

## Are fish oil supplements as effective as gemfibrozil for decreasing elevated triglyceride levels?

### Bottom Line

Both gemfibrozil and fish oil are effective in treating hypertriglyceridemia. In the largest single head-to-head comparison, however, gemfibrozil was more effective. Physicians and consumers should also be mindful that there is significant heterogeneity in the content of fish oil products.

### The Evidence

#### Triglycerides and health

Hypertriglyceridemia is associated with an increased risk of coronary events and pancreatitis. Interventions that lower triglyceride levels are associated with decreased cardiovascular events, although it is unclear if this effect is independent of alterations in other lipid parameters. Nonetheless, the American Heart Association has identified lowering triglyceride levels as a goal in the management of hyperlipidemia.

Treating hypertriglyceridemia, whether it is borderline (150–199 mg/dL), high (200–499 mg/dL), or very high ( $\geq 500$  mg/dL), should begin with therapeutic lifestyle modification.<sup>1</sup> In cases of high or very high hypertriglyceridemia, if lifestyle modification alone is ineffective, pharmacologic intervention is advised. For triglyceride levels less than 500 mg/dL, the primary goal of treatment should be to lower low-density lipoprotein cholesterol (LDL-C). When triglyceride levels are more than 500 mg/dL, the primary goal is to lower triglycerides to reduce the risk of pancreatitis.

Fibric acid derivatives (fenofibrate and gemfibrozil) and fish oil are 2 commonly used pharmacologic agents for the management of hypertriglyceridemia. In single-agent studies, gemfibrozil at a dose of 600 mg twice a day has been shown to effectively lower triglyceride levels 40% to 60% from baseline. Fish oil, 1,000 mg 3 times a day, has shown similar effectiveness in lowering triglyceride levels 30% to 50% from baseline. Both interventions have been associated with slightly increased LDL-C and high-density lipoprotein cholesterol (HDL-C).

#### Direct comparison studies

A small, randomized, short-term crossover study compared the effects of gemfibrozil with fish oil for the treatment of hyperlipidemia in 10 patients with diabetes mellitus type 2.<sup>2</sup> Each patient was treat-

ed for 2 weeks, with washout periods of 8 weeks before and between interventions. Daily dosages used were 22 mL fish oil (containing 4.6 g omega-3 fatty acids) and 900 mg gemfibrozil. Plasma lipid levels were determined on days 1 and 15 of each treatment period. A 39% decrease in triglyceride levels was noted with gemfibrozil, compared with an 18% decrease with fish oil ( $P < .05$ ).

In another study, 89 patients with triglyceride levels of more than 4.5 mmol/L (81 mg/dL) were randomized to receive, in a double-blinded fashion, either Omacor™ 4 g/d (now known as Lovaza®) or gemfibrozil at 1,200 mg/d for 12 weeks.<sup>3</sup> Omacor is a capsule containing the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Serum lipid levels were measured at the beginning and end of treatment. Baseline characteristics were similar in both randomized groups. Gemfibrozil reduced triglyceride levels 51.2% compared with 28.9% with Omacor ( $P = .007$ ). Gemfibrozil decreased total cholesterol 13.0% compared with 10.2% with Omacor ( $P = .51$ ), and decreased very-low-density lipoprotein cholesterol 19.4% compared with 11.8% with Omacor ( $P = .49$ ). HDL-C was increased by both compounds; Omacor elevated HDL-C by only 1.2%, whereas HDL-C was elevated 27.9% by gemfibrozil ( $P = .012$ ).

Another crossover study enrolled 12 men with endogenous hypertriglyceridemia and gave them all fish oil 12 g/d (3.6 g EPA and DHA) for 3 weeks. After an interval period of at least 6 weeks they were given gemfibrozil 900 mg/d for another 3 weeks. Again in this study gemfibrozil was shown to be more effective for decreasing serum triglyceride levels than fish oil. However, the difference did not reach statistical significance.<sup>4</sup>

EBP

Eric S. Graham, MD  
Richard Chadek, MD  
James Mold, MD, MPH

Southwest Oklahoma Family Medicine Residency

#### REFERENCES

1. Pejic RN, Lee DT. Hypertriglyceridemia. *J Am Board Fam Med* 2006; 19:310–316. [LOE 5]
2. Fasching P, Rohac M, Liener K, Schneider B, Nowotny P, Waldhäusl W. Fish oil supplementation versus gemfibrozil treatment in hyperlipidemic NIDDM. A randomized crossover study. *Horm Metab Res* 1996; 28:230–236. [LOE 4]
3. van Dam M, Stalenhoef AFH, Wittekoek J, Trip MD, Prins MH, Kastelein JJP. Efficacy of concentrated n-3 fatty acids in hypertriglyceridaemia. A comparison with gemfibrozil. *Clin Drug Investig* 2001; 21:175–181. [LOE 2b]
4. Szostak-Wegierek D, Nowicka G. Comparative study of the influence of fish oil and gemfibrozil on levels of serum lipoprotein in endogenous hypertriglyceridemia [article in Polish]. *Pol Arch Med Wewn* 1994; 92:184–191. [LOE 4]