Diabetes Management:
A case scenario

John Hickner, MD, MSc
Chairman, Family Medicine
Vice-Chair for Research
Medicine Institute
Cleveland Clinic

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Which is most important in preventing cardiovascular morbidity and mortality in patients with type 2 diabetes mellitus?

• Control of blood pressure
• Control of blood sugar
• Control of lipids
• Stop smoking
Management of an Adult With Type 2 Diabetes With Antidiabetic Medications: A Case Scenario

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Patient History

• The patient is a 51 year old male that weighs 195 lbs with a BMI of 29.5 kg/m² and a history of hypertension and dyslipidemia.

• He has a family history of type 2 diabetes, coronary artery disease (CAD) and renal insufficiency. He is currently asymptomatic.

• The review of systems reveals polyuria and nocturia, generally twice during the night, for the past two months.

• He experienced weight gain for the past several years, but has lost about 5 pounds in the last month.

• Current medication regimen includes simvastatin 40 mg po daily and metoprolol 50 mg po daily.
Physical Examination

- Eyes: No retinal changes
- Blood pressure: 130/85 mm Hg
- Heart rate: 65 bpm
- Lungs: Clear to auscultation
- Heart: Normal heart sounds
- Neurologic exam: Normal except for mild, symmetric diminution of sensation in the toes by monofilament examination

Laboratory Tests

- Fasting blood sample reveal the following
  - Normal serum chemistries
  - Creatinine 1.0 mg/dL
  - Normal liver functions
  - Normal blood counts
  - LDL-C 105 mg/dl
  - HDL 33 mg/dL
  - Triglycerides 170 mg/dL
  - Fasting blood glucose is 245 mg/dL and HbA1c is 8.8%
  - Urinalysis shows trace proteinuria
Clinical Decision

Does this patient meet the criteria for a diagnosis of type 2 diabetes?

A. No
B. Yes

Clinical Decision: Treatment

In addition to diabetes education, and advice regarding diet, exercise, and weight management, would you prescribe an antidiabetic medication?

A. No
B. Yes
Management of HbA1c, Adult With Type 2 DM

When making a reasonable clinical decision regarding the initiation of treatment with an antidiabetic medication, what evidence about the management of HbA1c is most accurate?

A. Any of the oral antidiabetic agents can be used, because all are equally efficacious as monotherapy in lowering the HbA1c levels.

B. One of the following should be used because they have the greatest (and about equal) efficacy at lowering HbA1c as monotherapy: metformin, pioglitazone, a second-generation sulfonylurea, or repaglinide.

C. One of the following should be used because they have the greatest (and about equal) efficacy at lowering HbA1c as a monotherapy agent: acarbose, sitagliptin, saxagliptin, nateglinide.

D. Insulin therapy would be preferable to an oral antidiabetic agent to initiate treatment of this patient.

Patient Discussion

• You discuss with the patient the pros and cons of initiating treatment with an oral antidiabetic medication

• The patient asks about the source of the information that you have given him, and you explain it is a summary of a large analysis done at a university that included many studies on the benefits and adverse effects of the currently available antidiabetic agents either alone or in different two-drug combinations.

• This information was summarized in a way that would allow patients to make decisions with their doctors regarding their course of treatment.
Risk Reduction With Glycemic Control

You explain that current research shows there is good evidence that achieving excellent glycemic control (an HbA1c of 7%) may offer him:

A. Reduced risk of mortality
B. Reduced risk of nonfatal myocardial infarction
C. Reduced risk of diabetes-related hospitalizations
D. Reduced risk of microvascular complications of diabetes
E. All the above

Treatment Decision

In addition to lifestyle interventions, what is the best choice for the first antidiabetic drug in this patient’s treatment?

A. Acarbose
B. Sitagliptin
C. Repaglinide
D. Metformin
Treatment Decision: Benefits Associated With Metformin Monotherapy

Compared to monotherapy with other antidiabetic medications, the benefits of using metformin may include:

A. Lowering HbA1c by about 1 absolute percentage point
B. Reducing or maintaining body weight
C. Decreased LDL levels
D. Decreased triglyceride levels
E. All the above

Treatment Decision: Adverse Effects Associated With Metformin Monotherapy

While reviewing the consumer research review, the patient asks about possible side effects of taking metformin. You tell him that the most important adverse effect of metformin is:

A. Marked weight gain
B. Unpredictable episodes of hypoglycemia
C. Gastrointestinal upset
D. Hip and nonhip fractures
E. Severe lactic acidosis
Patient Discussion: Informed Decision making

To help the patient make an informed decision about starting metformin, you:

A. Tell the patient about the evidence of the benefits and adverse effects for metformin.
B. Discuss the evidence in light of the patient’s personal medical history, current lab results, and examination findings.
C. Discuss the impact that starting metformin would have on the patient’s lifestyle, ensuring that the patient would adhere to the regimen.
D. Discuss the cost of the medication and the impact the additional cost might have on the patient, ensuring that the cost of the medication might not impact adherence.
E. Discuss the likelihood of benefits and adverse effects, and incorporate his personal preferences into weighing the individual benefits and risks when agreeing on this course of action.
F. All of the above.

Patient Discussion: Other Treatment Options

The patient says he has heard that pioglitazone has additional benefits that could reduce his risks of cardiovascular complications to a greater extent than metformin, so why not prescribe pioglitazone for him? You tell him:

A. While pioglitazone may have some beneficial effects on the lipid profile (specifically in lowering triglycerides), there is no strong evidence for protection against adverse cardiovascular events.
B. Metformin tends to decrease LDL-C, a known risk factor for atherosclerosis progression, to a greater extent than pioglitazone.
C. Pioglitazone might make him gain weight, while metformin would tend to make him lose a little weight.
D. All of the above.
During the discussion about the possibility of initiating oral drug therapy with pioglitazone rather than metformin, the patient points out that his father achieved excellent glycemic control with rosiglitazone.

