

Risk of muscle symptoms while taking statins

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Clinical question

What are the effects of statins on muscles?

Bottom line

Statins increase the risk of muscle symptoms (pain, cramps, weakness) in the first year of use, from 14.0% (placebo) to 14.8%, but are similar to placebo after 1 year. Only 1 patient-reported muscle symptom in 15 is due to the statin. Statins may increase muscle symptoms with creatine kinase rising to 10 times normal levels for 1 in about 3000 patients over placebo.

Evidence

Seven systematic reviews (11 to 135 RCTs; N=18,192 to 192,977) from the past 5 years examine this.¹⁻⁷ We focus on the most recent (23 RCTs; 154,664 patients over 4.3 years).¹ Results are statistically significant unless indicated.

- Any muscle symptoms for statin versus placebo ...
 - Anytime: 27.1% versus 26.6% (placebo).¹
 - Within the first year: 14.8% versus 14.0%, number needed to harm of 125.
 - After the first year: 14.8% versus 15.0% (not statistically different).
 - Other systematic reviews²⁻⁷ had similar but not statistically different results for myalgia,⁵ those 65 and older,⁴ and intensity versus placebo.² No difference by statin type,³ lipophilic or hydrophilic statins,⁶ or age group.^{1,5,6}
- Any muscle symptoms, more- versus less-intense statin ...
 - Any time point: 36.1% versus 34.8% (less intense).¹
 - Other systematic reviews found similar results.²
- Creatine kinase level more than 10 times the upper limit of normal (myopathy): 0.077% versus 0.044% (placebo).¹
 - Four other systematic reviews²⁻⁵ found no difference.
 - More- versus less-intense statin^{1,2}: No difference for approved statins and doses (excluding simvastatin 80 mg).
- Rhabdomyolysis: 3 systematic reviews^{4,5} found no difference.
- Discontinuation for muscle symptoms^{2,4} or any adverse event^{4,5,7} was not statistically increased.

Two large n-of-1 trials (60 to 200 patients with previous statin intolerance due to muscle symptoms) randomized to 3 to 4 cycles of about 4 to 8 weeks each of statin,^{8,9} placebo,^{8,9} and no pill.⁸

- Muscle symptom scores ...
 - Statin versus placebo^{8,9}: no difference.
 - Statin versus no pill⁸: pain score of 16 versus 8 (no pill) (scale of 0 to 100, with higher scores being worse).

Context

- Mean creatine kinase rise¹ with statins was about 2%.
- Myopathy and rhabdomyolysis are too infrequent to discern statin effects in meta-analysis of more than 100,000 RCT participants. Statin-induced rhabdomyolysis is estimated to be 2 to 3 excess cases per 100,000 patient-years.¹

Implementation

Statins are the most effective lipid-lowering drugs to prevent cardiovascular (CV) diseases, with a relative risk reduction of 25% to 35% for CV events and about 10% for mortality.^{10,11} For nonsevere muscle symptoms possibly caused by a statin, other causes should be excluded.¹² If none is identified, stop the statin and try a rechallenge in a few weeks with the same dose, a lower dose, a different statin, or alternate-day dosing, as most patients will tolerate rechallenge.^{8-10,12} Non-statin therapies appear to have fewer CV benefits and no mortality effect and should be considered only if statin intolerance is severe or unmanageable.^{10,11}

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Competing interests

None declared

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