Management of Hyperglycemia in Type 2 Diabetes:
A Patient-Centered Approach

SELF-ASSESSMENT PROGRAM

(FOR REFERENCE ONLY)

The content of this program is based on the Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

This program is intended to measure baseline knowledge; therefore, there is not a mandatory pre-requisite for participating in this program.

Target Audiences:
All health care professionals involved in treating individuals with diabetes, including physicians, family physicians, physician assistants, nurses, dietitians, pharmacists, and other health care professionals.

Learning Objectives:

Upon completion of this self-assessment program participants should be able to:

1. Discuss the pathophysiology and disease progression of diabetes
2. Identify the best treatment pharmacotherapy strategy for patients with hyperglycemia
3. Apply appropriate treatment strategies for patients with diabetes and hyperglycemia
4. Incorporate treatment strategies to minimize and manage hypoglycemia in patients with type 2 diabetes on insulin
5. Utilize the guidelines for management of diabetes in order to achieve lower A1C levels and reduce the risk of hyperglycemia
6. Avoid adverse outcomes associated with hyperglycemia and hypoglycemia
Single Statement Multiple Choice Questions

1. More stringent hyperglycemia management (target A1C 6-6.5%) in type 2 diabetes might be supported by which one of the following factors.
   A. Long-standing disease duration
   B. Moderate-severe vascular complications
   C. Shorter life expectancy
   D. Absent-few comorbidities

CORRECT ANSWER: D

Rationale

In 2008, the American Diabetes Association, the American Heart Association and the American College of Cardiology, released a joint position statement providing clarified guidance for determining individualized A1C targets based upon analysis of findings from the ACCORD, ADVANCE and VADT studies. Ismail-Beigi, et al. further reiterated the importance of utilizing these elements of decision-making when determining appropriate individualized glycemic targets. Some factors favor more stringent efforts to lower A1C, while others favor less stringent efforts. Patient elements that favor more stringent pursuit of lower A1C are: high motivation, excellent self-care capabilities, and adherent patients attitudes and efforts; low potential for risks associated with hypoglycemia or other adverse effects; newly diagnosed disease stage; long life expectancy; absent-few/mild important comorbidities; absent-few-mild established vascular complication; and readily available resources and support system.

References


2. During the United Kingdom Prospective Diabetes Study (UKPDS), patients with type 2 diabetes were assigned to the intensive treatment arm (received a sulfonylurea or insulin, or metformin if overweight) or a conventional treatment arm (dietary interventions only). In the intensive treatment arm, which one of the following benefits became apparent only
when a 10-year follow-up study was conducted?

A. Reduced risk of microvascular complications
B. Clinically lower overall BMI
C. Reduced risk of myocardial infarction
D. Lower overall mean A1C

CORRECT ANSWER: C

Rationale

The United Kingdom Prospective Diabetes Study (UKPDS) was designed to assess whether intensive blood-glucose control would impact not only microvascular, but also macrovascular complications in patients with type 2 diabetes. All participants (N=5102) received 3 months of dietary therapy. At the 3-month mark, those who had fasting plasma glucoses of 110-270 mg/dL (N=3867) were randomly assigned to either continue with the dietary therapy or receive more intense glycemic control (either a sulfonyurea or insulin, or in overweight individuals, metformin).

Differences in outcomes between the dietary therapy only group and the intensive treatment group were assessed through three aggregate endpoints: any diabetes-related endpoint, diabetes-related death, and all-cause mortality. The intensive regimen group had lower overall mean A1C, 12% lower risk for any diabetes-related endpoint (in this aggregate, a significant portion was due to a 25% risk reduction in microvascular endpoints), 10% lower risk for diabetes related-death, and a 6% lower risk for all-cause mortality. When compared to the dietary therapy only group, patients in the intensive treatment arm had significantly greater weight gain.

While there was a reduction in nonfatal MIs, fatal MIs, or sudden death, at that time it was concluded that intensive blood glucose control in patients with type 2 diabetes resulted in decreased risk of microvascular, but not macrovascular complications. Patient participants were followed for a 10-year period to assess the durability of the risk reductions. Although differences in A1C were lost, the risk reduction in microvascular complications was maintained. Over the 10-year period risk reductions for myocardial infarction and death from any cause emerged.

References


3. Based upon a meta-analysis of cardiovascular outcomes in type 2 diabetes studies, findings suggest that a 15% relative risk reduction in nonfatal myocardial infarcts is associated with an A1C reduction of approximately:
   A. .50%
   B. 1.0%
   C. 1.5%
   D. 2.0%
CORRECT ANSWER: B
Rationale
A meta-analysis of cardiac outcomes in the Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation (ADVANCE) and Veteran Affairs Diabetes Trial (VADT) found every approximate 1% A1C reduction was positively correlated with a 15% relative risk reduction for myocardial infarct. The A1C benefits did not extend to stroke or all-cause mortality.
References

4. In the fasting state, hyperglycemia is directly related to:
   A. Increased hepatic glucose production
   B. Defective insulin stimulation of target tissue glucose disposal
   C. Decreased adipocyte lipolysis
   D. Loss of pancreatic α-cell functionality
CORRECT ANSWER: A
Rationale
Hyperglycemia is caused by a number of factors. Increased hepatic glucose production is the primary mechanism in the fasting state. In type 2 diabetes, while the islet β-cells are still able to produce insulin, they are producing relatively insufficient amounts for the degree of insulin insensitivity. In the postprandial state, insufficient suppression of hepatic glucose production as well as decreased insulin stimulated glucose uptake at the target tissues (primarily skeletal muscle) lead to increased plasma glucose. In type 2 diabetes, pancreatic α-cell functionality also changes to a hypersecretory state of glucagon release, leading to further hepatic glucose production. Adipocyte lipolysis generates free fatty acids, which contribute to gluconeogenesis.
References


5. Which of the following is the correct diagnostic cut-point for diabetes?
   
   A. A1C ≥ 7%
   
   B. Fasting plasma glucose (FPG) ≥ 130 mg/dL
   
   C. 2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test
   
   D. Random plasma glucose ≥ 300mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis
   
   CORRECT ANSWER: C

Rationale

Patients who meet one or more of the following criteria meet the diagnostic cut-point for Types 2 Diabetes:

- A1C ≥ 6.5%
- Fasting plasma glucose (FPG) ≥ 126 mg/dL
- 2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test
- Random plasma glucose ≥ 200mg/dL in a patient with classic symptoms of hyperglycemia hyperglycemic crisis.

The diagnostic test results should be confirmed by a repeat test, unless clinical picture clearly supports the diagnosis.

References


6. The American Diabetes Association recommends many non-pregnant adults with type 2 diabetes work to achieve an A1C ≤ 7%. Which one of the following glycemic patterns would support this goal?

   A. Fasting glucose <70, postprandial glucose<140, mean plasma glucose<120-140
   
   B. Fasting glucose <126, postprandial glucose<200, mean plasma glucose<180
   
   C. Fasting glucose <130, postprandial glucose<180, mean plasma glucose<150 -160
The American Diabetes Association recommends the following glycemic targets for most adult, non-pregnant individuals with type 2 diabetes:

- Fasting glucose < 130
- Postprandial glucose < 180
- Mean plasma glucose < 150-160
- A1C ≤ 7%

Goals should be individualized based upon specific patient considerations and may be adjusted to more-or-less stringent goals.

References

7. **Less-stringent A1C goals (7.5 – 8.0%) may be acceptable in certain individuals with type 2 diabetes. Which factor(s) support less stringent goals?**

A. Limited life expectancy
B. History of severe hypoglycemia
C. Multiple comorbidities
D. All of the above

CORRECT ANSWERS: D

Rationale
In 2008, the American Diabetes Association, the American Heart Association and the American College of Cardiology, based upon analysis of findings from the ACCORD, ADVANCE and VADT studies, released a joint position statement providing clarified guidance for determining individualized A1C targets that reiterated the importance of considering these factors when determining appropriate individualized glycemic targets. Some factors favor more stringent efforts to lower A1C, while others favor less stringent efforts (Table 1).

Table 1. Patient Characteristics that Inform More or Less Stringent A1C Targets

<table>
<thead>
<tr>
<th>MORE STRINGENT EFFORTS</th>
<th>LESS STRINGENT EFFORTS (A1C ≤ 7.5 to 8.0%)</th>
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### (A1C ≤ 7%)

- Highly motivated
- Excellent diabetes self-care
- Adherent to treatment plan
- Relatively healthy
- Low risk for hypoglycemia and other adverse effects
- Newly diagnosed
- Long life expectancy
- Few/mild comorbidities
- Absent/few/mild vascular complications
- Has support/resources

### Low motivation

- Poor diabetes self-care
- Poor adherence to treatment plan
- Frail or with additional conditions
- High risk for hypoglycemia and other adverse effects
- Long-standing disease duration
- Short life expectancy
- Many/severe comorbidities
- Many/severe vascular complications
- Limited support/resources

### References


8. Weight loss has been shown to have a positive impact on glucose control and cardiovascular risk factors. At which weight loss threshold do these positive benefits start to become meaningfully apparent?

   A. Weight reduction of 0-4%
   B. Weight reduction of 5-10%
   C. Weight reduction of 11-15%
   D. Weight reduction of 16-20%

   CORRECT ANSWER: B

### Rationale

Modest weight loss of 5-10% has been shown to positively influence glucose control and
cardiovascular risk factors. Weight loss may be through dietary, pharmacological or surgical means.

**References**


9. **Clinicians treating patients with type 2 diabetes should include lifestyle interventions when developing diabetes management plans. Which of the following is NOT appropriate?**

A. Weight reduction if necessary

B. A minimum of 150 minutes/week of moderate activity (aerobic, resistance training, flexibility)

C. General diabetes education

D. A high-fiber, low-fat diet

E. A high-energy, high-protein, low-fat diet

**CORRECT ANSWER: E**

**Rationale**

All patients with diabetes should participate in a diabetes education program with ongoing support. Lifestyle interventions are a key component of type 2 diabetes management and should address dietary intake and activity levels. Both should be adjusted for individual patient needs. Weight reduction has been shown to improve glycemic control as well as improve cardiovascular risk factors. Physical activity promotes weight loss/maintenance as well as having beneficial effects on lipid profiles, carbohydrate metabolism and insulin sensitivity. Dietary modification should emphasize high-fiber, low-fat foods and minimize high-energy foods such as those high in saturated fats, cholesterol or sugar. Dietary protein intake should be moderated in individuals with proteinuria and diabetic nephropathy.

