Canadian Diabetes

Le diabète au Canada Volume 19, Number 3 Autumn 2006

Aggressive Cardiovascular Treatment Needed for People With Diabetes

Robin Conway MD, Lynn Nabata RD MA CDE, Danièle Pacaud MD FRCPC

Editor's Note

Diabetes has long been recognized as a multifactorial disease affecting primarily the cardiovascular (CV) system and leading to premature death. People with diabetes are 2 to 4 times more likely to die of a CV event than those who do not have diabetes (1). Abnormal cholesterol levels result in higher mortality. In secondary prevention of CV events, the value of aggressive lipid reduction is recognized. Yet, in people with diabetes without manifest vascular disease, there is a tendency to be much less aggressive, despite the fact that these patients have as high risk of a CV event as a person with diabetes who has had a CV event (1). Thus, primary prevention in persons with diabetes should be as aggressive as secondary prevention in those without diabetes. Lifestyle modifications—including nutrition interventions, weight control, smoking cessation and exercise—remain key components of CV prevention and management. However, many patients will able be unable to achieve lipid targets without pharmacologic intervention.

In this issue of *Canadian Diabetes*, Leiter and colleagues present highlights of the Canadian Diabetes Association 2006 Clinical Practice Guidelines entitled "Dyslipidemia in Adults With Diabetes" (2), an update of the Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada (3). The Clinical Practice Guidelines Expert Committee recognized the high CV risk associated with diabetes and the impact of dyslipidemia on CV morbidity and mortality. Two key recommendations in these guidelines are (2):

- In adults, the primary goal of lipid treatment is to achieve a low-density lipoprotein cholesterol (LDL-C) target of ≤2.0 mmol/L to decrease the risk of CV events (4). This has been reduced from the previous recommendation of <2.5 mmol/L. To achieve these levels, Leiter et al recommends that first line pharmacological treatment should consist of optimally dosed statin therapy.
- The secondary target is to reduce the total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-C) ratio to <4.0 mmol/L.

As more evidence becomes available, clinical practice guidelines are being changed to reflect this new evidence. It remains undisputed that evidence-based guidelines are the framework for the provision of good care, but what are the challenges in the dissemination and application of these guidelines? Are people with diabetes always managed according to guidelines-based care? As Leiter and colleagues note in their paper, the Third American National Health and Nutrition Examination Survey (NHANES III) data showed that 82% of people with diabetes have at least 1 additional CV risk factor (e.g. age, smoking, hypertension, family history, dyslipidemia etc.) and should be receiving aggressive risk reduction interventions (5,6). Yet, a recent Canadian study demonstrated that only 21% of people with type 2 diabetes are treated with any lipid-lowering agents at all (7).

This illustrates a care gap that may result from any disruption of the chain of events leading from the publication of evidence-based clinical practice guidelines through to its actual application to patient care. The publication of guidelines in itself has not been shown to have a significant effect on physicians' case management behaviour or patient outcomes. Rather, an effective dissemination plan is required, which includes presentation of guidelines in "manageable, continuous and reinforcing formats, as well as in settings that are known to facilitate understanding and change" (8). Facilitating the ease of implementing new guidelines is paramount, as family physicians' practices include medical issues that encompass the entire lifespan; moreover, they are swamped with a myriad of guidelines related to multiple diseases, and keeping up to date on all of them is a mammoth job. Thus, implementation tools to help them integrate recommendations into their practice should be included in any clinical practice guidelines dissemination plan.

Patient adherence to treatment recommendations presents another barrier to reducing mortality from diabetes. We must tackle this barrier with patient education and empowerment, consistent follow up and encouragement. Family physicians may not have control over barriers to optimal care, including socioeconomic issues (e.g. financial constraints, mobility, employment status), but they must be cognizant of the fact that these challenges exist.

Despite these challenges, it remains undisputed that evidence-based guidelines

Continued on page 7

In This Issue

Canadian Diabetes Association 2006 Dyslipidemia Clinical Practice Guidelines: A Review

Lawrence A. Leiter MD FRCPC FACP
Head, Division of Endocrinology & Metabolism, St. Michael's Hospital, Toronto, Ontario, Canada

Cynthia N. Lank BSc
Halifax, Nova Scotia, Canada

Note to readers: *This paper highlights key messages from the 2006 clinical practice guidelines entitled "Dyslipidemia in Adults With Diabetes," which were published recently in:* Canadian Journal of Diabetes. *2006;30(3): 230-240. Readers seeking more detailed information and complete references are directed to the guidelines, which are available at http://www.diabetes.ca.*

