



Triglyce-Ride that High?

CLINICAL QUESTION

Do triglyceride-lowering medications (fibrates, statins, niacin, omega-3s) reduce the risk of pancreatitis in patients with hypertriglyceridemia?

BOTTOM LINE

No randomized controlled trials (RCTs) have assessed the effect of fibrates or any other triglyceride-lowering medication on pancreatitis risk in patients with “very high” triglycerides (≥ 5.6 mmol/L). In patients with triglycerides < 5.6 mmol/L, fibrates either have no effect on pancreatitis or increase the absolute risk by $\sim 0.1\%$ over 5 years, whereas statins lower the risk by 0.1% .

EVIDENCE

- No RCT examined triglyceride-lowering medications in patients with triglycerides ≥ 5.6 mmol/L.
- Systematic review¹ of cardiovascular RCTs of fibrates (7 RCTs, 40,162 patients, average baseline triglycerides 1.6-2.1 mmol/L) and statins (21 RCTs, 153,414 patients, average baseline triglycerides 1.3-2.1 mmol/L):
 - Pancreatitis at ~ 5 years (differences statistically significant):
 - Fibrates: 0.4% versus 0.3% with placebo.
 - Statins: 0.2% versus 0.3% with placebo.

- Largest RCT² (not included in above review) compared pemafibrate (not available in Canada) to placebo in 10,497 patients with type 2 diabetes, fasting triglycerides 2.0-5.5 mmol/L (median 3.1 mmol/L), and high-density-lipoprotein cholesterol <1.0 mmol/L. After 3.4 years:
 - Pancreatitis: 0.5% in both groups.
- No evidence for niacin or omega-3 fatty acids on pancreatitis risk in any triglyceride group.

CONTEXT

- Alcohol overuse and gallstones account for the majority of acute pancreatitis,^{3,4} whereas hypertriglyceridemia account for <5% of cases.^{4,5}
 - Fibrates (except possibly pemafibrate)² increase risk of developing gallstones by ~1% over 6 years,⁶⁻⁸ potentially explaining how they lead to a net increase in pancreatitis.
- Guidelines recommend fibrates to lower triglyceride-related pancreatitis risk in patients with “elevated” triglycerides, but differ in threshold triglyceride levels to consider treating (5.6-11.2 mmol/L).⁹⁻¹⁰
- In a cohort study of 1.5 million patients, the 5-year risk of acute pancreatitis based on triglyceride concentration ranges:¹¹
 - 4.5-10mmol/L: 0.8%
 - 10-20 mmol/L: 1.5%
 - >20 mmol/L: 3.5%
- Cardiovascular benefits:
 - Fibrates only reduce non-fatal coronary events (19% relative risk reduction), with no benefit when added to statins.¹²
 - Statins reduce cardiovascular events (25-35% relative risk reduction) and all-cause mortality (10% relative risk reduction).¹³

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AUTHORS

Blair J. MacDonald,
PharmD, **Scott Garrison,**
MD PhD CCFP, **Ricky D.**
Turgeon, BSc(Pharm)
ACPR PharmD

*Authors do not have any
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