**References**


For Questions 10-13, please refer to the graph below and indicate the parameter that best
describes each curve.

Figure 1. The Natural Progression of Uncontrolled Hyperglycemia

10. Please refer to the graph below and indicate the parameter that best describes Curve 1.
   A. Insulin Secretion
   B. Postprandial glucose
   C. Fasting glucose
   D. Insulin Resistance

   CORRECT ANSWER: B

11. Please refer to the graph below and indicate the parameter that best describes Curve 2.
   A. Insulin Secretion
   B. Postprandial glucose
   C. Fasting glucose
   D. Insulin Resistance

   CORRECT ANSWER: C

12. Please refer to the graph below and indicate the parameter that best describes Curve 3.
A. Insulin Secretion
B. Postprandial glucose
C. Fasting glucose
D. Insulin Resistance

CORRECT ANSWER: D

13. Please refer to the graph below and indicate the parameter that best describes Curve 4.

A. Insulin Secretion
B. Postprandial glucose
C. Fasting glucose
D. Insulin Resistance

CORRECT ANSWER: A

Rationale
Generally, type 2 diabetes is characterized by increasing insulin resistance at target tissues, although the underlying reasons for this increasing resistance are not yet well understood. Insulin-dependent process, such as glucose uptake by peripheral tissues, inhibition of hepatic gluconeogenesis and inhibition of lipolysis are all impaired, leading to elevated plasma glucose. Initially, the β-cells are able to secrete enough insulin to compensate for this hyperglycemia and insulin levels at this time may appear normal to elevated (hyperinsulinemia). However, progressive β-cell insulin secretory loss, the driving force in the progression from normal glucose tolerance to IGT to frank type 2 diabetes, eventually occurs leading to postprandial hyperglycemia and further loss of β-cell functionality. The underlying cause of this loss is uncertain, but is most likely a combination of environmental/genetic factors and functional and anatomic defects, but interventions that improve glycemia can help offset the degree of β-cell dysfunction. Hepatic glucose production also increases due to increased pancreatic α-cell glucagon secretion. Eventually, the combination of increasing resistance, increasing hepatic glucose production and decreasing insulin secretion lead to fasting hyperglycemia as well as postprandial hyperglycemia.

References


Inzucchi S, Sherwin R. Type 2 Diabetes Mellitus. In: Goldman’s Cecil Medicine, 24th ed.
14. The development of type 2 diabetes is multifactorial. All of the following are thought to play a role in the development EXCEPT:

A. Genetics
B. Environmental factors
C. Elevated circulating free fatty acid levels
D. Pancreatic α-cell defects
E. Increased skeletal GLUT4 glucose transporters translocation capacity

CORRECT ANSWER: E

Rationale
Insulin resistance in thought to be multifactorial. While it appears that the insulin receptor may be defective in some type 2 diabetes individuals, distal post-receptor pathways are thought to play a significant role. One element of this is the decreased capacity for translocation of GLUT4 the muscle/fat cell surface. GLUT4 is contained in intracellular membrane vesicles that move to the cell surface under the presence of insulin. GLUT4 transporters are responsible for facilitating the facultative movement of glucose from outside to inside the cell cytoplasm where the glucose is then phosphorylated.

References


15. Please select the drug class that best fits the description. Each drug class can only be used once.

A. Biguanides
B. Sulfonylureas
C. Meglitinides

Thiazolidinediones

This drug class should be used with caution in patients at risk for lactic acidosis. ______
This drug class is the oldest oral agent and stimulates insulin release. _____

This shorter-acting insulin secretagogue may be associated with less hypoglycemia than the other secretagogues. _____

16. This drug class decreases hepatic glucose production and increases skeletal muscle insulin sensitivity. While one drug in this class may decrease the risk of myocardial infarct, the other drug is used very infrequently due to an associated increased risk of myocardial infarct. _____

Answer: A, B, C, D

References


17. Please select the drug class that best fits the description. Each drug class can only be used once.

A. α-glucosidase inhibitors
B. DPP-4 inhibitors
C. Bile Acid sequestrants
D. Dopamine-2 agonists

This oral drug class slows the intestinal digestion and absorption of carbohydrates. _____

The compound Bromocriptine belongs to this class and at this time, it is only available in the U.S. for use as an antihyperglycemics. Its mechanism of action and role in decreasing glucose levels is unclear. _____

This oral drug class focuses on the incretin system and its use leads to increased postprandial GLP-1 and G1P levels. _____

This drug class is infrequently used in the U.S. and Europe. Studies suggest this drug class may modulate FXR- and TGR5-mediated pathways involved in glucose homeostasis. One of its disadvantages is that it may decrease the absorption of other medications. _____
ANSWER: A, D, B, C

References


18. Please select the drug class that best fits the description. Each drug class can only be used once.

A. GLP-1 receptor agonists

B. Amylin mimetics

C. Insulin

This class of drugs is typically reserved for individuals with Type 1 Diabetes or others receiving intensive insulin therapy. It inhibits glucagon secretion and slows gastric emptying. _____

This injectable drug class focuses on the incretin system and leads to increased insulin secretion, decreased glucagon secretion and slowed gastric emptying. One of its advantages is that its use can lead to weight loss. _____

This drug class is universally effective at reducing plasma glucose levels. _____

Answer: B, A, C

References


What physiological feature puts East Asians at increased risk for type 2 diabetes?

F. Greater insulin resistance
G. Lower levels of endogenous incretins
H. Increased β-cell dysfunction
I. Increased incidence of dyslipidemias

CORRECT ANSWER: C

Rationale

The risk of developing TYPE 2 DIABETES is increased in some racial/ethnic groups. East Asians experience more β-cell dysfunction and Latinos experience greater insulin resistance. However, there have not been many studies conducted to evaluate matching the optimal treatment approach to these characteristics.

According to the CDC “many researchers think that some African Americans, Hispanic/Latino Americans, American Indians, Asian Americans, and Pacific Islander Americans inherited a ‘thrifty gene’ which helped their ancestors store food energy better during times when food was plentiful, to survive during times when food was scarce. Now that ‘feast or famine’ situations rarely occur for most people in the United States, the gene which was once helpful may now put these groups at a higher risk for type 2 diabetes.”

References


19. According to the Standards of Medical Care in Diabetes- 2013, the use of which medication class(es) place asymptomatic patients at increased risk of developing type 2 diabetes and are an additional indication for diabetes screening?

A. Atypical antipsychotics
B. Glucocorticoids
C. Both A and B
D. Neither A nor B

CORRECT ANSWER: C.
**Rationale**

The use of certain medications, such as atypical antipsychotics and glucocorticoids, put patients at increased risk of developing type 2 diabetes. Hyperglycemia, in patients with known or unknown diabetes, is a known side effect of glucocorticoid use. A recent study concluded that the use of atypical antipsychotics in older adults (>65 years) for conditions other than bipolar disorder or schizophrenia, was associated with increased initiation of antidiabetic medications.

**References**


**20. According to available evidence, which of the following is a treatment strategy for the delay or prevention of macrovascular complications?**

A. Antiplatelet therapy  
B. Blood pressure management  
C. Glycemic control ≤ 7% (individualized for patients)  
D. Smoking cessation  
E. Lipid management  
F. All of the above

**CORRECT ANSWER: F**

**Rationale**

All of these factors contribute to the prevention or delay of macrovascular complications.
Studies (Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation (ADVANCE) and Veteran Affairs Diabetes Trial (VADT) have found glycemic control (as measured by A1C) is an important component in the prevention of microvascular complications. In addition, for most non-pregnant adults, glycemic control (A1C≤7%) early in diabetes disease course has been associated with a reduction in macrovascular complications. Diabetes is considered to be a risk factor for atherosclerosis, independent of other cardiovascular risk factors such as hypertension, dyslipidemia and smoking. It has been suggested that in a diabetic state, insulin induces pathogenetic changes such as: increased synthesis of atherogenic factors (endothelin and plasminogen activator inhibitor), increased expression of insulin-like growth factor-1 and insulin induced stimulation of vascular endothelial and smooth muscle cells. Other risk factors should be addressed as they apply to individual patients. Current recommendations are:

- Blood Pressure < 130/80 mmHg
- Lipids: LDL<100 mg/dL (no overt CVD)
- LDL<70 mg/dL (overt CVD)
- HDL>40 mg/dL (males), HDL>50 mg/dL (females)
- TG<150 mg/dL
- Smoking cessation
- Low-dose aspirin (75-162 mg/day) for diabetic patients with increased cardiovascular risk.

References


21. **Hypoglycemia is a potential side effect of which of the following classes of drugs?**

   A. Insulins
   B. Sulfonylureas
   C. Meglitinides
   D. Amylin mimetics
   E. All of the above

   **CORRECT ANSWERS: E**

**Rationale**
These four drug classes can lead to hypoglycemia. Insulin works by activating the insulin receptors, leading to increased glucose uptake at peripheral tissues and decreased hepatic glucose production. The Sulfonylureas and Meglitinides are both secretagogues. They work by closing the pancreatic β-cell plasma membrane K_{ATP} channels, leading to an increase in insulin secretion. Amylin mimetics act as agonist and activate the amylin receptors leading to decreased glucagon secretion and slowed gastric emptying (their use requires decreased insulin dose adjustments). All of these four drug classes can lead to hypoglycemia.

References


22. The United Kingdom Prospective Diabetes Study early results data suggested metformin conferred greater cardiovascular benefits to the overweight diabetic participants than dietary interventions alone. All of the following were observed for the metformin group EXCEPT:

A. a relative risk reduction for myocardial infarction of 39%.
B. a relative risk reduction for all-cause mortality of 36%.
C. a relative risk reduction for diabetes related death of 42%.
D. an overall mean A1C reduction of 1.5%.