INTRODUCTION

A recently published national chart audit study of 2473 Canadian patients with type 2 diabetes revealed that 55% of patients with a diagnosis of diabetes of 2 years had dyslipidemia. This proportion rose to 66% in those who had had diabetes for ≥15 years (1). This high burden of dyslipidemia in patients with diabetes, as well as the increasing compelling trial evidence on the benefits of aggressive management of dyslipidemia in diabetes, led to a review of the lipid recommendations published in the Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada (2). The 2006 Lipid Expert Committee used the same evidence-based methodological principles of the 2003 guidelines to develop these revised recommendations for adults with diabetes.

ASSESSMENT OF VASCULAR RISK IN PATIENTS WITH DIABETES

Most patients with established diabetes are at high risk for vascular events (3-5) and should be treated accordingly (6,7). Clinical assessment can identify the minority of patients whose risk level might be considered lower. This would include people who meet all the following criteria: younger patients with recent onset of diabetes and without other risk factors for vascular disease (e.g. the metabolic syndrome, smoking) and without other complications of diabetes (including cardiovascular disease [CVD]). It is important to consider, however, that the average patient with newly diagnosed type 2 diabetes may have had the disease for many years prior to diagnosis. In addition, all patients with diabetes have an extremely high lifetime risk of CVD; thus, even if their short-term risk is lower, early interventions to improve their lipid profile may be justified in order to reduce long-term risk. Finally, the fact that both the short- and long-term clinical prognosis of patients with diabetes who experience an ischemic cardiac event continue to be worse than for those who do not have diabetes, also warrants an aggressive CV risk factor-reduction approach (7).

Several software programs are very useful tools to help physicians assess vascular risk in people with diabetes, e.g. the United Kingdom Prospective Diabetes Study risk engine (available at http://www.dtu.ox.ac.uk/riskengine/) and the Cardiovascular Life Expectancy Model (available in both French and English at http://www.chiprehab.com/CVD). These programs can also be powerful teaching and motivational tools to demonstrate to patients the cumulative effect of CV risk factors.

SCREENING

Fasting lipid levels (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], triglycerides [TG] and calculated low-density lipoprotein cholesterol [LDL-C]) should be measured at the time of diagnosis of diabetes and then every 1 to 3 years, as clinically indicated. More frequent testing should be performed if treatment for dyslipidemia is initiated.

TARGETS

Table 1 outlines lipid targets for adults with diabetes at high risk for CVD. Based on trials published since the release of the 2003 clinical practice guidelines (and reviewed below), the target **LDL-C** for high-risk patients has been lowered from <2.5 mmol/L to ≤2.0 mmol/L. In addition, LDL-C lowering is now recommended as the primary therapeutic goal in improving patients' lipid profiles.

The total cholesterol to HDL-C (**TC/HDL-C**) ratio is recommended as a secondary goal of therapy. Once the primary goal of an LDL-C of ≤2.0 mmol/L has been reached, one can consider lowering the TC/HDL-C ratio to the recommended goal of <4.0.

Specific goals for **TG** are not provided in these guidelines because there are little clinical trial data to support a specific TG target. Nonetheless, a TG level of <1.5 mmol/L is considered optimal, since

Table 1. Lipid targets for adults with diabetes at high risk for CVD

Index	Target value
Primary target	
LDL-C	2.0 mmol/L*
Secondary target	
TC/HDL-C ratio	<4.0

*Clinical judgment should be used to decide whether additional LDL-C lowering is required for patients with an on-treatment LDL-C of 2.0 to 2.5 mmol/L.

HDL-C = high-density lipoprotein cholesterol
LDL-C = low-density lipoprotein cholesterol
TC = total cholesterol

below this level of hyper-TG there are fewer associated metabolic abnormalities such as low HDL-C, small, dense LDL particles and postprandial lipemia.

The revised guidelines recognize the growing body of literature supporting apo B and the apo B/apo A1 ratio as sensitive indices for predicting CV risk (8). However, there is little clinical trial evidence for specific targets, and the measurement of these biomarkers is not widely available in Canada. At this time, knowledge of the apo B may be most clinically useful to guide the aggressiveness with which lipid-lowering therapy is pursued, with a goal of ~<0.9 g/L in the high-risk patient (9).

