VIEWPOINT

Hypertriglyceridemia
What the Dermatologist Needs to Know

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At times, dermatologists care for patients whose sole problems relate to the skin and are without primary care providers. In addition, these patients' dermatologic issues may relate to cutaneous manifestations of systemic cholesterol or triglyceride imbalances. Normal serum triglyceride levels range from 10 to 70 mg/dL (to convert to millimoles per liter, multiply by 0.0113); values greater than 150 mg/dL are considered abnormal. Triglycerides are generally measured after fasting for 8 to 12 hours.[1] Hypertriglyceridemia, defined as a triglyceride level above 200 mg/dL, is an occasional adverse effect of certain dermatologic therapies, particularly vitamin A derivatives (eg, isotretinoin, acitretin, bexarotene), used in acne, psoriasis, and cutaneous T-cell lymphoma, and atypical antipsychotics (eg, aripiprazole, quetiapine fumarate), used in delusions of parasitosis. Furthermore, elevated triglyceride level may be a component of certain dermatologic conditions, such as xanthelasma, eruptive xanthomas, and psoriasis. Hypertriglyceridemia is also associated with diabetes, hypertension, hypothyroidism, chronic kidney disease, obesity, physical inactivity, very high-carbohydrate diets, cigarette smoking, excess alcohol intake, pregnancy, and use of various medications such as corticosteroids, thiazides, protease inhibitors, β-blockers, estrogen-containing oral contraceptives, agents used in hormone therapy, and tamoxifen citrate.[1]

Major complications associated with hypertriglyceridemia are uncommon, but risk of pancreatitis increases when triglyceride levels are greater than 500 mg/dL. Several epidemiological studies have also demonstrated a relationship between elevated triglyceride level and increased incidence of cardiovascular disease.[1,2] Furthermore, drugs that reduce triglyceride level are associated with decreased cardiovascular risk.[1]

Given that dermatologists will likely interact with patients at risk for hypertriglyceridemia, we present a brief overview of the approach to managing this common condition. For patients with primary care physicians, we recommend consulting these physicians for management advice. While diet modification or discontinuation of pharmacotherapies causing hypertriglyceridemia should always be considered, this approach is not always optimal when treating conditions such as eruptive xanthomas. Furthermore, because not all patients will respond to lifestyle modifications, it is important to be aware of the common triglyceride-lowering drugs and their potential adverse effects. The primary objective for patients with very high-triglyceride levels is to prevent acute pancreatitis, and the secondary priority is to prevent cardiovascular disease.[1]

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Management Strategies

Lifestyle modifications are recommended for borderline-high and high triglyceride levels (150-499 mg/dL), and systemic treatment is recommended for very high levels (≥500 mg/dL) based on the National Cholesterol Education Program–Adult Treatment Panel III guidelines.[1] Systemic agents used to lower triglyceride levels include niacin (nicotinic acid or vitamin B_3), fibric acid derivatives (fibrates), ω-3 fatty acids present in fish oil, and occasionally hydroxymethylglutaryl–coenzyme A (HMG-CoA) reductase inhibitors (statins) (**Table**).[1]

First-line treatment should always be therapeutic lifestyle and habit changes, such as weight control, low-fat diet, exercise, and smoking and alcohol cessation.[3] Aerobics in particular can significantly lower triglyceride levels; the American Heart Association recommends 30 to 60 minutes of aerobics on most weekdays and 20 to 30 minutes of toning twice weekly. Patients not responsive to lifestyle modifications should be started on therapy with a lowering agent.

Niacin is available in sustained- and immediate-release formulations and can decrease triglyceride levels by 30% to 50% at high doses (≥1.5 g/d).[1,4] Niacin can also increase high-density lipoprotein cholesterol (HDL-C) concentrations by 20% to 40% and decrease low-density lipoprotein cholesterol (LDL-C) concentrations by 15% to 25%. Common adverse effects include flushing, pruritus, and xeroderma. Hepatotoxicity is a rare complication and is more common with sustained-release preparations, particularly when changing formulations. Cutaneous adverse effects are less common with sustained-released niacin compared with immediate-release niacin. Niacin-induced flushing is caused by release of prostaglandins and can occasionally be prevented by taking aspirin, 325 mg, 30 minutes prior to dosing.[1,4]

Fibrates (eg, gemfibrozil, fenofibrate) should be used when patients with hypertriglyceridemia are not responsive to niacin or are intolerant of its adverse effects. Fibrates can reduce triglyceride levels by 40% to 60% and can also increase HDL-C concentrations by 15% to 25%; however, fibrates can potentially raise LDL-C concentrations, although this is less common with fenofibrate.[1,5] Potential adverse effects include bloating, constipation, and transaminitis. Although gemfibrozil is considerably less expensive than fenofibrate, it has a higher incidence of adverse affects. However, gemfibrozil should not be used with a statin, given the increased risk of rhabdomyolysis.