CORRECT ANSWER: D

Rationale

Overall, participants in this study who received metformin, as opposed to only dietary interventions, had significantly fewer MIs, all-cause and diabetes related death events. However, the overall mean A1C reduction was only 0.6%. Subsequent follow-up of this cohort demonstrated that A1C differences were lost after the first year of follow-up. At the 10-year follow-up, relative risk reductions, while lower, were still significant.

References


Brief Clinical Scenarios
23. A 34-year old female presents to your office for a new patient visit. Her medical history is positive for gestational diabetes mellitus (GDM). The Diabetes Prevention Program Research Group found that implementing intensive lifestyle modifications and prescribing metformin resulted in an equivalent risk reduction of developing diabetes by:

A. 15%
B. 25%
C. 50%
D. 65%

CORRECT ANSWER: C

Rationale
A past history of GDM is considered a significant risk factor for the development of diabetes, in particular, type 2. The Diabetes Prevention Program (DPP) was a large prospective study that examined the impact of intensive lifestyle interventions or metformin therapy on the development of type 2 diabetes for individuals with impaired glucose tolerance. Participants were assigned either to a placebo, metformin or intensive lifestyle intervention group. Ratner, et al. (2008) conducted an analysis of the women enrolled in the DPP; parous women, with or without a history of GDM. Women, with a history of GDM, who received intensive lifestyle interventions or metformin therapy showed a 50% reduction in the incidence of diabetes compared to the placebo group. Women, with no history of GDM, who received intensive lifestyle interventions or metformin therapy showed 49% (ILS) and 14%(metformin) reductions in the incidence of diabetes compared to the placebo group. The authors concluded that both intensive lifestyle interventions and metformin therapy confer significant benefit in delaying or preventing the development of diabetes in women with a history of GDM or IGT.

References


24. A 78-year old patient with a 15-year history of type 2 diabetes arrives in your office for a check-up. He suffers from stage 3 chronic kidney disease and lives alone. From previous visits you have learned he has very few support services. What would be a realistic A1C treatment target for this individual?
A. A1C 6.0-6.5%
B. A1C 7.5-8.0%
C. A1C 8.5-10.0%
D. A1C 10.5-11%

CORRECT ANSWER: B

Rationale

Less-stringent A1C targets are acceptable in certain individuals, such as those with a history of severe hypoglycemia, extensive comorbidities/complications, limited life expectancy and difficulty achieving target A1c despite education, support and polypharmacy.

References


25. Your patient has been systematically titrating his basal insulin dose for the last 6 months; his daily dose is NPH .90 U/kg/day. Despite his good efforts you decide it would be prudent to add a prandial insulin dose to his treatment regimen. Which of the following scenarios might lead you to this conclusion?

A. A1C=7.4%, FPG<130 mg/dl, PPG>180 mg/dl
B. A1C=7.0%, FPG<130 mg/dl, PPG<180 mg/dl
C. A1C=7.0%, FPG<120mg/dl, PPG<160mg/dl
D. A1C=6.8%, FPG<120 mg/dl, PPG<160 mg/dl

CORRECT ANSWER: A

Rationale

Prandial insulin administration is meant to diminish the postprandial glucose elevations. The addition of prandial insulin to a patient’s diabetes management should be considered when the glycemic target of A1C<7.0%, FPG<130 mg/dl, PPG<180 mg/dl are not being met. These targets are general and should be individualized to each patient depending on their unique needs. Basal insulin doses are generally titrated with fasting plasma glucose levels, however as daily doses exceed .5 U/kg/day and get closer to 1.0U/kg/day, there is an increased likelihood that the addition of prandial insulin will become necessary.

References

26. A 72-year old patient arrives in your office complaining of shakiness and sweating before he went to bed the previous night. He doesn’t recall checking his blood glucose level at the time, however he felt better after a glass of milk and a few graham crackers. His current medications are metformin, pioglitazone and glyburide. Which one of the following medications is the most likely cause of his symptoms?

A. Metformin  
B. Pioglitazone  
C. Glyburide  

CORRECT ANSWER:  C  

**Rationale**

Dizziness and sweating are both signs of hypoglycemia (plasma glucose <70mg/dl). The risk of hypoglycemia due to antihyperglycemic medications increases exponentially with age. The sulfonylureas (glyburide is in this drug class), meglinitides, amylin mimetics and insulins can all cause hypoglycemia as a side effect. Glyburide is inexpensive and commonly used. However a systematic review comparing glyburide with other secretagogues/insulin (Gangji et al, 2007) found the risk and rates of hypoglycemia associated with its use are approximately 50% higher than with other sulfonylureas and other nonsulfonylurea secretagogues. Therefore, its use should be minimized. Metformin (a biguanide) and pioglitazone (a thiazolidinedione) do not cause hypoglycemia as a side effect. An alternative three-drug combination could substitute a meglinitide (while this drug class is a secretagogue, it is shorter-acting and is associated with less hypoglycemia that the sulfonylureas), DDP-4 Inhibitor or a GLP-1 receptor antagonist for the sulfonylurea. When patients are able to self-treat their hypoglycemia, generally 15-20 g of a quick-acting carbohydrate should raise the blood glucose by 15-20 mg/dl in approximately 15-20 minutes.

**References**


27. Your patient has been newly diagnosed with type 2 diabetes (A1C 7.7%) and you have prescribed metformin. Metformin should be titrated to minimize which side effect?

A. Rebound hyperglycemia
B. Reactive hypoglycemia
C. Weight gain
D. Gastrointestinal-side effects

CORRECT ANSWER: D

Rationale

If well tolerated and not contraindicated, metformin is considered the preferred first-line treatment for TYPE 2 DIABETES. While generally well tolerated, gastrointestinal side effects are considered a common problem unless metformin is titrated.

References


28. At her last visit, your patient’s labs showed a eGFR 55 ml/min/1.73 m². At this visit, her labs measured an eGFR of 44 ml/min/1.73 m². Dose reduction/cessation should be considered for all of the following agents EXCEPT:

A. Glyburide
B. Sitagliptin
C. Metformin
D. Pioglitazone

CORRECT ANSWER: D
Rationale

Moderate–severe renal functional impairment is common in type 2 diabetes, with a 20-30% prevalence of moderate-severe chronic kidney disease (CKD). Patient with impaired renal function are at increased risk of hypoglycemic events due to slower renal elimination of insulin, the incretin hormones and some antihyperglycemic medications. As a result, medications with renal excretion need to be evaluated for counterindications and undergo appropriate dosing adjustments or discontinuation. Antihyperglycemic medications that undergo renal clearance and should be avoided, used with caution or dose-adjusted are: metformin, most insulin secretagogues (except repaglinide and nateglinide), most dpp-4 inhibitors (except linagliptin, which is enterohepatically eliminated), the GLP-1 receptor agonists exenatide (liraglutide is not dependent on renal clearance, however its safety has not been established in CKD) and the insulins. Pioglitazone does not undergo renal elimination so there are not any limitations on its use (be aware that its use can lead to water retention in predisposed individuals).

References


29. A 42-year old patient was diagnosed with type 2 diabetes approximately one year ago and is currently taking metformin, a DPP-4 inhibitor, and a basal insulin dose (current daily dose .9 U/kg/day). Despite good compliance with her diet, exercise and medication regimen, she reports postprandial glucose measurements of usually about 190 mg/dL. Her current A1C is 7.6%. Which of the following changes in her management do you consider most important?

A. Add a sulfonylurea to her regimen
B. Increase her basal insulin dose
C. Add a pre-meal rapid-acting insulin
D. Discontinue her basal insulin dose and add a prandial insulin dose

CORRECT ANSWER: C

Rationale

While the ADA/EASD’s implementation strategies to pharmacologically achieve glycemic targets while minimizing side-effects, need to be individualized for each patient, a general progression exists. Assuming there are not any contraindications, metformin is the optimal first-line medication. Individualized A1c goals are assessed approximately every 3-6 months with additional drugs being added/adjusted as needed to achieve or the A1C goal (1-drug monotherapy, 2-drug combo therapy, 3-drug combo therapy, complex insulin strategies). After
a patient starts a basal insulin regimen they can self-titrate their insulin dosing to their pre-agreed fasting glucose goals. The American Diabetes Association recommends the following glycemic recommendations for most adult, nonpregnant individuals with TYPE 2 DIABETES. Fasting glucose <130, postprandial glucose<180, mean plasma glucose<150-160, A1C≤7%. When fasting glucose is at target, but postprandial glucose levels (PPG>180 mg/dL) and A1C remain above target, the addition of prandial insulin should be considered.

References


30. One of your patients is currently taking metformin, glyburide and an evening basal dose of insulin. After discussing how best to achieve better glycemic control, he has agreed to add a pre-meal insulin dose. Which modification should be made with the addition of the prandial dose?

A. Discontinue the glyburide
B. Discontinue the metformin
C. No modifications should be made
D. Discontinue the metformin, glyburide and evening insulin

CORRECT ANSWER: A

Rationale
Secretagogues should be discontinued with the addition of a prandial insulin dose. The secretagogues may be useful in conjunction with basal insulin by providing some protection against initial glycemic control deterioration. However, after insulin dosing is stabilized, even if the secretagogues do not provide any additional benefit on A1C reduction, their discontinuation will help decrease the risk of hypoglycemia or weight gain.

References
Inzucchi S, et al. Management of hyperglycemia in type 2 diabetes: A patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European
31. One of your patients is a 3-state regional salesman who has a fairly unpredictable work schedule. When he gets hungry while on the road, he tends to eat at the first restaurant he sees. For the past 3 months, he has managed his type 2 diabetes with metformin, glipizide and glargine. Despite this regimen, his current A1C is 7.8%. You are in agreement that he needs to add a bolus insulin dose to his regimen. Which type of insulin would be the most appropriate choice?

A. Rapid-acting insulin analogues
B. Premixed insulin
C. Long-acting insulin analogues
D. Intermediate-acting insulin

CORRECT ANSWER: A

Rationale

This patient would benefit from the addition of a prandial insulin dose with a shorter-acting insulin. While human regular insulin is generally less expensive, the rapid-acting insulin analogues (lispro, aspart, glulisine) result in better postprandial glycemic control than human regular insulin. These insulins can be added to the patient’s day in a graduated fashion, starting with the largest/highest carbohydrate meal, then the next largest and finally, the smallest meal. This approach allows self-monitored glucose results to guide the titrations to the appropriate dose. The long-acting and intermediate acting-insulins are generally used for basal insulin dosing. While a premixed insulin may be a more convenient and simpler choice (dosed before breakfast and before supper) than basal-bolus, it is not well suited to individuals who do not have a consistent and predictable lifestyle with regular timing of meals as delayed or missed meals raise the risk of hypoglycemia with these formulations.

