

Case Study: Glycemic Control in the Elderly: Risks and Benefits

Evan M. Benjamin, MD, FACP

Presentation

R.B. is a 67-year-old woman with obesity, hypertension, and coronary artery disease (CAD). Eighteen months ago, she suffered an inferior wall myocardial infarction (MI). Cardiac catheterization revealed an occluded right coronary artery and a 40% stenosis in the proximal left anterior descending artery.

The patient was placed on β -blocker and aspirin therapy and was provided education regarding lifestyle modification. A lipid panel revealed mild hypertriglyceridemia and a slightly depressed HDL cholesterol level. Blood glucose was not measured. The patient initially did well, denying chest pain, shortness of breath, or any symptoms related to her cardiac condition.

Over the past month, R.B. complained of increasing fatigue and episodes of polyuria and polydipsia. A fasting blood glucose level was 168 mg/dl. Physical examination revealed a mildly obese woman with blood pressure of 142/86 mmHg and a pulse of 78. A dilated eye exam revealed mild nonproliferative diabetic retinopathy. Only trace pedal edema bilaterally was found. Additional laboratory examination revealed a hemoglobin A_{1c} (A1C) concentration of 9.4%, blood urea nitrogen 11 mg/dl, creatinine 0.9 mg/dl, and urine microalbumin 1,993 μ g/dl on a spot urine sample.

Questions

1. What is the relationship between diabetes and complications in the elderly?
2. What are the risks of intensive therapy for elderly patients?

3. What approach might be used for glycemic management?

Commentary

Diabetes affects nearly 20% of those over 65 years of age in the United States. The Diabetes Control and Complications Trial (DCCT) demonstrated that tight glucose control in patients 13–39 years of age with type 1 diabetes was associated with a marked decrease in microvascular complications. The United Kingdom Prospective Diabetes Study (UKPDS) confirmed the relationship between glycemic control and complications in type 2 diabetes. It is now generally agreed that all patients with diabetes should have as tight glycemic control as possible.

Although specific trials with elderly patients who have type 2 diabetes are ongoing, there is indirect evidence supporting the concept that tight glycemic control may help to decrease or prevent microvascular and macrovascular disease in this population. Tight glycemic control in older diabetic patients after MI has been associated with reduced long-term mortality. Other studies have found that elderly patients with elevated fasting blood glucose levels had a 50% higher cardiovascular and all-cause mortality.

The chief concern about tight control in elderly patients with diabetes is the risk for hypoglycemia. The elderly are, in general, less aware of the signs of hypoglycemia and are particularly at risk for this complication. Intensive glucose control in all patients is a trade-off between benefits and risks. Improved glycemic control may reduce the risk of

micro- and macrovascular disease, yet the tighter the control, the greater the risk of treatment-induced hypoglycemia.

Until recently, the preference for loose glycemic control for elderly patients has been supported by the notion that elderly patients are more susceptible to oral agent-induced hypoglycemia and less sensitive to the warning signs of hypoglycemia. However, findings from the UKPDS showed that severe hypoglycemia among patients with type 2 diabetes is a rare event. Now, with the recent increased use of newer agents that are less associated with hypoglycemia, it is timely to consider tighter glycemic control for many elderly diabetic patients.

It is important to take into account co-morbid factors when deciding whether an elderly patient is a candidate for tight glycemic control. Certainly, a patient with significant end-organ disease, malignancy, or dementia may not be a good candidate for tight glycemic control. However, in healthy elderly diabetic patients without significant co-morbid disease, one needs to look at the life expectancy and quality of life of each individual. The life expectancy of the average healthy 65-year-old woman is 19 years, and therefore, attention to glucose control with resultant decrease in vascular damage could significantly affect the quality and quantity of the final years of life.

R.B. is a typical patient entering the last decade or two of her life. She has been otherwise healthy yet has significant risk factors for cardiovascular disease. She clearly manifests signs and

symptoms of the insulin resistance syndrome, and her only major co-morbid condition is CAD, which is now being medically managed. Given what we now know about a relationship between glycemic control and mortality from macrovascular disease, it is imperative that R.B. be able to achieve as tight glycemic control as possible. Given the existence of a partially obstructed left anterior descending artery, it will be very important to aggressively treat cardiovascular risk factors and to maintain euglycemia to prevent further progression of this coronary lesion.

In addition, R.B. is manifesting early signs of microvascular disease from diabetes. In all likelihood, her diagnosis of diabetes lagged the clinical development of hyperglycemia. She has had enough time to manifest microvascular changes in her retina, as well as in her glomeruli. By starting R.B. on an aggressive regimen to achieve near-normal glycemic control, we may be able to limit further progression of her microvascular disease. R.B.'s care will need to take into account her current medical condition, drug regimen, and ability to detect hypoglycemic reactions.

