Statins in Liver Disease: Oh the Pain!

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Case Presentation

HPI: A 42-year-old female with **cryptogenic cirrhosis,** Type II diabetes mellitus, hyperlipidemia, pancytopenia, and awaiting liver transplant presents with acute progressive **myalgias** and proximal muscle **weakness** with **dark urine** over five days. Review of systems was negative for fever and upper respiratory symptoms, but positive for a recent sick contact and increase in **atorvastatin** dosing a month prior.

Medications:
- **atorvastatin 40 mg daily**
- insulin glargine
- insulin aspart
- Vitamin D3
- furosemide
- lactulose oral solution
- metformin
- spironolactone

Social History:
- remote drinking history
- no IVDU
- no other drug use

Physical Exam:
- *Vital signs*: normal (BP 106/90 mmHg)
- *HEENT*: scleral icterus
- *MSK*: moderate **tenderness** of bilateral thighs, calf muscles, shoulders
- *Neurologic*: **4 / 5** UE and LE proximal muscle **weakness**

Labs:
- CK **7500 U/L**
- chronic pancytopenia
- normal electrolytes except K 3.1 mmol/L
- **Cr 1.32 mg/dL (prior 0.6 mg/dL)**
- **AST 540 U/L, ALT 135 U/L, AP 297 U/L**
- **Total bilirubin 7.0 mg/dL**
- albumin 1.5 g/dL
- normal ESR, CRP, and thyroid function

Other tests:
- **Viral testing negative** for adenovirus, coronavirus, metapneumovirus, influenza A/B, parainfluenza, RSV, *Bordetella pertussis*, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, rhinovirus/enterovirus, HIV, CMV, and EBV.

Brief Hospital Course

She was admitted for management of **rhabdomyolysis** and treated with **aggressive IV hydration**. After hydration, patient had return of muscle strength, CK levels gradually improved, and her renal function normalized.

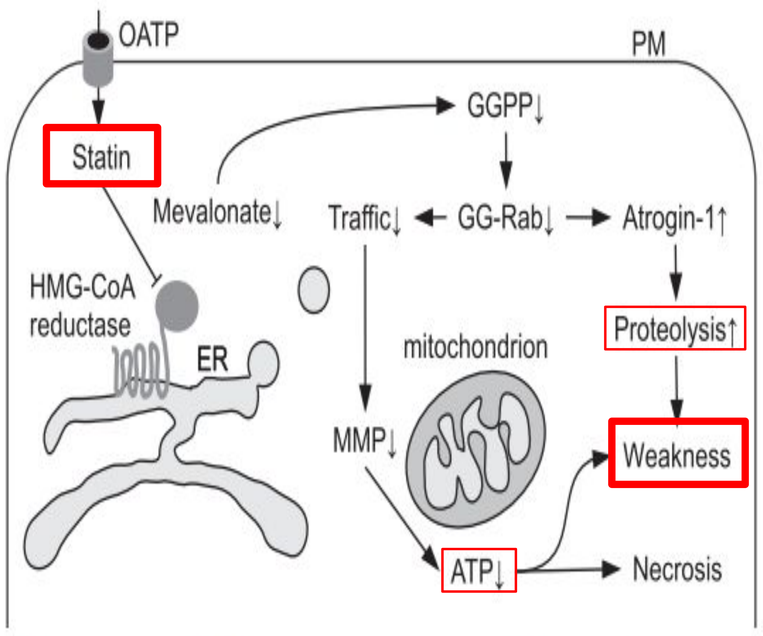
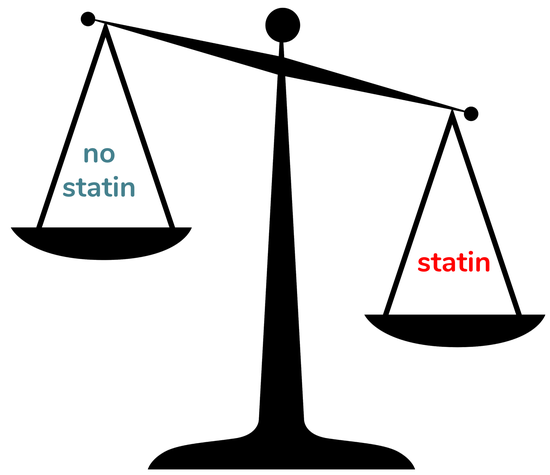


Figure 1. Scheme for statin-induced rhabdomyolysis.
ER: endoplasmic reticulum, GGPP: geranylgeranylpyrophosphate, GG-Rab: geranylgeranylated Rab GTPase, MMP: mitochondrial membrane potential, OATP: organic anion transporting polypeptide, PM: plasma membrane. [3]

Discussion

- Statins can lead to rhabdomyolysis by inhibiting **HMG-CoA reductase.** This causes a decrease in mitochondrial ATP synthesis and an increase in proteolysis, leading to muscular weakness.
- **Myalgias** from statin use occur in **1-10%** of the general population**,** while **rhabdomyolysis** occurs less than **0.1%** of the time. The risk is **dose-dependent**.
- However, routine monitoring of liver enzymes is ineffective in assessing who will develop liver injury from statin therapy.
- **Decompensated liver cirrhosis** and **acute liver failure** are still **contraindications** to statin use.
- On the other hand. patients with **liver disease** have an increased risk of **cardiovascular disease.**
- Statins also slow progression of fibrosis, prevent hepatic decompensation, and may **reduce all-cause mortality** in patients with chronic liver disease.
- Overall, statin therapy in patients with chronic liver disease is likely **more beneficial than harmful.**



References

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Teaching Points

Teaching point 1:
- Rhabdomyolysis is a rare complication of statin therapy.

Teaching point 2:
- Clinicians should be aware of the potential increase in the use for patients with cirrhosis due to reduction in cardiovascular disease and all-cause mortality. The overall benefit likely outweighs the risk.