References


32. A 41-year old patient with a BMI of 39 kg/m^2 returns for a follow-up visit 3 months after initiating metformin. She is highly sensitive to her weight and has tried to implement lifestyle modifications, but is finding it difficult to make any meaningful changes in her diet or exercise routines. Her current A1C is 7.7%, with a target goal A1C<7%. In addition to discussing consideration of bariatric surgery, which drug class might you add?

A. Thiazolidinedione  
B. Sulfonylurea  
C. DDP-4 inhibitor  
D. GLP-1 receptor agonist

CORRECT ANSWER: D

**Rationale**

Thiazolidinediones have been shown to be effective at improving insulin sensitivity, however their use can lead to an overall increase in body weight due to an increase in lower body fat secondary to adipocyte proliferation. Sulfonylureas are associated with weight gain as well. The use of metformin has been associated weight reduction/maintenance in heavier patients, DDP-4 inhibitors are considered weight neutral and GLP-1 receptor agonists are associated with weight loss, which can be significant in some patients. Bariatric surgery has been associated with a rapid and significant resolution of type 2 diabetes in severely obese individuals, with some individuals able to decrease or even discontinue their antihyperglycemic medications and may be considered in adults with type 2 diabetes and BMI>35 kg/m^2 with type 2 diabetes associated comorbidities or type 2 diabetes that is difficult to control with medications or lifestyle modifications. There is currently insufficient evidence to recommend bariatric surgery for those with a BMI of 30-35 kg/m^2, although small trials have demonstrated a benefit. Dietary modifications and increased physical activity are known to improve glycemic control, aid in weight loss and improve other cardiovascular risk factors.

**References**


33. Your 42-year old, overweight patient was diagnosed with type 2 diabetes (A1C 7.7%) five months ago. You discussed the diagnosis with him, prescribed metformin and provided lifestyle modification education resources. He missed his follow-up appointment, so you called him to schedule a return visit. At this appointment, he shares some of the positive lifestyle modifications he has made and that he has been taking his metformin consistently. He currently takes 2000 mg metformin per day. At this visit his A1C is 9.4%. All of the following are reasonable treatment options EXCEPT:

A. Metformin+ lifestyle modifications
B. Metformin + once-daily evening basal insulin dose + lifestyle modifications
C. Metformin + sulfonylurea+ lifestyle modifications
D. Metformin + GLP-1 receptor agonist + lifestyle modifications

CORRECT ANSWER: A

Rationale
According to ADA/EASD guidelines, once A1C≥9%, glycemic targets are hard to achieve with monotherapy. If, after approximately a 3-month treatment period, monotherapy does not achieve or maintain target A1C, a second oral agent, a GLP-1 receptor agonist or a basal insulin should be added. Adding a second agent is associated with an additional A1C reduction of 1%. A, B, and C are all acceptable 2-drug combinations. Additional education, support and more frequent follow-up would be warranted.

Reference

34. A 43-year old patient with a 2-year history of type 2 diabetes presents to your office for a follow-up visit. She is a highly motivated patient and doesn’t have any significant comorbidities, so together, you have set a target A1C≤ 6.5%. Her current medications are metformin and sulfonylurea. Despite her good efforts, her current A1C is 7.3%. You would like to add a third agent to her regimen, however she is concerned about any additional weight gain as she has gained a few pounds since starting the sulfonylurea. Which drug class would you add to minimize any additional weight gain?

A. Basal insulin
B. GLP-1 agonist
C. Thiazolidine
D. DPP-4 Inhibitor

CORRECT ANSWER: B

**Rationale**

The use of GLP-1 receptor agonist is associated with weight loss. Metformin is considered to be weight neutral and can also be associated with weight loss. DPP-4 inhibitors are considered weight neutral and the sulfonylureas, meglitinides and thiazolidinedione are associated with weight gain. All insulin and insulin analogues can lead to weight gain, however both insulin analogue detemir and insulin analogue glargine have been associated with less weight gain, compared to NPH, when used as basal insulin. Detemir causes the least amount of weight gain, followed by glargine. The mechanism for this is still not clearly understood. One 6-month study in individuals with type 2 diabetes receiving basal–bolus therapy, found insulin detemir was associated with a 0.4 kg weight gain vs 1.3 kg weight gain in patients receiving NPH insulin. A 24-week comparison of either NPH insulin or insulin detemir as an add-on therapy to oral agents in type 2 diabetes, found detemir was associated with a mean weight gain of 1.2 kg vs. NPH insulin mean weight gain of 2.8 kg.

**References**


35. A 62-year old Asian-American female arrives at your office for a new patient appointment. Her current medications are metformin, pioglitazone, enalapril, lovastatin, alendronate, calcium supplements and vitamin D. Her A1C is on target at 6.9%, however you decide to replace her pioglitazone with a different antihyperglycemic medication. Why would you make this decision?

A. Pioglitazone increases the risk of hypertriglyceridemia
B. Pioglitazone increases the risk for cardiovascular events
C. Pioglitazone increases the risk for of fractures
D. Pioglitazone increases the risk for hypoglycemia
CORRECT ANSWER: C

**Rationale**

Increased risk of bone fractures is a recognized side effect of piogliatazone (thiazolidinediones) and therefore would not be the best choice for this post-menopausal patient. For this particular patient, her ethnic background and age also place her at increased risk for osteoporosis and low bone density. Piogliatozone advantages are: no risk of hypoglycemia as a side effect, it has durability of effectiveness, it has been associated with a decreased risk of cardiovascular events and it decreases triglycerides.

**References**


36. Your patient has been taking metformin, glipizide and a daily basal insulin dose (.85 U/kg/day). While his fasting glucose levels are on target, he have not yet been able to reach his individualized glycemic target of A1C<7%. In your discussion with him about the addition of a prandial insulin dose to his regimen, you compare and contrast his options. Compared to basal insulin alone, premixed insulins:

   A. tend to lower A1c to a larger degree.
   B. are associated with less weight gain.
   C. cause less hypoglycemia.
   D. are a good option for people with irregular meal schedules.

CORRECT ANSWER: A

**Rationale**

Compared to basal insulin alone, the premixed insulins tend to lower A1C to a more significant degree. However, their use has been associated with slightly increased rates of hypoglycemia and weight gain. Due to the fixed ratios of shorter-acting and longer-acting insulins in premixed insulins, individuals lose their ability to titrate their insulin needs to their meal size and timing. Thus, the premixed are more suitable for those who have a regular eating schedule and predictable meal size.

**Reference**

Inzucchi S, et al. Management of hyperglycemia in type 2 diabetes: A patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European
A 64-year female presents to your office for her 3-month follow-up. She has previously been diagnosed with mild diastolic heart failure, secondary to hypertension. She currently takes an ace-inhibitor and a diuretic with good control of her heart failure symptoms and hypertension. At her last visit, she had a FPG 118 mg/dl. In a subsequent conversation with her, you discussed how she has developed prediabetes and suggested lifestyle modifications. Since her last visit, she has taken up very gentle walking four times/week and has changed her diet to a more healthful one. Despite these positive changes, this visit’s labs return an A1C 7.8%; her remaining labs are within normal limits. Which one of the following antihyperglycemic medication classes would you choose to initiate treatment?

A. Sulfonylureas  
B. Biguanides  
C. Insulin  
D. Thiazolidinediones

CORRECT ANSWER: B

Rationale

Metformin would be considered the first-line drug of choice for this patient. The use of metformin in patients with diabetes and heart failure used to be contraindicated (its use in patients with compromised renal function being associated with lactic acidosis). However, it can now be used in select patients with heart failure if renal function is normal, CV status is stable and ventricular dysfunction is not severe. Eurich, et al. (2005) conducted a retrospective analysis of type 2 diabetes patients treated with metformin vs. sulfonylureas and found overall decreased mortality in the metformin group. Masoudi et al (2005) examined metformin vs. thiazolidinediones and found the reduced risk of death at 1-year and lower hospital admission rates in the metformin group, while increased hospital admissions (primarily due to heart failure readmissions) was seen in the thiazolidinedione group. Thiazolidinediones increase renal sodium and water reabsorption, causing fluid retention and worsening of heart failure signs/symptoms. A recent retrospective analysis (Tzoulaki, et al., 2009) found an association between the use of sulfonylureas and increased risk of developing/worsening heart failure. Both classes of drugs should not be used in patients with diabetes and heart failure.

References


38. A 54-year old male presents to your office for an initial visit. His past medical history is significant for hypertension, hypertriglyceridemia and acute pancreatitis. His current lab results show an A1C 9.1%, which is confirmed on a repeat lab. You would like to start him on an antihyperglycemic treatment regimen. Which of the following two-drug combinations is contraindicated for this patient?

A. Metformin + a sulfonylurea
B. Metformin + an insulin
C. Metformin + a meglitinide
D. Metformin + a GLP-1 receptor agonist

CORRECT ANSWER: D

Rationale

Given this patient’s A1C, initiating a 2-drug combination therapy would be an appropriate
The incretin-based drugs (GLP-1 receptor agonist and DPP-4 inhibitors) are contraindicated if there is a history of pancreatitis as they have been linked to reports of acute pancreatitis, although their possible role increasing the risk of pancreatitis is not clear. The GLP-1 receptor agonists are glucose dependent and work at the pancreatic level to stimulate insulin secretion and suppress glucagon production. DPP-4 inhibitors inhibit DDP-4 (DDP-4 inactivates the incretins), leading to an increase in active incretin levels.

Reference


39. A 47 year-old patient has done an excellent job with lifestyle modifications and medication adherence, however she has not been able to yet achieve her individualized A1C goal. Her current regimen consists of a metformin, sitagliptin and insulin detemir (insulin started 4 months prior). However, over the past month as she has titrated her basal insulin towards her A1C goal, her self-glucose blood monitoring log shows large drops in her overnight glucose levels. After consulting with the treatment team, you decide to add rapid-acting prandial insulin to her regimen. How would you implement this strategy?