TREATMENT

Lifestyle modification

Many people with diabetes will have additional traditional CV risk factors that compound their already high risk of events. Accordingly, lifestyle interventions remain a key component of CVD prevention strategies and diabetes management in general. While lifestyle modification should be encouraged in all patients with dyslipidemia, the vast majority will be unable to achieve recommended lipid targets without pharmacologic intervention. Thus, for most people with diabetes, lifestyle interventions should be seen as an important adjunct to, but not a substitute for, pharmacologic treatment.

Smoking cessation should be encouraged and actively supported. In individuals with a body mass index (BMI) ≥25 kg/m^2 and/or abdominal obesity, weight reduction is strongly recommended. Even a modest 5 to 10% weight loss can be associated with an improved lipid profile in people with dyslipidemia and diabetes. An energy-restricted, well-balanced diet that is low in dietary cholesterol, saturated fats, trans fatty acids and refined carbohydrates is essential. Regular aerobic exercise helps individuals lose weight and maintain this weight loss over time, and may be associated with improvements in TG and HDL-C. Regular exercise can also improve glycemic control in people with type 2 diabetes, and is associated with substantial reductions in CV morbidity and mortality in both type 1 and type 2 diabetes.

LDL-C

The LDL-C target of ≤2.0 mmol/L is achievable in the vast majority of patients with a statin alone or, less commonly, a statin in combination with a second agent, such as a cholesterol absorption inhibitor. Studies have shown that the degree of LDL-C lowering with statins and the beneficial effects of LDL-C lowering are similar in people with and without diabetes (10-15). While statin therapy across all subgroups has shown the same relative risk reduction in outcomes, the absolute benefit depends on absolute risk, which is increased in people with diabetes. Sub-group analyses from statin trials have also shown similar benefits of LDL-C lowering, regardless of baseline LDL-C (13,15). Therefore, statin use should be considered for any person with diabetes at high risk of a vascular event. In the very small group of lower-risk patients with type 2 diabetes, the relative reduction in CVD risk with statin therapy is likely to be similar to those at higher global risk for CVD, but the absolute benefit from statin therapy will be lower.

The Collaborative Atorvastatin Diabetes Study (CARDS) (13) is the first completed statin trial to be conducted exclusively in patients with type 2 diabetes without known vascular disease. Mean baseline LDL-C was only 3.1 mmol/L and all patients had at least 1 additional CV risk factor (i.e. in addition to known diabetes). CARDS demonstrated that treatment with atorvastatin 10 mg daily was safe and highly efficacious in reducing the risk of first CVD events, including stroke. Treatment resulted in a mean LDL-C of 2.0 mmol/L, and was associated with a 37% reduced risk for CV events and a 48% reduced risk for stroke. The study provided important new evidence to support the value of treating even so-called "normal" LDL-C levels in patients with type 2 diabetes and no known vascular disease. CARDS patients all had at least 1 additional CV risk factor— a profile that would also apply to an estimated 70 to 80% (13) of type 2 diabetes patients. Analysis of the Third American National Health and Nutrition Examination Survey (NHANES III) data indicates that 82% of people with diabetes and no clinically evident coronary artery disease (CAD) have at least 1 of the CARDS entry criteria risk factors (13). CARDS authors conclude that the data "challenge the use of a particular threshold level of LDL-cholesterol as the sole arbiter of which patients with type 2 diabetes should receive statin therapy. … The absolute risk, determined by other risk factors in addition to LDL-cholesterol, should drive the target levels." Indeed, the authors question whether any patients with type 2 diabetes can be considered at sufficiently

Canadian Diabetes
Le Diabète au Canada

Autumn 2006

Canadian Diabetes/le Diabète au Canada is published four times a year by the Canadian Diabetes Association. All articles published in *Canadian Diabetes* are the sole opinions of the authors and are not necessarily endorsed by the Canadian Diabetes Association.

Change of address notices to:
Canadian Diabetes Association
522 University Avenue, 13th Floor
Toronto, Ontario M5G 1W7

The publication of Canadian Diabetes/ le Diabète au Canada is made possible by an unrestricted educational grant from Merck Frosst and Merck Frosst/Schering.

Canada Post Publication agreement number 40063447.

ISSN0841-9388

low risk for statin therapy to be withheld (13). A recently published sub-analysis of the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm (ASCOT-LLA) revealed similar benefits of atorvastatin 10 mg vs. placebo in patients with type 2 diabetes, hypertension and at least 3 additional risk factors (16).

