



# Drug Monitor

ONLINE EDITION

## When Statins Aren't Enough, Try Fibrates

Statins have long been considered the gold standard of cholesterol treatment. There are some patients, however, who don't respond to or can't tolerate them. Others may be receiving the maximum allowable dose of statins without having reached their cholesterol goals. For patients such as these, fibrates could be the answer, say researchers from Jewish General Hospital and McGill University, both in Montreal, Canada, and Hôpital Laval and Royal Victoria Hospital, both in Quebec City, Canada. They performed a systematic review of data from 20 double-blind, placebo-controlled, randomized trials of fibrates, involving a total of 25,655 patients.

The researchers identified four trials of bezafibrate, nine trials of fenofibrate, and seven trials of gemfibrozil that met their inclusion criteria. When compared to placebo, all three fibrates were associated with greater reductions in total cholesterol levels (range, -101.3 mg/dL to -5.0 mg/dL) as well as triglyceride levels (range, -321.3 mg/dL to -20.8 mg/dL). The fibrates also increased levels of high-density lipoprotein (HDL) (range, +1.1 mg/dL to +17.9 mg/dL) and were associated with an "important decrease" in nonfatal myocardial infarctions (odds ratio, 0.78). Rates of all-cause mortality were not significantly reduced by fibrates, however.

Although fibrates as a class showed similar effects on lipid profiles, the researchers found minor differences between individual fibrates: Bezafibrate may have a greater beneficial effect on HDL, while fenofibrate may improve total cholesterol more than bezafibrate and gemfibrozil.

The researchers advise clinicians to consider fibrates as monotherapy for patients who are intolerant or resistant to statins or who have hypertriglyceridemia. Furthermore, they may be used as an adjunct for patients who are receiving the maximum dose of statins. This combination therapy was examined in a previous study and was associated with a 42% reduction in triglyceride levels, a 23% reduction in total cholesterol levels, and a 25% increase in HDL levels.

Source: *Am J Med.* 2009;122(10):962e1-962e8.  
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## Combination Therapy for Neuropathic Pain

More effective and better tolerated monotherapies for neuropathic pain are "much anticipated," say researchers from University of Manitoba, Winnipeg, Canada and Queen's University and Kingston General Hospital, both in Kingston, Canada. In the meantime, findings from their study of 56 patients suggest that combining the drugs gabapentin and nortriptyline is more effective than using either drug alone.

The double-blind, double-dummy, crossover trial involved patients with either diabetic polyneuropathy or postherpetic neuralgia who reported a daily pain score of at least 4 (on a scale of 0 to 10) for at least six months directly preceding the start of the trial. The patients were assigned randomly to one of three groups. These groups all received the same treatments (gabapentin monotherapy, nortriptyline monotherapy, and gabapentin-nortriptyline combination therapy) but in different sequences. Each treatment was given for six weeks.

A total of 47 patients (84%) completed at least two of the three treatment periods and were included in the efficacy analyses. The researchers found that pain scores were significantly lower with combination therapy than with either drug alone. The mean daily pain score at maximum tolerated dose was 3.2 for the gabapentin group, 2.9 for the nortriptyline group, and 2.3 for the combination therapy group. No serious adverse events were recorded during the trial; the most common adverse event was dry mouth.

Combining gabapentin and nortriptyline also significantly improved pain intensity during sleep—an important finding given that sleep interference is a major complication of neuropathic pain, the researchers say. Additionally, combination therapy was associated with a significantly lower Beck Depression Inventory score and with improvements in mood and enjoyment of life when compared to gabapentin or nortriptyline monotherapy.

For both drugs, the researchers found that patients could tolerate higher doses in monotherapy than in combination therapy. This finding indicates there is at least some additivity of adverse events when combining the drugs, they say. Nevertheless, they conclude that, since the combination resulted in "superior efficacy" at lower doses without causing more adverse events, "additivity for analgesia was higher than for adverse events." Based on their results, the researchers recommend the combination for patients who respond to either drug alone but seek additional pain relief. ●

Source: *Lancet.* 2009;374(9697):1252-1261.  
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