A. Decrease the basal insulin dose and add 1 daily prandial injection before the smallest meal of the day
B. Decrease the basal insulin dose and add 1 daily prandial injection before the largest meal of the day
C. Maintain the basal insulin dose and add 1 daily prandial injection before the smallest meal of the day
D. Maintain the basal insulin dose and add 1 daily prandial injection before the largest meal of the day

CORRECT ANSWER: B

Rationale

Basal insulin is generally titrated against fasting glucose levels. The addition of prandial insulin should be addressed when postprandial glucose measurements are significantly elevated (>180 mg/dL). This should be suspected when fasting glucose is at target, but A1C remains above goal after 3-6 months of basal insulin titration. Prandial insulin should also be considered when self-monitoring of glucose levels during up-titration of the basal insulin reveals large drops in overnight or between meals glucose levels; as prandial insulin is added, basal insulin should be reduced. The addition of prandial insulin should be individualized to each patient needs and abilities. These rapid-acting insulins are added to the patient’s day in a graduated fashion,
starting with the largest/highest carbohydrate meal, then the next largest and finally, the smallest meal as needed. This approach allows self-monitored glucose results to guide the prandial insulin injection to the appropriate dose and frequency.

References


40. You have decided that one of your a 72-year old patients should add a basal insulin dose to her antihyperglycemic regimen. During your discussion with her, she voices concern that between her “arthritic hands and poor vision” she won’t be able to accomplish this. You make the recommendation that using an insulin pen will make injection easier for her. Which of the following statement regarding insulin pens is true?

A. They all require loading with an insulin cartridge
B. They have more accurate dosing than syringes
C. They can now dose insulin in .10 units increments
D. They are now available for all types insulin

CORRECT ANSWER: B

Rationale

Insulin pens are now widely available; some are prefilled/disposable while others are reusable and require an insulin cartridge to be loaded. Insulin pen pros: more discreet, convenient and easier to use than vial/syringe; they have features that allow for more accurate and repeated dosing; they are less painful as the needle is only used once vs. twice with the vial/syringe; can increase medication adherence Cons: more expensive than vial/syringe; may not be covered by insurance; not all insulin types are available in pen form and there may be pen/insulin compatibility issues.

References


41. One of your patients has referred her 21-year old stepson for a new patient exam. He has
recently arrived home from college for the summer and she is concerned because he always seems to be thirsty. When prompted, she recalls her husband saying his ex-wife struggled with her weight and took “pills for her blood sugar.” Physical examination is notable for mildly elevated BP (137/84) and BMI 26 kg/m². He denies any cigarette or alcohol use, states his favorite activities revolve around video games, and that he doesn’t really enjoy any physical activities. Labs are notable for random plasma glucose 312 mg/dl, UA positive for glucose. What would your initial drug therapy strategy be?

A. Initiate monotherapy with metformin
B. Initiate a combination therapy with two noninsulin agents
C. Initiate lifestyle modifications
D. Initiate insulin therapy

CORRECT ANSWER: D

Rationale

According to the ADA/EASD recommendations, insulin therapy should be strongly considered from the onset for patients who present with severe hyperglycemia (≥300-350mg/dl; A1C≥10-12%) with or without catabolic features. Insulin therapy is mandatory if patients exhibit catabolic features or if ketonuria is present. Once patients’ symptoms/glucotoxicity/metabolic state have been resolved and stabilized, unless there is evidence of type 1 diabetes, it may be possible to modify the treatment strategy to reflect partial or complete tapering of the insulin, switching to noninsulin hyperglycemic agents or combination therapy. Environmental factors and genetics strongly influence the development of type 2 diabetes; in general if 1 parent was diagnosed with type 2 diabetes before age 50, the child has a 1 in 7 risk of developing type 2 diabetes; if the parent was diagnosed after age 50, the child’s risk is 1 in 13; if both parents were diagnosed with type 2 diabetes, the child’s risk jumps to 1 in 2.

References


42. A 47-year old patient returns for a follow-up visit. He currently takes metformin 2000 mg daily, but is not achieving his glycemic target of A1C <7 %. His current A1C is 8.0%. You would like to add a second medication to his regimen, however he voices concern that he is no longer covered by any health insurance and is worried about how to pay for his medications.
Taking his concern into consideration, what drug would you add to metformin?

A. DPP-4 inhibitor  
B. Thiazolidine  
C. Sulfonylurea  
D. Meglitinide  

CORRECT ANSWER: C

**Rationale**

A 2-drug combination is the appropriate next management step for this patient. When the cost of medications is a concern, metformin + sulfonylurea is the lowest cost combination. Relative costs of antihyperglycemic medications are as follows. Low Cost: metformin, sulfonylureas. Moderate Cost: α-glucosidase inhibitors. High Cost: meglitinides, thiazolidinediones, DPP-4 inhibitors, bile acid sequestrants, dopamine-2 agonists, GLP-1 agonist, amylin mimetics. Variable: insulins.

**Reference**


43. A 75-year old man presents to your office with complaints of occasional mild hypoglycemia. His current antihyperglycemic regimen includes metformin and nateglinide. You would like to modify his treatment regimen to minimize his risk of hypoglycemia. Which one of the following 2-drug combinations would NOT be a suitable substitution?

A. Metformin + pioglitazone  
B. Metformin + glipizide  
C. Metformin + vildagliptin  
D. Metformin + exenatide  

CORRECT ANSWER: B

**Rationale**

In this case, the sulfonylureas (glipizide) and meglintinides (nateglinide) can lead to hypoglycemia (meglinitides less so than sulfonylureas). The thiazolidinediones (pioglitazone), DPP-4 inhibitors (vildagliptin), GLP-1 agonists (exenatide) and metformin have low hypoglycemic potential as a side effect. The thiazolidinediones (pioglitazone), DPP-4 inhibitors (vildagliptin) and GLP-1 agonists (exenatide) can be used in various combinations with
metformin to provide glycemic control when the goal is to minimize hypoglycemia.

Reference


44. A 43-year old patient presents to your clinic for an appointment. She has mild hypertension, which is currently well controlled with a β-blocker. She was diagnosed with type 2 diabetes 6-years ago, and has been taking metformin and glipizide. She has noticed that her recent self-blood glucose monitoring numbers have been creeping up and with a most recent FPG of 160 mg/dl. At today’s visit, she has an A1C 8.0%. She tells you that until now her job has required she travel several times a month. This week she was promoted to a managerial position that does not require travel. Which of the following approaches would be the best for her?

A. Add a basal insulin dose once a day
B. Add premixed insulin twice a day
C. Add pre-mixed insulin twice a day and change her noninsulin medications
D. Add a basal insulin dose once a day and change her noninsulin medications

CORRECT ANSWER: A

Rationale

Usually, the addition of basal insulin is considered the optimal initial insulin regimen; usually in conjunction with one or two noninsulin agents. Generally, therapeutic regimens should begin with some basal insulin before moving to more complex insulin strategies. Starting a pre-mixed insulin regimen as the initial insulin strategy can be considered in patients willing to take more than one injection a day and with higher A1C level (>9.0%). Pre-mixed regimens tend to lower A1C slightly more when compared to basal insulin alone. However, the use of pre-mixed insulin can lead to slightly more hypoglycemia and weight gain than basal insulin. When basal insulin is used, the continued use of secretagogues may provide some benefit in reducing initial glycemic control deterioration. However, with the addition of prandial insulin, while metformin is usually continued and may help prevent some weight gain, secretagogues should be stopped.. In addition to continued general diabetes education (SBGM, lifestyle modifications, disease course), patients should receive education on the avoidance, recognition and treatment of hypoglycemia.

Reference

45. A 51-year old patient returns to your office for a follow-up visit. She is currently taking metformin and glipizide after being diagnosed with type 2 diabetes 8-years ago. She shows you her self-care logs that indicate she has been eating a healthy diet and walking daily. She has been maintaining her weight (BMI 26kg/m²). Despite her excellent efforts, her A1C is 7.8%, above her target of A1C<7.0%. When you start to discuss adding a basal insulin dose to her regimen, she bursts into tears. All of the following are common barriers to insulin therapy initiations EXCEPT:

A. Fear that hyperglycemia will make her ill
B. Fear others will treat her differently because she needs regular injections.
C. Fear of needles or that insulin injections are painful
D. Fear that insulin causes death or complications

CORRECT ANSWER: A

Rationale

Common patient-identified barriers to initiating insulin therapy are: fear others will see them differently; insulin is not an effective treatment for diabetes; using insulin can lead to complications or death; concern that using insulin will negatively impact their lifestyle; fear of hypoglycemia: fear of weight gain; fear of needles of injection pain; and insulin cost concerns. Fear of hypoglycemia can be ameliorated with choosing insulin less likely to cause hypoglycemia (newer rapid-acting and longer-acting analogue insulins) as well as patient education on the frequency, avoidance, recognition and treatment of hypoglycemia.

Reference


46. A 39-year old, overweight (BMI 27 kg/m²) patient comes into your office for his annual wellness examine. Routine labs show random plasma glucose of 176 mg/dL, so you ask him to return for a fasting plasma glucose and A1C. The results show a FPG 139 mg/dL and A1C of 7.7%. He is resistant to the idea of starting medication and is very keen on pursuing a trial period of dietary modifications and an exercise program, especially after you tell him about the benefits of moderate exercise on diabetes. Which of the following statements about
exercise is true?

A. Exercise reduces basal insulin levels only when paired with proper diet
B. Exercise can lead to weight loss, but rarely reduces A1C levels
C. Exercise can reduce all-cause mortality by up to 38%
D. Exercise must be rigorous and regular to lead to greatest reduction in mortality

CORRECT ANSWER: C

Rationale

A recently published study (meta-analysis of 12 studies and prospective cohort data), led by Diewrtje Sluik form the German Institute of Human Nutrition Potsdam-Rehbrucke, confirmed that physical activity lowers basal insulin levels, lowers A1C levels and lowers the risk of cardiovascular disease and total mortality by up to 38% in patients with type 2 diabetes. Compared to physically inactive adults, moderately active persons were associated with the best improvement in risk for death. Participants who engaged in more intense/higher levels of exercise still showed impressive risk reduction, but it was slightly less than the moderate exercise group.