However, he is confused and somewhat concerned that his father’s physician asked him last year to discontinue rosiglitazone and switch to pioglitazone.

In response to this discussion about thiazolidinediones you review the evidence from the clinician research summary titled Comparing Medication for Adults With Type 2 Diabetes and tell him:

A. Pioglitazone is preferred to rosiglitazone because it achieves greater glucose lowering.

B. Rosiglitazone may be associated with increased risk of myocardial infarction.

C. There are no differences between rosiglitazone and pioglitazone with respect to efficacy or adverse effects, but pioglitazone is more expensive.

D. Rosiglitazone is associated with a higher incidence of liver function abnormalities.
Patient Discussion: Initiating Treatment

• After considering all the facts, the patient agrees to:
  – Follow dietary advice
  – Follow an exercise program
  – Start metformin at a dose of 500 mg twice daily
  – Contact you if he has any adverse effects before discontinuing the medication

• You send him home with the consumer research review titled “Medicines for Type 2 Diabetes: A Review of the Research for Adults” as a reference tool and advise him to call if he starts experiencing any side effects.

Patient Followup: Unsuccessful Glycemic Control

• After four weeks, he reports no symptoms of gastrointestinal upset, but his fasting blood glucose levels (monitored at home) are not satisfactory, so you ask him to increase the dose of metformin to 1000 mg twice daily.

• Three months later, at his next office visit, his HbA1c level is 7.4%.

• The patient states he has been compliant with the diet, exercise and drug prescriptions, and has lost 6 pounds of body weight.
Clinical Decision: Unsuccessful Glycemic Control

As a result of this follow-up visit, how do you decide to proceed?

A. Do nothing further, because the HbA1c level may decrease further with the current regime
B. Recommend switching metformin to glyburide
C. Recommend switching metformin to pioglitazone
D. Recommend switching metformin to sitagliptin
E. Add glyburide, pioglitazone, or sitagliptin to metformin

Patient Discussion: Addition of Pioglitazone

• You counsel him to take the consumer research review home to share with his family, refer to it from time to time to remind him why he’s taking the drugs, and refer to it for descriptions of the adverse effects.

• After this discussion, you and your patient determine that the likelihood of attaining an HbA1c of 7% and the attendant lowering of risk of microvascular complications are worth the increased risk of side effects from adding additional drugs.

• After further discussion that includes consideration of the “tiers” of pharmacy approval through his insurance company, his understanding of the side effects of each agent, and cost, the decision is made to add 15 mg pioglitazone daily to his regime, while continuing metformin at 1000 mg po daily.
**Patient Followup: Weight Gain From Pioglitazone**

- Six weeks later, he returns to your office with the complaint that he has gained about 4 pounds of body weight. There are no other complaints.

- You examine him and note that he has increased subcutaneous fat in the hip/buttock region, but no pitting edema in the lower extremities.

- There is no elevation of the jugular venous pulse or audible S3, and the lungs are clear.

**Adverse Effects Associated With Pioglitazone**

The most likely reason for the weight gain is:

A. Marked increase in appetite due to pioglitazone, leading to increased caloric intake.

B. Expansion of body adipose stores, more in the subcutaneous regions, due to the action of pioglitazone on adipocytes.

C. Heart failure that is difficult to detect on physical examination, requiring detailed cardiac imaging and function testing.

D. Increased muscle mass, especially in the proximal musculature, due to a growth hormone-like effect of pioglitazone.

E. A synergistic effect between pioglitazone and metformin that leads to increased adiposity.
You reassure the patient that his weight gain is not likely to be due to heart failure.

Explain to him that the thiazolidinedione mechanism may lead to fat depot expansion.

The patient’s HbA1c is now 6.8%, triglycerides 145 mg/dL, with no change in the other lipid parameters.

However, the patient is insistent that weight gain is interfering with his overall sense of well-being.

You then discuss with him the treatment options going forward. Which of the following lines of information do you use to help inform his decision?

A. Explain to him that many interventions that lower blood glucose may tend to make you gain some weight (except metformin) emphasizing that it is important to keep a strict diet in addition to the drug therapy.

B. Explain that he could be switched to a different combination, such as metformin + glyburide or metformin + sitagliptin, and would probably still achieve HbA1c of 7%, but there is no way to tell except to try the new combination for 3 months.

C. Other combination therapies may have a more favorable effect on his weight.

D. All of the above.
Informed Decision-making: Adverse Effects

Following discussion of the evidence, as well as considering cost and insurance coverage, the patient decides that he would like to try a combination of metformin + glyburide. You would explain to him that this change would increase the possibility of which adverse effect?

A. Marked weight gain
B. Photosensitive skin rash
C. Liver function abnormalities
D. Hypoglycemic episodes
E. Hypokalemia

Closing Remarks

• After discussing the potential benefits and the small risk of adverse effects, you decide to prescribe a combination of 1000 mg po daily metformin and 5 mg daily glyburide and schedule him a followup visit.

• After reviewing the consumer research review again with him, you remind him of the benefits and potential adverse effects of this combination of oral antidiabetic agents.

• Once he is comfortable with this decision, you remind him to refer to the consumer research review when he has questions regarding his treatment.

• In his next regularly scheduled visit, you will recheck the HbA1c level and lipid levels, review his home blood glucose measurements, and ask him about any symptoms and any further questions he may have.
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