Therapeutics

Review: Statin monotherapy is safe in hyperlipidemia except for increased risk for transaminase elevation


Clinical impact ratings: GM/FP/GP ★★★★★★✩✩ Cardiology ★★★★★★✩✩

Question
In patients with hyperlipidemia, how safe is statin monotherapy?

Methods

Study selection and assessment: English-language, randomized, double-blind, placebo-controlled trials (RCTs) that evaluated statin monotherapy (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, or simvastatin) in ≥ 100 adult patients with hyperlipidemia. 35 RCTs (n = 74,102, mean age range 44 to 76 y) met the selection criteria. Follow-up ranged from 1.5 to 65 months (median 4.5 mo). Individual study quality was assessed using the Jadad scale (mean score 4.1 out of 5).

Outcomes: Myalgia, creatine kinase elevation, rhabdomyolysis, transaminase elevation, and discontinuation caused by adverse events.

Main results
Meta-analysis showed that groups did not differ for myalgia, creatine kinase elevation, rhabdomyolysis, or discontinuation caused by any adverse events (Table). Statin monotherapy increased the risk for transaminase elevation more than did placebo (Table). Subgroup analysis showed that atorvastatin (but not the other statins) resulted in more patients with myalgia than did placebo (n = 567, 5.1% vs 1.6%, number needed to harm 32, 95% CI 17 to 477).

Conclusion
In patients with hyperlipidemia, statin monotherapy increases the risk for transaminase elevation but not myalgia, creatine kinase elevation, or rhabdomyolysis.

Source of funding: No external funding.

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Commentary

The review by Kashani and colleagues provides further reassurance of the safety of monotherapy with hydroxymethylglutaryl-CoA reductase inhibitors in the management of patients at risk for cardiovascular events or death. The doses used in the included studies were typical of current practice, although study patients were commonly younger and healthier. The findings are consistent with the conclusions of the National Lipid Association Statin Safety Assessment Task Force (1). To place these findings in perspective, the mortality risk from fatal rhabdomyolysis is < 0.3/100,000 person-years, a level that is close to the background level of the disorder. Risk for serious hepatic toxicity remains minimal, and transaminase elevation is usually reversible with reduction of statin dose or termination of therapy.

Recently published work shows that generic simvastatin is cost-effective in preventing cardiovascular events across a wide range of age groups (35 to 85 y) (2), a finding that will probably result in increased use of the therapy in older patients. At the same time, treatment goals are evolving, and the drive to reduce low-density lipoprotein levels to ≤ 70 mg/dL (1.8 mmol/L) will involve higher doses of statins with potentially increased risk for adverse events, particularly in older patients with more comorbid conditions. The bottom line is that statins are remarkably safe and effective as monotherapy. However, as we push doses higher, treat patients with comorbid conditions, and use combination therapy, we need to be aware that statins are not risk free, and prudent monitoring will be still needed.

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References
2. Heart Protection Study Collaborative. Lifetime cost effectiveness of simvastatin in a range of risk groups and age groups derived from a randomised trial of 20,536 people. BMJ. 2006;333:1145.

Statin monotherapy vs placebo for hyperlipidemia at median 4.5 months*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials (n)</th>
<th>Weighted event rates</th>
<th>RRI (95% CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transaminase elevation</td>
<td>28 (62,184)</td>
<td>1.5%</td>
<td>1.1%</td>
<td>30% (6 to 59)</td>
</tr>
<tr>
<td>Creatine kinase elevation</td>
<td>16 (41,467)</td>
<td>0.45%</td>
<td>0.43%</td>
<td>18% (9-11 to 56)</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>20 (68,110)</td>
<td>0.17%</td>
<td>0.13%</td>
<td>9% (35 to 83)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>21 (48,138)</td>
<td>19%</td>
<td>19%</td>
<td>1% (3-3 to 4)</td>
</tr>
<tr>
<td>Discontinuation caused by any adverse events</td>
<td>26 (45,268)</td>
<td>6.1%</td>
<td>6.1%</td>
<td>4% (3-3 to 11)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article using a random-effects model.

†Information provided by author.