DSEN ABSTRACT

Implementation of Pharmacogenomics to Identify Patients at Risk of Statin-Induced Myopathy

Summary

We observed a 45-fold variation in statin concentration among patients taking the same dose. Clinical factors including age and genetic polymorphisms within uptake and efflux transporter genes had the greatest effect on statin exposure in patients taking atorvastatin and rosuvastatin. A dosing decision support algorithm incorporating both clinical and genomic variables was developed to avoid high plasma levels of statins.

Key messages

To reduce the risk of statin-induced myopathy it may be beneficial to limit statin exposure. Patients with loss-of-function polymorphisms in SLCO1B1 and ABCG2 should be prescribed lower doses of statins especially if the patient is of an advanced age. Our study revealed that approx. 50% of patients in routine practice taking the highest doses were predicted to have statin levels above the 90th percentile using our algorithm implying that current practices do not adequately identify patients at risk for high statin exposure.

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What is the issue?

- Muscle pain and weakness are common side effects of statin use, and in some cases statins can cause significant muscle injury, including a rare but life-threatening form known as rhabdomyolysis.
- Exposure to high doses of statins has been linked to an increased risk for statin-associated muscle injury, but some patients prescribed high doses do not experience muscle side effects while some prescribed low doses suffer from muscle damage.

What was the aim of the study?

- To better understand the clinical and pharmacogenetic determinants that underlie the interpatient variability in statin concentrations as a way to pre-emptively identify patients at risk for statin myopathy.

How was the study conducted?

- 299 patients taking atorvastatin or rosuvastatin were prospectively recruited from an outpatient referral center.
- Measurement of statin plasma levels was performed by liquid chromatography-tandem-mass spectrometry and pharmacogenomics were assessed by TaqMan allelic discrimination assays.
- Clinical variables including age, sex, body mass index and concomitant medications were collected.
- The contribution of clinical variables and genetic polymorphisms was assessed using multiple linear regression.
- A second cohort of 579 patients from primary and specialty databases was retrospectively assessed.

What did the study find?

- Statin plasma concentrations vary by approximately 45-fold among patients taking the same dose.
- Common loss-of-function polymorphisms in the drug transporter genes, SLCO1B1 and ABCG2 are significantly associated with statin exposure.
- Patient age was highly associated with statin levels.
- An algorithm incorporating genomic and clinical variables to avoid high atorvastatin and rosuvastatin levels was developed.

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