Patients, who are newly diagnosed with type 2 diabetes, have A1Cs near target (<7.5%) and who are highly motivated to engage in lifestyle modifications may be given the opportunity to pursue lifestyle modifications for a 3-6 month period. If lifestyle modifications are not successful, pharmacotherapy can be initiated after the trial period.

References


47. A 59-year old patient who was diagnosed with type 2 diabetes five years ago presents to your clinic for an appointment. He has a history of hypertension and dyslipidemia, both currently well controlled with medication. He has been taking metformin and a DPP-4 inhibitor. He tells you he is concerned about a sore on his foot that is taking a long time to heal. At today’s visit, his office A1C is 8.8%. After discussing his options, you decide to add basal insulin analogue detemir to his regimen. Compared to insulin NPH, what would you expect him to experience while taking detemir?

A. Less weight gain
B. More hypoglycemia
C. More weight gain
D. No weight gain or hypoglycemia difference

CORRECT ANSWER: A

Rationale
Compared to NPH, the use of long-acting insulin analogues (glargine and detemir) have been associated with modestly less weight gain and overnight hypoglycemia.

Reference

48. A 68-year male presents to your office for a follow-up visit. His past medical history is significant for a myocardial infarction (five years ago) and type 2 diabetes. His current medications include an ACE inhibitor, a statin, aspirin and metformin. Despite good compliance with his medications and beneficial lifestyle changes, he is not able to achieve his individualized target A1C of 7.5-8%. You decide it would be beneficial to add second antihyperglycemic agent. Which of the following medications should be avoided?

A. Pioglitazone
B. Exenatide
C. Rosiglitazone
D. Sitagliptin

CORRECT ANSWER: C

Rationale
Cardiovascular disease is a frequent complication in type 2 diabetes patients with approximately 65% dying of cerebrovascular or coronary artery disease. Rosiglitazone is not recommended for use as meta-analysis suggests is associated with an increased risk of cardiovascular events. In addition, agents that can cause hypoglycemia should be used with caution as hypoglycemia can worsen myocardial ischemia and may cause arrhythmias. Very limited studies suggest pioglitazone, GLP-1 receptor agonists and DPP-4 inhibitors may lead to modest improvements in cardiovascular risk.

Reference
49. You are reviewing lifestyle modifications with a 42-year old, relatively sedentary patient that has been newly diagnosed with prediabetes. Your screening for any cardiovascular risk factors was negative, so she has agreed to a 3-month trial of dietary modifications and increased physical activity. Structured exercise interventions and modest weight loss have been shown to lower the risk of developing type 2 diabetes in high-risk populations by an average of:

A. 22%
B. 35%
C. 58%
D. 70%

CORRECT ANSWER: C

Rationale
The Da Qing study in China found even modest changes in exercise (20 minutes mild-moderate, 10 minutes strenuous, 5 minutes very strenuous exercise 1-2 times per day) reduced the risk of developing diabetes by 46%. The Finnish Diabetes Prevention Study and the U.S. Diabetes Prevention Program (DPP) looked at the effects of intensive lifestyle modifications (diet and increased physical activity) on the development of diabetes in individuals with either IGT or IFG. The Finnish study participants were assigned to either 30 minutes/day of moderate physical activity or a “no-change” group. The DPP participants were randomized to either control, metformin or lifestyle modifications (dietary changes, weight loss goals and 150 minutes of weekly aerobic activity) groups. The Finnish Diabetes Prevention Study and the U.S. Diabetes Prevention Program (DPP) both showed 58% reduction in diabetes incidence. Participants in the DPP metformin group had a 31% reduced incidence of developing diabetes. The benefits of increased physical activity on diabetes prevention endured across ethnic groups, both sexes and those who did not meet weight loss goals.

References


50. A patient that you haven’t seen for several years comes to your clinic for a wellness check-up. Since her last visit, she has gained about 15 pounds (5’6”, BMI 27 kg/m²). Her stage 1 hypertension is controlled with hydrochlorothiazide. As you discuss her weight gain, you learn that she doesn’t get more than 30 minutes a week of physical activity. You decide it would be best to check her A1C. Which of the following information from her history leads you to screen her for type 2 diabetes?

A. Her youngest child weighed 8.5 pounds at birth.
B. Two of her cousins have type 2 diabetes.
C. She just celebrated her 41st birthday.
D. She has a history of hypertension.

CORRECT ANSWER: D

Rationale

According to the ADA standards, hypertension (BP≥140/90 or on therapy for hypertension) in conjunction with BMI ≥ 25 kg/m² is an indication for diabetes screening in asymptomatic adults. The ADA’s criteria for testing for diabetes in asymptomatic adult individuals follows:

Testing should be considered in all adults who are overweight (BMI≥25/kg/m²)* and have an additional risk factor (*at-risk BMI may be lower in some ethnic groups), including:

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity (e.g. African American, Latino, Native American, Asian
American, Pacific Islander

- Women who delivered a baby weighing >9 lb or were diagnosed with GDM
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or triglyceride level 250 mg/dL (2.82 mmol/L)
- Women with polycystic ovary syndrome
- A1C ≥5.7%, IGT, or IFG on previous testing
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- History of CVD

In the absence of the above criteria, testing for diabetes should begin at age 45 years. If the results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., those with prediabetes should be tested yearly) and risk status.

Reference

CLINICAL CASE VIGNETTES

CASE 1

Mrs. O’Doole is a 34 year-old of Irish descent. She works as florist who and is married with three children. She arrives at your clinic for her annual wellness exam. Her blood pressure is 130/84 mmHg, pulse 65, BMI 24 kg/m² and her physical exam is notable for acne and mild hirsutism. Her only current medication is oral birth control pills. She recalls starting OCP, 15 years prior, due to irregular menses.

51. What clinical diagnosis would suggest screening Mrs. Hernandez for type 2 Diabetes?

   A. Thyroid dysfunction
   B. Cushing syndrome
   C. Polycystic ovary syndrome
   D. Premature ovarian failure

CORRECT ANSWER: C

Rationale

The ADA has developed criteria for testing asymptomatic adults for type 2 diabetes. In this case, while she normal weight, she has one or more additional risk factors and should be screened for type 2 diabetes. Mrs. O’Doole’s clinical picture (acne, hirsutism, overweight, irregular menses) is suggestive for polycystic ovary syndrome (PCOS), a significant risk factor for type 2 diabetes. While hirsutism/acne/menstrual irregularities can occur in Cushing syndrome, other physical findings are also usually present (abdominal striae/central fat/moon facies/hypertension). Signs of hyperandrogenism are absent in thyroid dysfunction and premature ovarian failure.

Wang et al (2011) examined data from the Coronary Artery Risk Development in Young Adults (CARDIA) study to estimate whether women with PCOS (overweight and normal-weight) were at increased risk for the development of incident diabetes, dyslipidemia and hypertension. Study authors concluded that PCOS, independent of BMI, is associated with an increased risk of diabetes and dyslipidemia, but not hypertension. The risk of developing diabetes was three times higher in normal weight women with PCOS vs. normal weight women without PCOS.

References


Based upon her medical history and physical, you believe it would be prudent to screen Mrs. O’Doole for type 2 diabetes. You discuss your recommendations with her and she agrees to be tested. The lab returns a fasting plasma glucose (FBG) of 112 mg/dL. You share these results with your patient and inform her, that while only mildly elevated, she has impaired fasting glucose. What is the best choice for initial management of Mrs. O’Doole’s prediabetes?

A. Metformin
B. Metformin + Pioglitazone
C. Lifestyle modifications + Pioglitazone
D. Lifestyle modifications (dietary modifications, weight loss and exercise)

CORRECT ANSWER: D

Rationale

Mrs. O’Doole’s FPG 112 mg/dL is indicative of impaired fasting glucose and she is considered to have prediabetes. The ADA recommends patients with IGT, IFG or A1C 5.7-6.4% should target a 7% weight loss and at least 150 minutes/week of moderate activity. Dietary modifications (reduced calories/low fat/high fiber/limited use of sugar-sweetened beverages) have been part of lifestyle interventions that prevent diabetes. Findings from the Da Qing study, the Finnish Diabetes Prevention study and the U.S. Diabetes Prevention Program Outcomes study showed lifestyle interventions to be highly effective in reducing the conversion rate from prediabetes to diabetes. These studies also showed that lifestyle interventions were more effective than metformin in preventing diabetes development, except in very-high risk individuals (BMI≥35 kg/m², history of GDM and/or more severe or progressive hyperglycemia). Given her impaired fasting glucose, it would reasonable to recommend lifestyle modifications and provide follow-up counseling and support. For patients with prediabetes, monitoring for the development of diabetes should occur, at a minimum, annually.

References


53. At a follow-up appointment 6-months later, Mrs. O’Doole tells you despite good intentions, she has not been able to adhere to any meaningful lifestyle changes, in fact she has gained 5 pounds. At this time her repeat fasting plasma glucose shows FPG 138 mg/dL. After discussing management options with her, you decide the best management would be:

A. lifestyle modifications only
B. metformin only
C. metformin + lifestyle modifications
D. repaglinide only

CORRECT ANSWER: C

Rationale
Mrs. O’Doole’s FPG (138 mg/dL) suggests she has progressed from prediabetes to diabetes (this should be confirmed on a repeat FPG). Highly motivated, newly diagnosed patients, with an A1C already near target, may be given the chance to try lifestyle modifications before the introduction of antihyperglycemic medications for glycemic control. However, this patient has not been able to implement these modifications to a clinically beneficial degree. At the time of diagnosis, unless there are contraindications, metformin is considered first-line therapy for type 2 diabetes. Incidentally, the addition of metformin may decrease her PCOS-associated hirsutism.

References
You discuss the benefits of lifestyle changes with Mrs. O’Doole and tell her that you are referring her to an exercise program specifically for individuals with type 2 diabetes. What schedule of exercise is recommended for patients like Mrs. O’Doole?