In the subset with diabetes (n=1051) of the Treating to New Targets (TNT) trial (14) conducted in patients with stable coronary heart disease, patients treated with atorvastatin 80 mg daily who achieved a group mean LDL-C of 2.0 had 25% fewer subsequent major CV events than those treated with atorvastatin 10 mg daily who achieved a mean LDL-C of 2.6 mmol/L (p=0.026). Intensive therapy with atorvastatin 80 mg vs. therapy with 10 mg also reduced the rate of all CV events and cerebrovascular events. Notably, an increased event rate for all primary and secondary efficacy outcomes was noted for the diabetes subgroup compared with the overall study population, reinforcing the evidence that people with diabetes and CHD have an extremely high risk of CV events.

A recent meta-analysis of >90,000 statin-treated patients indicated that for every 1.0 mmol/L reduction of LDL-C, there was an approximately 20% reduction in CVD events, regardless of the baseline LDL-C. The proportional reductions were very similar in all subgroups, including those with diabetes without pre-existing vascular disease (17).

TC/HDL-C, HDL-C, TG

An elevated TC/HDL-C ratio in the face of an optimal LDL-C of ≤2.0 mmol/L is usually associated with a low HDL-C and/or elevated TG. This form of dyslipidemia is more amenable to lifestyle modification (increase in physical activity and weight reduction) and improvement in glycemic control than is an isolated LDL-C elevation. Initially, treatment should consist of intensification of lifestyle modification and improvement of glycemic control, using glucose-lowering therapies as needed. If the ratio remains elevated after a 4- to 6-month trial of these measures and once glycemic control and LDL-C have been optimized, adjuvant lipid-modifying therapy may be used in conjunction with statin therapy. Even with such aggressive measures, this secondary target is frequently not achieved.

If low HDL-C is the major cause of a persistently elevated TC/HDL-C ratio (in those whose LDL-C is already optimally controlled with a statin), niacin (immediate-release or extended-release formulation) is the adjuvant agent of choice. Combination lipid-lowering therapy with niacin is generally safe (18).

Recognizing the atherogenicity of small, dense LDL particles and remnant lipoproteins and the important anti-atherogenic role of HDL particles, it is important to improve these metabolic parameters by lifestyle modification, improvement in glycemic control and pharmacotherapy when indicated. The atherogenic impact of LDL-C particle size will be minimized and reductions in the TC/HDL-C will occur if very low plasma concentrations of LDL-C are achieved.

The LDL-C target is achievable in the vast majority of patients with a statin alone, or less commonly, a statin in combination with a second agent.

To reduce the risk of pancreatitis, a fibrate is recommended for patients with fasting TG levels >10.0 mmol/L who do not respond to other measures such as tight glycemic control, weight loss and restriction of refined carbohydrates. For those with moderate hyper-TG (4.5 to 10.0 mmol/L), either a statin or a fibrate can be attempted as first-line therapy, with the addition of a second lipid-lowering agent of a different class if target lipid levels are not achieved after 4 to 6 months on monotherapy. While several studies have shown CVD prevention is associated with fibrate treatment (19,20), there is much less evidence for CVD risk reduction with fibrates relative to statins in people with diabetes. Furthermore, in some studies, no statistically significant reduction in the primary endpoint was demonstrated with fibrate therapy (21,22). Combination therapy with fenofibrate (23,24) or bezafibrate plus a statin appears relatively safe if appropriate precautions are taken, but the efficacy of this approach with regard to outcomes has yet to be established. Statins should not be used in combination with gemfibrozil due to the increased risk of myopathy and rhabdomyolysis (25).

Although there is some clinical trial evidence that monotherapy with niacin or fibrates can prevent CVD events, there is currently insufficient evidence to routinely recommend statin + niacin and no evidence for fibrate + niacin combinations to reduce CV risk in patients with diabetes. For high-risk individuals who have a persistent elevation of TC/HDL-C despite achieving the primary LDL-C target of ≤2.0 mmol/L, niacin or fibrates can be added to statin therapy at the physician's discretion.

CONCLUSIONS

Dyslipidemia is a major risk factor for CVD in people with diabetes. Despite compelling evidence on the benefits of LDL-C lowering, many Canadians with diabetes and at high risk of CVD remain untreated or under-treated. Assessing global risk for CVD (i.e. obesity, hypertension, hyperglycemia, dyslipidemia, microalbuminuria, family history, smoking, sedentary lifestyle, diet) is essential in every patient. Effective risk reduction requires a multi-faceted approach targeting all risk factors. Physicians now have more evidence than ever before to convince them to lower LDL-C well below previously recommended targets in their patients with diabetes.

