disease.
- Liver enzymes should be monitored in all patients who take statins. If the alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level doubles, the statin should be stopped.
- Elevation in liver enzymes with statin therapy is dose related.
- It is recommended to start statin therapy at low doses in patients with chronic liver disease and check liver enzymes after any increase in dose.

Elevated HDL:

- LDL-lowering potency varies between agents. Cerivastatin is the most potent, (withdrawn in August, 2001 due to risk of serious Rhabdomyolysis) followed by rosuvastatin, atorvastatin, simvastatin, lovastatin, pravastatin, and fluvastatin
- Doubling a statin dose produces only about a 5% decrease in total cholesterol and a 7% decrease in LDL concentration, so a more potent statin may be necessary in the case of sub-therapeutic response.
- Statins may decrease triglycerides by 10-33% and LDL by 20-60% and increase HDL by 5-10%.

Statin Equivalent Dosages						
% LDL Reduction (approx.)	Atorvastatin	Fluvastatin	Lovastatin	Pravastatin	Rosuvastatin	Simvastatin
10-20%	--	20 mg	10 mg	10 mg	--	5 mg
20-30%	--	40 mg	20 mg	20 mg	--	10 mg
30-40%	10 mg	80 mg*	40 mg	40 mg	5 mg	20 mg
40-45%	20 mg	--	80 mg*	80 mg*	5–10 mg	40 mg
46-50%	40 mg	--	--	--	10–20 mg	80 mg*
50-55%	80 mg	--	--	--	20 mg	--
56-60%	--	--	--	--	40 mg	--
* 80mg dose no longer recommended due to increased risk of rhabdomyolysis						
Starting dose						
Starting dose	10–20 mg	20 mg	10–20 mg	40 mg	10 mg; 5 mg if hypothyroid, >65 yo, Asian	20 mg
Optimal timing	Anytime	Evening	With evening meals	Anytime	Anytime	Evening

Pregnancy:

FDA: all statins are pregnancy category X (contraindicated)

Statins Administration

- Increased absorption with food: lovastatin
- Decreased absorption with food: atorvastatin, fluvastatin, and pravastatin
- Not affected by food intake: simvastatin and rosuvastatin
- Administered at any time of day: rosuvastatin and atorvastatin (longer half-life compared to other statins) should be administered in the evening: other statins (shorter half-life), when synthesis of endogenous cholesterol occurs.

References

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