A. 30 minutes daily of moderate-intensity physical activity at least 4 days per week
B. 30 minutes daily of moderate-intensity physical activity at least 5 days per week
C. 45 minutes daily of moderate-intensity physical activity at least 4 days per week
D. 45 minutes daily of moderate-intensity physical activity at least 5 days per week

CORRECT ANSWER: B

Rationale

Patients with type 2 diabetes who are previously sedentary should aim to accumulate a minimum energy expenditure of 1000 kcal/wk. This corresponds to the American College of Sports Medicine and the American Diabetes Association guidelines for moderate-intensity physical activity for a minimum of 30 minutes at least 5 days week.

ADA recommendations advise patient with type 2 diabetes should participate in at least 150 minutes per week of moderate intensity exercise (50-70% maximum heart rate). No more than 2 days should pass without exercise and the exercise should be distributed over at least a 3-day period. In addition, at least 2 times week, individuals should engage in resistance training. Providers should use their clinical judgment in regarding the need to assess for cardiovascular risk factors before recommending a physical activity program. Individuals with type 2 diabetes have been shown to lower their A1C levels by an average of .66% when participating in structured exercise interventions of at least 8-weeks duration.

References


CASE 2

Mr. Hernandez is an overweight (BMI 30 kg/m$^2$), 45-year old plumber of Hispanic heritage who arrives at your office for a first-time visit. He has not been to a physician during the last 7 years because he hasn’t always had health insurance and “doesn’t like going to the doctor.” However, he has been noticing lately that his vision seems a little blurry and he’s developed a red, itchy rash in his groin. He is a non-smoker and recalls being told a long time ago that he should eat a low salt diet, but he can’t remember why. On examination, his BP is 154/96 mm/Hg, and his pulse is 72, RR 22. His physical exam is notable for signs of a yeast infection in his groin. You order a CBC and A1C to be drawn that day before he leaves. You advise him how to treat his skin infection.

55. When you receive the results of the CBC, it shows a random plasma glucose of 162 mg/dL and A1C 7.3%. You call Mr. Hernandez and ask him to return the next morning, before he has eaten, for additional labs. In this individual, you might order all the following labs EXCEPT:

A. A1C.
B. chem 12 panel.
C. fasting lipid profile.
D. urine ketones.

CORRECT ANSWER: D

Rationale

Urine and/or blood ketone tests are usually ordered to monitor the progress of patients being treated for ketoacidosis or who present with symptoms of acute/moderate-severe hyperglycemia, ketosis, ketonuria or ketoacidosis. The other listed test are all part of the initial laboratory evaluation. In order to meet the ADA’s criteria for the diagnosis of diabetes, initial lab results showing elevated A1C, FGP or OGTT levels, need to be confirmed by repeat testing. The laboratory components of a comprehensive diabetes evaluation are:

- A1C, if results not available in the past 2-3 months
- Fasting lipid profile,
- Liver function tests,
- Test for urine albumin excretion with urine albumin-to-creatinine ratio
- Serum creatinine and calculated GFDR
- TSH in type 1 diabetes, dyslipidemia or women over age 50 years

References

56. Mr. Hernandez labs return and are notable for A1C 7.5, FPG 137 mg/dL, LDL-cholesterol 190 mg/dL, HDL-cholesterol 38 mg/dL and triglycerides 232 mg/dL. You discuss his lab results, his diagnosis and how to manage diabetes and make referrals to the appropriate diabetes team clinicians. You start Mr. Hernandez on metformin, lifestyle modifications, an ACE inhibitor, and a statin. What clinical parameters are you looking to achieve?

A. A1C<7%, BP<130/80 mmHg, LDL<100 mg/dL
B. A1C<7%, BP<130/90 mmHg, LDL<100 mg/dL
C. A1C<7%, BP<140/80 mmHg, LDL<100 mg/dL
D. A1C<7%, BP<140/90 mmHg, LDL<150 mg/dL

CORRECT ANSWER: C

Rationale
For most individuals with diabetes, glycemic control (A1C<7%, FPG 70-130 mg/dL, PPG <180mg/dL) has been associated with reduced microvascular complications, managing blood pressure (BP<140/80 mmHg) and lipid profiles has been shown to be effective in reducing macrovascular complications. The ADA recommends LDL<100 mg/dL in individuals without overt CVD; LDL<70mg/dL in individuals with overt CVD. While there are not recommended HDL or TG goals, TG levels <150 mg/dL and HDL levels >40 mg/dL in men and HDL levels >50mg/dL in women are desirable.

Reference

57. You ask Mr. Hernandez to return in 3-months time to evaluate how everything is going. However, he fails to keep his appointment. He returns 1 year after his initial diagnosis for a recurrent yeast infection. His A1C is currently 7.7%. Upon questioning, he admits that while he has been good about taking his “heart meds”, he has not taken the “sugar pill” because he didn’t like it. What side effect did the patient most likely find intolerable?

A. Diarrhea and abdominal cramping
B. Paresthesias
C. Increased appetite
D. Insomnia
CORRECT ANSWER: A

**Rationale**

Metformin may be contraindicated in some patients and other patients may not tolerate its side effects well. Gastrointestinal side effects are common. If metformin is not tolerated or is contraindicated, the ADA/AED guidelines recommend initiating therapy with a drug from another class and proceeding accordingly.

**References**


**CASE 3**

Mrs. Hunter is 36-year old African American who comes to your office for her annual wellness exam. She is overweight (BMI 27 kg/m²), but is otherwise healthy. She jokes that she “just can’t seem to lose that extra baby weight” after giving birth 3 years ago. However, her daughter recently started preschool so she has been able to go to her new gym several times per week. In fact, one of the added bonuses of her membership is that she has been participating in their free, weekly nutrition and exercise support groups. In addition to her routine labs, you order an A1C, which comes back elevated at 7.1%. This measurement is confirmed several days later.

58. Based on Mrs. Hunter’s profile, what would a reasonable next step be?

A. Encourage lifestyle modifications and start metformin with an A1C target of < 7.0%
B. Encourage lifestyle modifications and start metformin with an A1C target of < 6.0%
C. Encourage lifestyle modifications and do not initiate drug therapy at this time
D. Encourage lifestyle modifications and start metformin and a sulfonylurea

CORRECT ANSWER: C

**Rationale**

Encourage lifestyle modifications and do not initiate drug therapy at this time. In general, it is reasonable to give patients that are already near target (A1C<7%) at time of diagnosis and are highly motivated to engage in lifestyle modifications, a window of opportunity to engage in lifestyle modifications for a trial period of 3-6 months before embarking on pharmacotherapy. In select patients (highly motivated, newly diagnosed, long life expectancy, no significant comorbidities), more stringent A1C targets (<6.5%) may be considered as along as they can be
achieved without adverse treatment effects or significant hypoglycemia.

**Reference**


59. You and Mrs. Hunter set a goal for A1C<6.5%. She returns 3 months later for a follow-up visit and her office labs show an A1C 6.8%. You congratulate her on her progress and ask her to return in another 3-4 months. When she does, she is above her goal with an A1C 8.1%. She explains that she has gone back to full-time work and just doesn’t have the time to get to the gym anymore. At this time, what would your next step be and what would her individualized glycemic targets be?

A. Encourage lifestyle modifications and start metformin with a target A1C< 6.5%
B. Encourage lifestyle modifications and start metformin with a target A1C <7.5%
C. Encourage lifestyle modifications and start a 2-drug combination target A1C target < 7%
D. Encourage lifestyle modifications and do not initiate drug therapy at this time

CORRECT ANSWER: A

**Rationale**

After allowing a 3-6 month trial period of lifestyle modifications, if on a repeat visit the A1C indicates the attempt has been unsuccessful, pharmacotherapy should be initiated. With her current A1C at 8.1%, monotherapy, typically with metformin unless there are contraindications, would be started. The glucose-lowering effect of metformin is considered to be high and would be expected to lead to an A1C reduction of 1-1.5%. While she has had difficulty maintaining lifestyle modifications, the more stringent A1C goal, as long as it is well tolerated (no significant hypoglycemia, treatment side effects) would still be appropriate given her age, health status and disease duration. A1C goals should be individualized and modified as necessary. She should be encouraged to continue with lifestyle modifications as well.

**Reference**

60. After 4 years of good glycemic control with metformin 1500 mg q day, Mrs. Hunter returns for her 6-month follow-up visit. At this time, her office A1C is 8.2% and she has gained 7 pounds. She is very concerned about her weight gain. If weight is a concern, what would be the best antiglycemic drug to add to her regimen?

A. A sulfonylurea  
B. A DPP-4 inhibitor  
C. A thiazolidinedione  
D. A GLP-1 receptor agonist  

CORRECT ANSWER: D  

Rationale  
The use of GLP-1 receptor agonists is associated with modest-significant weight reduction. The other medications listed are either associated with weight gain or are weight neutral.  

Reference  

CASE 4  
Mr. Carlson is 52-year old Caucasian grocery store manager you saw last week for a new patient visit. His labs from that visit were significant for elevated random plasma glucose 166 mg/dL, A1C 7.4% and elevated lipids (TG=175 mg/dL, LDL 148 mg/dL, HDL 38 mg/dL, total cholesterol 221 mg/dL).  

He has returned to your clinic for a follow-up appointment. His physical exam is notable for central abdominal obesity (waist circumference 42”), left eyelid xanthelasma, BP 147/91, HR 72, RR 18, BMI 36 kg/m² but otherwise normal. A repeat A1C test shows A1C 7.6% Mr. Carlson smokes between 1 and 1.5 packs of cigarettes daily. After discussing the labs and your findings with Mr. Carlson, you begin collaborating on a management plan. You write prescriptions for metformin, a statin and ACE inhibitor.  

Mr. Carlson doesn’t think “taking medication will be too tough” but expresses skepticism about your recommendations for a change in his diet, exercise and smoking programs because he has tried them, without success in the past.
61. What is considered the starting BMI for consideration of bariatric surgery?

