CASE STUDY

Case Study: Colesevelam Hydrochloride for Management of a Patient With Type 2 Diabetes Mellitus and Hyperlipidemia

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Key Point: Welchol® (colesevelam hydrochloride) is indicated for lowering hemoglobin A1C in adult patients with type 2 diabetes mellitus (T2DM) and lowering low-density lipoprotein-cholesterol (LDL-C) in patients with primary hyperlipidemia. This is an important add-on choice for patients with T2DM at high risk for cardiovascular disease as it provides an option to treat both disorders with one medication. The effect of Welchol® on cardiovascular morbidity and mortality has not been determined.

Background

Alice† is a 63-year-old Caucasian woman who works at her local hospital as a case manager in the pediatric wing. She presents to her primary care physician (PCP) 7 months after her last visit. Her PCP has the latest reports from her cardiologist to keep him updated on her cardiovascular health. She reports no exertional chest pain, and a recent stress echocardiogram showed normal wall motion with apical dyskinesis and an ejection fraction of 55%. Alice's PCP does a thorough workup to determine her overall health status.

Current Visit

Exam Findings

- Height — 5 ft 4 in
- Weight — 163 lb
- Body Mass Index (BMI) — 29 kg/m^2
- Waist — 35 inches
- Blood Pressure (BP) — 126/76 mmHg
- Heart Rate — 68 beats per minute (BPM)
- Cardiac exam — Normal
- Peripheral pulses — Normal and no edema

Current Treatment Regimen

- Atorvastatin 40 mg daily (2004)
- Aspirin 81 mg daily (2007)
- Lisinopril 10 mg daily (2007)
- Metformin 1000 mg at bedtime (2008)
- Low fat diet
- Exercise for 20 minutes 3 times per week

Health History

- Myocardial infarction 2 years ago
- T2DM diagnosed 1 year ago
- Dyslipidemia diagnosed 5 years ago
- A family history of T2DM and coronary heart disease (CHD)

Laboratory Results

	Last Visit (7 months ago)	Current Visit
Glycated hemoglobin (A1C)	6.6%	7.1% ↑
Fasting plasma glucose (FPG)	115 mg/dL	125 ↑
Low-density lipoprotein-cholesterol (LDL-C)	100 mg/dL	108
High-density lipoprotein-cholesterol (HDL-C)	45 mg/dL	45
Triglycerides (TG)	210 mg/dL	215
Total cholesterol (C)	187 mg/dL	196
Non-high-density lipoprotein-cholesterol (non-HDL-C)	142 mg/dL	151
Aspartate aminotransferase/alanine aminotransferase (AST/ALT)	WNL	WNL

WNL=within normal limits

Clinical Discussion

Alice's outstanding health issues are her rise in A1C and LDL-C levels since her last visit to her PCP 7 months ago. Alice's A1C level has gone up from 6.6% to 7.1% despite her treatment with metformin for 1 year, and she has a rise in her LDL-C level. The recommended LDL-C goal by the American Diabetes Association/American College of Cardiology Foundation (ADA/ACC) consensus statement is <70 mg/dL for an individual with high cardiometabolic risk (CMR)[1]; Alice's LDL-C level of 108 mg/dL is not consistent with current National Cholesterol Educational Program Adult Treatment Panel III (NCEP ATP III) guidelines for patients at high risk of CHD.[2] Alice followed a regimen of diet, exercise, and weight loss, but she feels a recent family trip to Italy lessened her resolve to stick to her regimen; she is still overweight with a BMI of 29 kg/m^2.

A review of Alice's current treatment regimen shows that she was first placed on atorvastatin (40 mg daily) in 2004 for dyslipidemia. After Alice had a myocardial infarction in 2007, she was started on low dose aspirin (81 mg daily), and lisinopril (10 mg daily) was added to lower her blood pressure. Most recently, metformin (1000 mg at bedtime) was added in 2008. Metformin is the first-line drug for the treatment of T2DM, particularly in overweight people; it is the most commonly prescribed oral antidiabetes agent.[3,4]

Since Alice is in the highest risk category for CHD and is not at goal for LDL-C or A1C levels, her PCP returns her to the cardiologist to further manage her care.