Summary Of Key Guidelines Changes

- The vast majority of people with established diabetes continue to be considered at high risk of a vascular event and should be treated accordingly. The targets for people with diabetes previously considered at "moderate risk" of a vascular event, however, were eliminated.
- The LDL-C target has been lowered from <2.5 mmol/L to ≤2.0 mmol/L and is now recommended as the sole primary goal in the management of dyslipidemia. First-line treatment should consist of optimally dosed statin therapy. Once the LDL-C target has been achieved, physicians can consider additional therapies to achieve the secondary target of a TC/HDL-C of <4.0.

2006 Recommendations for the Management of Dyslipidemia

Note: Readers are referred to the original guidelines document for supporting references and evidence grading.

◆ = New Recommendation

Prevention

People with type 1 or type 2 diabetes should be encouraged to adopt a healthy lifestyle to lower their risk of CVD. This entails adopting healthy eating habits, achieving and maintaining a healthy weight, engaging in regular physical activity, and smoking cessation.

Risk Assessment

◆ Most people with type 1 or type 2 diabetes should be considered at high risk for vascular disease. The exceptions are younger people with type 1 or type 2 diabetes with shorter duration of disease and without complications of diabetes (including established CVD) and without other CVD risk factors. A computerized risk engine (e.g. UKPDS risk engine, Cardiovascular Life Expectancy Model) can be used to estimate vascular risk.

Screening

Fasting lipid levels (TC, HDL-C, TG and calculated LDL-C) should be measured at the time of diagnosis of diabetes and then every 1 to 3 years as clinically indicated. More frequent testing should be performed if treatment for dyslipidemia is initiated.

Targets

◆ The primary target of therapy is the LDL-C; the secondary target is the TC/HDL-C ratio.

◆ If the TC/HDL-C ratio is ≥4.0, consider strategies to achieve a TC/HDL-C ratio <4.0, such as improved glycemic control, intensification of lifestyle (weight loss, physical activity, smoking cessation) and, if necessary, pharmacologic interventions.

Plasma apo B can be measured, at the physician's discretion, in addition to LDL-C and TC/HDL-C, to monitor adequacy of lipid-lowering therapy in the high-risk patient. Target apo B should be <0.9 g/L.

Treatment

◆ Patients at high risk of a vascular event should be treated with a statin to achieve an LDL-C ≤2.0 mmol/L. Clinical judgment should be used as to whether additional LDL-C lowering is required for patients with an on-treatment LDL-C of 2.0 to 2.5 mmol/L.

◆ In patients with serum TG >10.0 mmol/L despite best efforts at optimal glycemic control and other lifestyle interventions, a fibrate should be prescribed to reduce the risk of pancreatitis. For those with moderate hyper-TG (4.5–10.0 mmol/L), either a statin or a fibrate can be attempted as first-line therapy, with the addition of a second lipid-lowering agent of a different class if target lipid levels are not achieved after 4 to 6 months on monotherapy.

For patients not at target(s), despite optimally dosed first-line therapy as described above, combination therapy can be considered. Although there are as yet no completed trials demonstrating clinical outcomes in patients receiving combination therapy, pharmacologic treatment options include (listed in alphabetical order):

- Statin plus ezetimibe
- Statin plus fibrate
- Statin plus niacin

Looking Ahead: Ongoing Lipid Research

Clinical practice guidelines will continue to evolve as trial evidence is published. Adequately powered, event-reduction, prospective, randomized, controlled, clinical trials are currently underway with various classes of lipid-lowering agents to examine whether the addition of other therapies in individuals already treated with statins further reduces cardiovascular events and/or prolongs survival:

- **Action to Control Cardiovascular Risk in Diabetes (ACCORD)**
  – statin + fibrate
- **Atherothrombosis Intervention in Metabolic Syndrome with Low HDL-cholesterol/High Triglyceride and Impact on Global Health Outcomes (AIM HIGH)**
  – statin + extended-release niacin
- **Investigation of Lipid Level management to Understand its Impact In Atherosclerotic Events (ILLUMINATE)**
  – statin + cholesterol ester transfer protein inhibitor.