R.B.'s treatment plan will include aggressive hypertension control, lipid management, use of angiotensin-converting enzyme inhibitors or angiotensin receptor therapy for renal disease, and a stepwise management plan to achieve euglycemia. Goals for hypertension control will be established to minimize cardiovascular disease while avoiding hypotension. In general, the target will be to keep blood pressure below 130/80 mmHg. In addition, the target for LDL cholesterol will be <100 mg/dl. It is very important that we establish a target blood glucose as well as a target A1C concentration for her.

R.B. will need to be aware of the complications and risks associated with tight control. It will also be important to explain the perceived benefits of tight glycemic control on slowing the progression of her CAD and microvascular dis-

ease. She should be referred to a certified diabetes educator to learn more about diabetes and to outline a self-management plan. A nutritional assessment needs to be performed, and a food plan needs to be initiated.

Blood glucose awareness training may be of special utility for R.B. She will continue to take a β -blocker because she is status-post an acute MI, and this may further impair her ability to detect hypoglycemia.

Additionally, R.B. should be referred to social services or counseling for financial case management, if necessary. Many Medicare risk plans may pay for medication and monitoring supplies when Medicare itself will not.

If R.B. does not achieve her target glucose levels and A1C concentration, she should be started on an oral hypoglycemic agent and followed closely to see if she is achieving her target glycemic control. The use of metformin (Glucophage) or a thiazolidinedione (Actos or Avandia) may be the best first choice in this elderly patient with obesity and insulin resistance. Neither produces hypoglycemia in the absence of insulin or a sulfonylurea agent.

If glycemic targets are not achieved within a short time frame after starting an oral agent, the patient should have her medications increased to the maximum dose and then should be considered as a candidate for combination therapy with other oral hypoglycemic agents. Finally, there should be no hesitation to initiate R.B. on a regimen that includes insulin. Although there is a relationship between endogenous insulin levels and atherosclerosis, it is clear that hyperglycemia is far worse than the use of exogenous insulin for patients who will no doubt benefit from tighter glycemic control.

Our current understanding of the relationship between glycemic control and microvascular disease suggests that tight glycemic control should be considered for select elderly patients with diabetes. With proper education, medication choices, and consideration of

co-morbid diseases, elderly patients with diabetes can improve their quality and quantity of life with improved glycemic control.

Clinical Pearls

1. The elderly comprise an increasingly larger proportion of diagnosed cases of diabetes in the United States.
2. All complications of diabetes can occur in elderly patients.
3. Reduction in risk for microvascular and macrovascular disease should be the goal for all patients with diabetes. Elderly diabetic patients should be considered candidates for intensive blood glucose control.
4. The risk of hypoglycemia in type 2 diabetes, while rare, may be higher among the oldest patients and those who are cognitively impaired.
5. Certain patients with significant co-morbid disease may not be appropriate candidates for tight control.
6. Careful selection of elderly patients for aggressive glycemic control will result in lower rates of diabetic complications and hypoglycemia.

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Evan M. Benjamin, MD, FACP, is director of the Division of Healthcare Quality at Baystate Medical Center and an assistant professor of medicine at Tufts University School of Medicine in Springfield, Mass.

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Case Study: Nondysphoric Depression in a Man With Type 2 Diabetes

Patrick J. Lustman, PhD; Marty L. Caudle, BS, PA-C; and Ray E. Clouse, MD

Presentation

R.A. is a 58-year-old married man seen by his primary physician for scheduled care of diabetes. Diagnosed 4 years ago with type 2 diabetes, he is mildly obese (5 feet, 11 inches, 218 lb, body mass index 30.4 kg/m²) and hypertensive (blood pressure 165/92 mmHg), but otherwise has no evidence of coronary heart disease or other complications of diabetes. He uses insulin and has insufficient control of hyperglycemia (recent hemoglobin A_{1c} [A1C] concentrations range from 10 to 11.5%). He does not perform blood glucose testing.

Six months ago, the patient started having difficulty falling and staying asleep. As a result, he felt tired and fatigued most of the time. He became less physically active, stopped exercising, and gained 12 lb. Then he gradually stopped socializing and eventually lost interest in most things, including sexual activity. During this time, he earnestly denied feeling sad or depressed. He has continued to work but has trouble concentrating, frequently forgets things, and feels impatient, irritable, and frustrated. For the past month, the constella-

tion of symptoms has been persistent and interfering.

Physical examination was remarkable only for mild obesity. Routine laboratory and CT scan of the head were normal. R.A. was treated with alprazolam (Xanax), 0.25 mg at bedtime, which relieved the insomnia but had no effect on his other symptoms.

Questions

1. Can a diagnosis of depression be established?
2. Which treatment would be effective for R.A.?
3. What are the potential benefits of depression treatment?

Commentary

Can a diagnosis of depression be established?