†Not an actual Welchol® patient.

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Cardiologist Visit

First and foremost, Alice's cardiologist wants to reduce Alice's LDL-C and A1C levels to goal. According to the NCEP ATP III guidelines, a LDL-C goal <70 mg/dL and a non-HDL-C goal <100 mg/dL are preferred recommendations for a patient such as Alice.[5] The American Heart Association and the American College of Cardiology (AHA/ACC) guidelines for secondary prevention state that these goals are reasonable, rather than optional, targets.[6]

Because of these guidelines, the cardiologist wants to further reduce Alice's LDL-C level. After careful consideration, the cardiologist decides that the best option is to switch Alice's treatment plan from atorvastatin 40 mg/d to rosuvastatin 20 mg/d to achieve at least an additional 6% reduction in her LDL-C level.[7] He also decides to add Welchol® 3.75 gm/day because he would like to reduce her LDL-C level by another 16%, as well as reducing her A1C level by an additional 0.5%, without risk for hypoglycemia.[8-10]

The cardiologist could have considered other options, such as increasing Alice's atorvastatin dosage to 80 mg/day and/or adding ezetimibe (to reduce her LDL-C level), increasing her metformin dosage to 2000 mg/day, and/or considering the addition of a dipeptidyl peptidase IV (DPP-IV) inhibitor (to reduce her A1C level); none of these options would provide the dual benefits of reducing both her LDL-C and glucose levels with one agent. In addition, prescribing Welchol® would eliminate a branded co-pay for an additional drug. Welchol® is available as 6 (325 mg) tablets, which she can take all at once, 3 tablets twice daily, or a once-daily oral suspension, which can be mixed with 4-8 ounces of water. Alice decides to take the oral suspension as she has difficulty swallowing pills.

Three Months After Visiting the Cardiologist

Three months later, Alice's laboratory values demonstrate a marked improvement in her cholesterol and glucose levels:

- LDL-C — 80 mg/dL ↓
- HDL-C — 47 mg/dL↑
- Non-HDL-C — 120 mg/dL↓
- A1C — 6.6%↓

Add-On Therapy With Welchol® for Patients With T2DM and CHD

The addition of a bile acid sequestrant (BAS) to a statin has long been recognized as a safe and effective way to lower LDL-C levels by an additional 20% to 25%. A clinical trial by Knapp and colleagues demonstrated that adding colesevelam hydrochloride 3.8 g to simvastatin 20 mg resulted in a 42% mean reduction from baseline in LDL-C level, with excellent safety and tolerability.[11]

Welchol® is the only BAS that is indicated as an adjunct to diet and exercise to reduce LDL-C and improve glycemic control in adults with T2DM.[12] Welchol® was originally approved in the United States in 2000 as a cholesterol-lowering agent; the US Food and Drug Administration approved Welchol® for use in the treatment of T2DM in 2008. Three pivitol clinical trials were the foundation for the approval of Welchol® as add-on therapy with other antidiabetes medications, including a combination with metformin, a sulfonylurea, or an insulin-based regimen. The baseline levels of A1C in these trials were in the range of 7.5% to 9.5%.[8-10] Welchol® was shown to consistently reduce A1C levels in these studies by 0.5%, irrespective of the background treatment.

In Alice's case, the addition of Welchol® to rosuvastatin resulted in a 25% reduction over her previous LDL-C level; additionally, Alice had a 0.5% reduction in her A1C level. Welchol® was well tolerated, and Alice did not experience a weight gain.

Treatment Goals for Alice

- Compliance with medications
- Continued weight loss
- Consultation with a certified diabetes educator on a more frequent basis
- Practice home glucose monitoring
- More frequent visits with PCP

Conclusion

Based on clinical studies, Welchol® is safe and effective add-on therapy for patients with T2DM who are not at their recommended A1C and LDL-C levels.

Please see adjacent pages for Important Safety Information and Brief Summary of Full Prescribing Information about Welchol®.

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Editorial support provided by Laurie R. Towle, PhD.

Faculty Disclosure: Dr Jones has disclosed that he has received support in the form of consulting agreements from Abbott Laboratories, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo, Inc., and Merck.