REFERENCES

1. Harris SB, Ekoé J-M, Zdanowicz Y, et al. Glycemic control and morbidity in the Canadian primary care setting (results of the diabetes in Canada evaluation study). *Diabetes Res Clin Pract.* 2005;70:90-97.
2. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes.* 2003;27(suppl 2): S1-S152.
3. Haffner SM, Lehto S, Rönnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med.* 1998; 339:229-234.
4. Booth GL, Rothwell D, Fung K, et al. Diabetes and cardiac disease. In: Hux JE, Booth G, Laupacis A, eds. *Diabetes in Ontario: An ICES Practice Atlas.* 2002:5. 95-5.127.
5. Krolewski AS, Kosinski EJ, Warram JH, et al. Magnitude and determinants of coronary artery disease in juvenile-onset, insulin-dependent diabetes mellitus. *Am J Cardiol.* 1987;59:750-755.
6. Gæde P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med.* 2003;348:383-393.
7. Grundy SM. Diabetes and coronary risk equivalency. What does it mean? *Diabetes Care.* 2006;29:457-460.
8. Barter PJ, Ballantyne CM, Carmena R, et al. ApoB versus cholesterol to estimate cardiovascular risk and to guide therapy: report of the thirty-person ten-country panel. *J Intern Med.* 2006: 259:247-258.
9. Walldius G, Jungner I, Holme I, et al. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. *Lancet.* 2001; 358:2026-2033.
10. Pyörälä K, Pedersen TR, Kjekshus J, et al. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. A subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). *Diabetes Care.* 1997; 20:614-620.
11. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *N Engl J Med.* 1996;335:1001-1009.
12. The Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med.* 1998;339:1349-1357.
13. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet.* 2004;364;685-696.
14. Shepherd J, Barter P, Carmena R, et al. for Treating to New Targets Investigators. Effect of lowering LDL cholesterol substantially below currently recommended levels in patients with coronary heart disease and diabetes. 2006:29;1220-1226.
15. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet.* 2003;361: 2005-2016.
16. Sever PS, Poulter NR, Dahlof B, et al. Reduction in cardiovascular events with atorvastatin in 2532 patients with type 2 diabetes. Anglo-Scandanavian Cardiac Outcomes Trial—Lipid-Lowering arm (ASCOT-LLA). *Diabetes Care.* 2005;28: 1151-1157.
17. Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: Prospective meta-analysis of data from 90 056 participants in 14 randomised trials. *Lancet.* 2005;366: 1267-1278.
18. Grundy SM, Vega GL, McGovern ME, et al. Efficacy, safety, and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes: Results of the Assessment of Diabetes Control and Evaluation of the Efficacy of Niaspan Trial. *Arch Intern Med.* 2002;162: 1568-1576.
19. Frick MH, Elo MO, Happa K, et al. Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia: safety of treatment, changes in risk factors, and incidence of coronary heart disease. *N Engl J Med.* 1987;317: 1237-1245.
20. Robins SJ, Rubins HB, Faas FH, et al. Veterans Affairs HDL Intervention Trial (VA-HIT). Insulin resistance and cardiovascular events with low HDL cholesterol: The Veterans Affairs HDL Intervention Trial (VA-HIT). *Diabetes Care.* 2003;26: 1513-1517.
21. Keech A, Simes RJ, Barter P, et al. Effects of long-term feno-fibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): Randomised controlled trial. *Lancet.* 2005; 26:1849-1861.
22. The BIP Study Group. Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease. The Bezafibrate Infarction Prevention (BIP) Study. *Circulation.* 2000;102:21-27.
23. Durrington PN, Tuomilehto J, Hamann A, et al. Rosuvastatin and fenofibrate alone and in combination in type 2 diabetes patients with combined hyperlipidaemia. *Diabetes Res Clin Pract.* 2004;64:137-151.
24. Athyros VG, Papageorgiou AA, Athyrou VV, et al. Atorvastatin and micronized fenofibrate alone and in combination in type 2 diabetes with combined hyperlipidemia. *Diabetes Care.* 2002;25:1198-1202.
25. Pasternak RC, Smith SC, Bairey-Merz C, et al. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. *J Am Coll Cardiol.* 2003;40;567-572.

Suite de la page 8
clinique sont modifiées. Il est indéniable que des lignes directrices factuelles sont l'assise de la prestation de bons soins, mais à quelles difficultés se heurtent la diffusion et la mise en application de ces lignes directrices? Les personnes diabétiques sont-elles toujours prises en charge selon les lignes directrices? Comme Leiter et ses collaborateurs le soulignent dans leur compte rendu, le sondage NHANES III (*Third American National Health and Nutrition Examination Survey*) a révélé que 82 % des personnes atteintes de diabète présentent au moins un autre facteur de risque cardio-vasculaire (p. ex. âge avancé, tabagisme, hypertension, antécédents familiaux et dyslipidémie) et devraient faire l'objet d'interventions énergiques pour réduire les risques (5,6). Une récente étude canadienne a toutefois démontré que seulement 21 % des personnes atteintes de diabète de type 2 reçoivent un hypolipidémiant quelconque (7).