Long-chain ω-3 polyunsaturated fatty acids (docosahexaenoic acid and eicosapentaenoic acid), which are present in fish oils, can be used to supplement the aforementioned medications and can lower triglyceride lev-

Table. Triglyceride-Lowering Medications and Potential Adverse Effects

Drug	Dosing	Triglyceride Level Reduction, %	Potential Adverse Effects
Fibric acid derivatives		40-60	Bloating, flatus, transaminitis, gastrointestinal disturbances, renal failure (elderly patients)
Fenofibrate	48-160 mg/d		
Gemfibrozil	600 mg, twice daily		
Niacin (nicotinic acid)		30-50	Pruritus, xeroderma, flushing, gastrointestinal disturbances, hepatitis[a]
Sustained release	500-2000 mg/d		
Immediate release	500-2000 mg, 2-3 times daily		
Fish oil supplements		30-50	Dysgeusia, gastrointestinal disturbances, pruritus, cutaneous eruption, eructation
ω-3 Fatty acids	2-9 g/d, DHA or EPA		
ω-3-Acid ethyl esters (Lovaza; GlaxoSmithKline)	1-4 g/d		
Statins		20-40	Hepatotoxicity, myopathy, rhabdomyolysis[b]
Rosuvastatin calcium	5-20 mg/d		
Simvastatin	5-80 mg/d		
Atorvastatin calcium	10-80 mg/d		
Pravastatin sodium	10-80 mg/d		
Lovastatin	10-80 mg/d		

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid.

[a] Cutaneous adverse effects are less common with sustained released; hepatotoxicity is more common with immediate release. Aspirin, 325 mg, administered 30 minutes prior to dosing may reduce flushing.

[b] Risk of rhabdomyolysis increases when statins are used in combination with gemfibrozil.

els by up to 30% at high doses (3 g/d); higher doses (9 g/d) can reduce triglyceride levels by up to 50%.[1,6] Fish oil supplements are generally well tolerated, but occasional adverse effects include unpleasant taste and gastrointestinal disturbances, including eructation and reflux. Fish oils are relatively inexpensive and are available over the counter, but patients usually need to take multiple capsules daily to achieve a triglyceride-lowering effect. Recently, a prescription fish oil capsule that is predominantly composed of eicosapentaenoic acid and docosahexaenoic acid (Lovaza; GlaxoSmithKline) was approved by the Food and Drug Administration for treatment of triglyceride levels greater than 400 mg/dL, although it is considerably more expensive than over-the-counter preparations.

Statins (eg, atorvastatin calcium, rosuvastatin calcium) can be used when patients are not responsive to the aforementioned therapies because they only decrease triglyceride levels by 20% with regular doses and 40% with high doses.[1,7] Statins should also be reserved for patients with concomitant elevation in LDL-C level or high-risk patients with cardiovascular disease or diabetes. Common adverse events include myalgias and occasional transaminitis; however, liver function tests do not need to be performed routinely. Although fairly safe, approximately 10% of patients will discontinue statins use because of intolerable adverse effects. Recently, a generic formulation of atorvastatin calcium (Lipitor; Pfizer Inc) became available in the United States and may be a more affordable option for some patients. For patients without insurance or sufficient funding, certain medications are available at Costco, Wal-Mart, or Target pharmacies for US $4 per month or US $10 for 3 months.

Conclusions

Hypertriglyceridemia is a common problem, particularly among high-risk patients using therapeutic agents that may cause this adverse effect. Hypertriglyceridemia can usually be managed with lifestyle modifications, but if pharmacotherapy is necessary, it is probably best to start with niacin and/or fish oil. Fibrates are also effective at lowering triglyceride levels, although adverse effects are more common. Statins only minimally lower triglyceride levels and should only be used in high-risk patients or those with increased LDL-C concentrations. For patients without general practitioners, it may be reasonable for dermatologists to consider initiating treatment.

ARTICLE INFORMATION

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REFERENCES

1. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106(25):3143-3421.

2. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol*. 1998;81(4A):7B-12B.

3. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults-the evidence report. *Obes Res*. 1998;6(suppl 2):51S-209S.

4. Martin-Jadraque R, Tato F, Mostaza JM, Vega GL, Grundy SM. Effectiveness of low-dose crystalline nicotinic acid in men with low high-density lipoprotein cholesterol levels. *Arch Intern Med*. 1996;156(10):1081-1088.

5. East C, Bilheimer DW, Grundy SM. Combination drug therapy for familial combined hyperlipidemia. *Ann Intern Med*. 1988;109(1):25-32.

6. Connor WE. Fish oil in hypertriglyceridemia: safety and recommendations. *Lipids*. 1999;34(suppl):S271.

7. Vega GL, Grundy SM. Management of primary mixed hyperlipidemia with lovastatin. *Arch Intern Med*. 1990;150(6):1313-1319.