The diagnosis of depression, or major depressive disorder, can be established even though, as in the case of R.A., the patient does not feel depressed, sad, or blue. Loss of interest or pleasure can serve as the major criterion for a depression diagnosis as long as at least four

other defining symptoms are present (significant weight loss or gain, hypersomnia or insomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt, impaired concentration or indecisiveness, and recurrent thoughts of death or suicide). The symptoms must occur together, be severe, and persist daily over a period of at least 2 weeks. Applying these criteria, R.A. qualifies for a diagnosis of depression.

Depression without sadness, or nondysphoric depression (NDD), occurs more often in men than women and more often in those who are medically ill than in those who are not. Irritability, social withdrawal, and indecisiveness often figure prominently in the clinical presentation. While patients are likely to acknowledge these symptoms, they may resist considering the possibility of being depressed given the absence of sadness. In these situations, it can be useful to include the spouse, other family members, or significant others in the clinical interview to help identify existing affective symptoms and the degree of their interference with patients' usual func-

tioning.

The link between diabetes and depression has been extensively studied. Diabetes doubles the likelihood of comorbid depression, making it present in ~20% of patients with type 1 or type 2 diabetes. This psychiatric illness is associated with hyperglycemia and an increased risk for all complications of the metabolic disorder. The risk for coronary heart disease is three times greater in depressed than in nondepressed diabetic women. The subset of depressed diabetic patients with NDD has not been systematically studied, but irritability, a seminal feature of NDD, is associated with abnormalities in glucose metabolism. Of interest, many of the adverse effects of affective illness on the course of diabetes, including poor treatment compliance and hyperglycemia, were evident in R.A.

Which treatment would be effective for R.A.?

Evidence from recent controlled trials indicates that depression in diabetic patients can be treated effectively with conventional antidepressant medications or with cognitive behavior therapy (CBT). Improvement in depression by either approach often produces reductions in A1C test results of 0.5–1.2%. CBT is a particularly potent approach and is recommended for patients who are receptive to counseling and have adequate insurance or find it affordable. Counseling can be especially useful in helping patients impaired by diabetes complications develop effective coping strategies.

Conventional tricyclic antidepressants (TCAs; e.g., amitriptyline [Elavil] and nortriptyline [Pamelor]) and newer antidepressants such as the serotonin reuptake inhibitors (SSRIs; paroxetine [Paxil], fluoxetine [Prozac], and sertraline [Zoloft]) have equivalent efficacy, relieving depression in 50–60% of patients who complete 8–16 weeks of therapy. Antidepressant selection is based on such factors as presenting

symptoms, concomitant medical conditions, drug interactions, and side effects. The potential for direct drug effects on glucose should also be considered and monitored. The available data suggest that the TCAs may induce mild hyperglycemia, whereas the SSRIs have an opposite effect. Consequently, the SSRIs and other contemporary antidepressants (such as nefazodone [Serzone] and venlafaxine [Effexor]) comprise the first-line pharmacotherapy for depression in diabetic patients. The TCAs, alone or in combination with a newer agent, may be favored when pain is a predominant complaint.

In all cases, it is important to set reasonable goals. Depression is rarely cured. Without specific antidepressant treatment, individual episodes do not rapidly remit and are not responsive to efforts focused solely on improving glycemic control. And although depression is acutely responsive to treatment, the disorder is highly recurrent. Afflicted patients suffer on average one episode annually throughout their lifetimes.

What are the potential benefits of depression treatment?

The benefits of depression management go beyond improved mood. Successful treatment produces a number of ancillary benefits, including restoration of normal sleep, pain relief and improved pain tolerance, decreased somatic preoccupation, enhanced sexual function, and improved illness coping and general functioning. Finally, relief of depression is associated with behavioral activation (increased social, occupational, and physical activity), improved compliance with diabetes treatment, and clinically significant improvements in glycemic control.

Clinical Pearls

1. Diabetes doubles the risk for depression, a psychiatric disorder that can be diagnosed in the absence of sadness. Loss of interest (including social withdrawal) and irritability are

prominent features of this nondysphoric presentation of depression.

2. Pharmacotherapy and counseling are viable treatment options. Depression in diabetes is a chronic condition; recurrent episodes requiring treatment are the norm, not the exception.
3. Restoring mental health improves glycemic control and has ancillary beneficial effects on sleep, appetite, mentation, and physical, social, and sexual functioning.

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Patrick J. Lustman, PhD, is a professor of medical psychology in the Department of Psychiatry; Marty L. Caudle, BS, PA-C, is a clinical research supervisor in the Department of Psychiatry; and Ray E. Clouse, MD, is a professor of medicine and psychiatry in the Department of Medicine, Division of Gastroenterology, at Washington University School of Medicine in St. Louis, Mo. Dr. Lustman is also a counseling psychologist at the Department of Veterans Affairs Medical Center in St. Louis.