Cette situation illustre une lacune des soins pouvant résulter de toute interruption de la suite des événements entre la publication de lignes directrices de pratique clinique factuelles et la mise en application chez les patients. On n'a pas démontré que la publication de lignes directrices en soi avait un effet important sur la gestion des cas par les médecins ni sur le devenir des patients. Il faudrait plutôt mettre en place un plan de diffusion efficace des lignes directrices mettant à profit «des méthodes gérables, soutenues et prévoyant des rappels et des milieux qui favorisent la compréhension et le changement» (8). Il est essentiel que la mise en application des lignes directrices soit facile, car les médecins de famille se penchent sur des questions médicales qui touchent toute la vie de leurs patients. En outre, ils sont inondés par une foule de lignes directrices sur diverses maladies et rester à jour dans de multiples domaines est une tâche phénoménale. Il faut donc que les moyens d'intégration des recommandations dans leur pratique fassent partie du plan de diffusion des lignes directrices.

La fidélité des patients aux traitements recommandés constitue un autre obstacle à la réduction de la mortalité associée au diabète. Nous devons surmonter cet obstacle en éduquant les patients, en leur donnant plus d'autonomie, en les suivant de près et en les encourageant. Les médecins de famille ne peuvent peut-être pas surmonter les obstacles aux soins optimaux, y compris les questions socio-économiques (p. ex. contraintes financières, mobilité, emploi), mais ils doivent être conscients de ces obstacles.

Malgré tout, il est indéniable que des lignes directrices factuelles permettent d'offrir de bons soins. Ainsi, les lignes directrices sur la dyslipidémie dont il est question dans ce numéro fournissent aux médecins de famille des données probantes, des connaissances et des moyens de prendre la dyslipidémie en charge en présence de diabète. Ces lignes directrices offrent aux médecins un cadre qui leur permet de réduire la morbidité et la mortalité cardio-vasculaires et, partant, d'améliorer la qualité de vie chez les patients diabétiques. Elles leur permettent de :

- prodiguer des soins conformes à des lignes directrices de pratique clinique factuelles;
- appuyer les personnes atteintes de diabète pour la prévention primaire de la maladie cardio-vasculaire au moyen de modifications du mode de vie, y compris une saine alimentation, la perte de poids, le sevrage du tabac et l'exercice;
- prescrire une statine en première intention chez les patients qui présentent une dyslipidémie;
- prescrire la *bonne statine* et à la *bonne dose* pour atteindre la cible;
- aider les patients à prendre leur maladie en charge en cernant et en surmontant les obstacles;
- faire un suivi pour s'assurer que les patients ont atteint l'objectif et surveiller les effets secondaires et les interactions médicamenteuses possibles.

Nous espérons que les médecins de premier recours mettront ces lignes directrices en application entièrement et sans tarder afin que nous puissions atteindre notre but de réduire au minimum le fardeau du diabète et de la dyslipidémie chez les personnes diabétiques.

RÉFERÉNCES (voir 3e colonne)

Editor's Note…continued from page 1
offer evidence for good care. Thus, the dyslipidemia guidelines highlighted in this issue provide family physicians with the evidence, knowledge and tools to manage dyslipidemia in diabetes. These guidelines offer physicians a framework reduce CV morbidity and mortality, and, in turn, achieve a better quality of life for clients with diabetes, by:

- Providing care in accordance to evidence-based clinical practice guidelines.
- Supporting people with diabetes in the primary prevention of CVD through lifestyle modifications, including nutrition modifications, weight control, smoking cessation and exercise.
- Prescribing a statin as a first-line therapy for those with dyslipidemia.
- Prescribing the *right* statin in the *correct* dosages to achieve target.
- Supporting patient self-management, by recognizing and addressing the barriers.
- Following up to ensure patients have reached target, and to monitor potential side effects and drug interactions.

It is our hope that primary care practitioners implement these guidelines swiftly and completely into practice to achieve the goal of minimizing the burden of diabetes and dyslipidemia for people with diabetes..

REFERENCES

1. Haffner SM, Lehto S, Rönnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med.* 1998; 339:229-234.
2. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Lipid Expert Committee. Dyslipidemia in adults with diabetes. *Can J Diabetes.* 2006;3:230-240.
3. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes.* 2003;27(suppl 2):S1-S152.
4. Shepherd J, Barter P, Carmena R, et al, for Treating to New Targets Investigators. Effect of lowering LDL cholesterol substantially below currently recommended levels in patients with coronary heart disease and diabetes: the Treating to New Targets (TNT) study. *Diabetes Care.* 2006:29;1220-1226.
5. Alexander CM, Landsman PB, Teutsch SM, et al. Third National Health and Nutrition Examination Survey (NHANES III); National Cholesterol Education Program (NCEP). NCEP defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes.* 2003;52:1210-1214.
6. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): Multicentre randomised placebo-controlled trial. *Lancet.* 2004;364;685-696.
7. Harris SB, Stewart M, Brown, JB. Type 2 diabetes in family practice. Room for improvement. *Can Fam Physician.* 2003;49:778-785.
8. Harris S, Webster-Boegart S, Lillie D, et al. A model for the dissemination of clinical practice guidelines—the Canadian Diabetes Association experience. *Can J Diabetes Care.* 2000;24:64-69.

Canadian Diabetes

Le diabète au Canada Volume 19 N° 3 Automne 2006

Nécessité d'un traitement cardio-vasculaire énergique en présence de diabète

Robin Conway, M.D., Lynn Nabata, diététiste, MA, ÉAD, et Danièle Pacaud, M.D., FRCPC

Note de la rédaction

Le diabète est depuis longtemps reconnu comme une maladie multifactorielle touchant surtout l'appareil cardio-vasculaire et aboutissant à un décès prématuré. Les personnes diabétiques sont de 2 à 4 fois plus susceptibles de mourir d'un trouble cardio-vasculaire que les personnes non diabétiques (1). Des taux anormaux de cholestérol entraînent une hausse de la mortalité. Pour la prévention secondaire des troubles cardio-vasculaires, la valeur d'une baisse importante des taux de lipides est reconnue. Pourtant, chez les personnes diabétiques qui ne présentent pas de maladie vasculaire avérée, la tendance est de prescrire un traitement beaucoup moins énergique, même si ces patients sont aussi exposés aux troubles cardio-vasculaires que les personnes diabétiques ayant déjà présenté un trouble cardio-vasculaire (1). Par conséquent, la prévention primaire chez les personnes diabétiques devrait être aussi énergique que la prévention secondaire chez les personnes non diabétiques. Les modifications du mode de vie, y compris une saine alimentation, la perte de poids, le sevrage du tabac et l'exercice, restent des éléments clés de la prévention et de la prise en charge des troubles cardio-vasculaires. Cependant, de nombreux patients sont incapables d'atteindre les cibles lipidiques sans intervention pharmacologique.

Dans ce numéro de *Le diabète du Canada*, Leiter et ses collaborateurs résument les points saillants des Lignes directrices de pratique clinique 2006 de l'Association canadienne du diabète intitulées «Dyslipidémie chez les adultes diabétiques» (2), une mise à jour des Lignes directrices de pratique clinique 2003 de l'Association canadienne du diabète pour la prévention et le traitement du diabète au Canada (3). Le Comité d'experts des lignes directrices de pratique clinique a reconnu que le diabète était associé à un risque accru de troubles cardio-vasculaires de même que l'impact de la dyslipidémie sur la morbidité et la mortalité cardio-vasculaires. Deux recommandations clés de ces lignes directrices sont (2) :

Chez les adultes, le principal objectif de la prise en charge des lipides est l'obtention d'un taux de cholestérol des lipoprotéines de basse densité (C-LDL) $\leq$ 2,0 mmol/L afin de réduire le risque de manifestations cardio-vasculaires (4). L'ancienne cible recommandée était $<$ 2,5 mmol/L. Pour atteindre cet objectif, Leiter et ses collaborateurs recommandent un traitement pharmacologique de première intention par une statine administrée à une dose optimale.

L'objectif secondaire est la réduction du rapport cholestérol total (CT):cholestérol des lipoprotéines de haute densité (C-LHD) à $<$ 4,0 mmol/L.

À mesure que d'autres données probantes font surface, les lignes directrices de pratique

Suite à la page 7

CANADA POSTES
POST CANADA
Postage paid Port payé
Publications Mail Poste-publications
40063447