A. BMI > 28 kg/m²
B. BMI > 30 kg/m²
C. BMI > 35 kg/m²
D. BMI > 37 kg/m²

CORRECT ANSWER: C

Rationale

Individuals with type 2 diabetes and BMI > 35 kg/m², may be considered a candidate for bariatric surgery, especially if their diabetes is hard to control with lifestyle modifications and antihyperglycemic medications. The decision to undergo this surgery should not be taken lightly as these patients will need lifelong support and medical management. The pros and cons of the surgery should be discussed with the patient and they should be referred only if they want to pursue it further. Bariatric surgery in individuals with BMIs 30-35 kg/m² has shown a glycemic benefit, however there is insufficient evidence at this time to routinely recommend it.

References


62. Mr. Carlson makes an appointment with a registered dietitian. She discusses with him the benefits of medical nutrition therapy on weight, glycemic control, blood pressure, lipid profile and overall wellbeing. Which following statement regarding macronutrients is true?

A. The ratio of carbohydrates, protein and fat is the same for all patients
B. Total calories consumed per day is the key strategy for achieving glycemic control
C. Reduced intake of trans fat lowers the HDL and raises the LDL
D. Saturated fat should be <7% of total calories

CORRECT ANSWER: D

Rationale

Saturated fat should be <7% of the total daily calories. Dietary modifications and the composition of carbohydrates/fats/protein should be adjusted to meet the needs and
preferences of the individual patients. Carbohydrate monitoring is still a key component for glycemic control. It can occur in the form of carbohydrate counting, estimation based on experience or educated food choices. Reduced trans fat intake results in a lower LDL and increased HDL.

Reference

63. You are concerned about Mr. Carlson’s cigarette use because cigarette smoking has been shown to have multiple physiological impacts on health. Which one of the following statements regarding smoking and type 2 diabetes is true?

A. It equally affects all-cause mortality in individuals with and without diabetes
B. In individuals with diabetes, it causes more rapid progression to micro- and macroalbuminuria
C. It has not been linked to worsening glycemic control
D. The use of bupropion in contraindicated in diabetes

CORRECT ANSWER: B

Rationale
Smoking cessation support for patients with diabetes is important and should be given high priority. In patients with diabetes, smoking is an independent risk factor for developing macrovascular and microvascular complications. In addition to being an independent risk factor, smoking causes more rapid progression to micro- and macroalbuminuria. Overall mortality is higher in smokers who have diabetes when compared to the non-diabetic smoking population. Studies suggest that smoking may induce diabetes and smoking has been shown to worsen glycemic control and insulin resistance. There are a variety of medications that can be used to help patients with diabetes stop smoking. Bupropion is one of them.

Reference
CASE 5

Mr. Huang is a 61-year old Asian American businessman who comes in to see you for a follow-up appointment. He was diagnosed with type 2 diabetes 4 years ago and has a long-standing history (15 years) of hypertension and hypercholesterolemia, which are currently well controlled. Current medications are metformin (1500 mg/day), lisinopril and simvastatin. He is overweight (BMI 29 kg/m²) but feels he has a healthy diet and gets out for a 25-30 minute walk 3 or 4 times per week. He feels great, but over the last nine months or so, he has noticed that his home average glucose levels are in the 180-198 mg/dL range. At today’s visit, his A1C is 8.3%.

64. Based on Mr. Huang’s individual glycemic target of A1C<7%, you would like to add another antihyperglycemic. You choose linagliptin over glimepiride. What is the best reason for your choice?

A. Greater weight loss benefits
B. More effective at lowering blood glucose levels
C. Lower cost of treatment

CORRECT ANSWER: A

Rationale

The DPP-4 inhibitors are considered to be weight loss-weight neutral, but have intermediate A1C lowering efficacy and are costly. In general, the noninsulin pharmacological agents metformin, sulfonylureas, TZDs and GLP-1 agonist are thought to have better glucose-lowering abilities than meglitinides, DPP-4 inhibitors, AGIs, colesvealam and bromocriptine (respective expected A1C reduction 1.0-1.5% vs. 0.5-1.0%). However, studies have shown the differential effects on glucose control are small. Thus, when progressing from a monotherapy to a two drug combination, selection of the second agent should be guided by agent- and patient-specific properties (e.g., dosing, costs, side-effects, weight impact).

In Mr. Huang’s case, he would benefit from the weight neutral/loss associated with the DPP-4 inhibitors as opposed to the sulfonylurea associated weight gain. An efficacy study of Tradjenta (linagliptin) vs. glimepiride in combination with metformin found “Patients treated with linagliptin had a mean baseline body weight of 86 kg and were observed to have an adjusted mean decrease in body weight of 1.1 kg at 52 weeks and 1.4 kg at 104 weeks. Patient on glimepiride had a mean baseline body weight of 87 kg and were observed to have an adjusted mean increase from baseline in body weight of 1.4 kg at 52 weeks and 1.3 kg at 104 weeks (treatment difference p<0.0001 for both timepoints)”. The average wholesale cost of linagliptin is $8.12 per tablet (2011).

References


65. Mr. Huang achieves good glycemic control with his lifestyle modifications, metformin and linagliptin and returns every 6 months for follow-up visits. Three years after initiating this treatment plan he returns to your clinic for his 6-month check-up. When asked how his diabetes management is going at home, he shares that recently he has been “unable to really get out and get as much exercise as he know he should due to his creaky, old knees acting up.” His current office A1C is 8.8%. You discuss with him what the next management steps may be to achieve his individualized glycemic goal. What would your next medical management step be?

A. Add a rapid-acting insulin analogue
B. Add a long-acting insulin analogue
C. Add a GLP-1 agonist
D. Add a sulfonylurea

CORRECT ANSWER: B

Rationale

Moving to a 3-drug combination would be appropriate in this individual. The addition of a basal dose of a long-acting insulin analogue would be the most appropriate choice for this individual. Rapid-acting insulin analogues are used for daytime bolus dosing. Both the DPP-4 inhibitors and the GLP-1 agonist are based on the incretin system. When new agents are added, they should have complimentary mechanisms of action. In some cases, when adding a third agent, sulfonylurea could be an appropriate choice. However, once A1C≥8.5%, it is unlikely that a noninsulin agent will be adequately effective at lowering blood glucose levels.

Reference

66. **What is the best advice you can give Mr. Huang regarding exercise?**

   A. He really needs to find a way to perform 150 min/week of moderate-intensity aerobic exercise.
   
   B. At his age, exercise doesn’t make a significant difference any more.
   
   C. He should do his best to be active and get as close to 150 min/week as he can.
   
   D. He should be as physically active as possible introduce resistance training at least 2 times per week to his routine.

   **CORRECT ANSWER: D**

**Rationale**

Current physical recommendations for individuals with type 2 diabetes are: 150 min/week of moderate-intensity aerobic exercise and in the absence of contraindications, be encouraged to perform resistance training at least 2 x week. Meta-analysis has shown the positive benefit of resistance training on metabolic control, weight management and quality of life. For those that have difficulty engaging in aerobic activity, resistance training has been shown to be safe and efficacious.

**References**


**CASE 6**

Mrs. Wilson is an overweight 71-year old African American patient who has come to your clinic today for a new patient visit. She recently moved to the area to live with her daughter and is concerned about her diabetes care plan. She was diagnosed with type 2 diabetes 12 years ago at a wellness check through routine screening. In hindsight, she wonders if maybe she “went undiagnosed for a while” because she “didn’t get to the clinic very often and was having some problems with frequent urination at night” before she was screened.

She currently takes metformin, glyburide, captopril, pravastatin, aspirin and has recently titrated to .6 U/kg/day insulin NPH as a nightly basal dose. Her current A1C goal is <7.5% and she has been working hard to get to that level. However, for the first time her life, she is
finding herself to be nauseated and irritable in the morning, but always feels better after a little breakfast. She states she feels “pretty good for her age” although she occasionally has “a little chest tightness when walking more than 4 or 5 blocks.” Last time she remembered to check it a few days ago, her postprandial glucose was a little high at 214 mg/dL. Her office A1C is 8.6%.

67. Based on what you know about the patient, what is the most likely cause of her morning distress?

A. Hyperglycemia
B. Hypoglycemia
C. Anxiety
D. Cognitive decline

CORRECT ANSWER: B

Rationale
Dizziness, anxiety, tremor, nausea, palpitations, diaphoresis, confusion, irritability, hunger, drowsiness are some of signs and symptoms of hypoglycemia (plasma glucose <70mg/dl). The risk of hypoglycemia due to antihyperglycemic medications increases exponentially with age. In her case, the sulfonylureas (glyburide is in this drug class) and insulin can cause hypoglycemia as a side effect. When patients are able to self-treat their hypoglycemia, generally 15-20 g of a quick—acting carbohydrate should raise the blood glucose by 50 mg/dl in approximately 15 minutes. While anxiety can produce similar symptoms, her antihyperglycemic medications are probably the most likely cause.

References


68. Based on her history, what would be an acceptable individualized A1C goal for this patient?

A. A1C < 6.5%
B. A1C < 7.0%
CORRECT ANSWER: C

Rationale
Less-stringent A1C targets are acceptable in certain individuals, such as those with a history of hypoglycemia, presence of important comorbidities/complications, limited life expectancy, long-standing disease duration, risks associated with hypoglycemia, established vascular complications and difficulty achieving target A1c despite education, support and polypharmacy. This patient has several factors that would support a less-stringent A1C: advanced age, polypharmacy, lives alone and doesn’t have an established network, has a history of hypoglycemia putting her at increased risk for falls, arrhythmias, confusion, symptoms of cardiovascular disease and comorbidities.

References

69. After discussing her situation with her, you decide to modify Mrs. Wilson’s antihyperglycemic regimen. Which of the following treatment options would you choose?

A. Metformin + long-acting analogue + rapid-acting analogue
B. Metformin + glyburide + long-acting insulin analogue + rapid-acting analogue
C. Metformin + glyburide + NPH + rapid-acting analogue
D. Metformin + NPH + rapid-acting analogue

CORRECT ANSWER: A

Rationale
Metformin should be continued as it has been shown that there is less weight gain when it is used in conjunction insulin vs. insulin alone. Mrs. Wilson is having periodic episodes of overnight hypoglycemia suggesting her basal insulin is too high for her nighttime needs and needs to be reduced. However, she is having postprandial glucose excursions and her most recent A1C of 8.6% is above her individualized A1C goal. This would indicate the need for prandial insulin. Long-acting insulin analogues have been shown to cause slightly less overnight hypoglycemia when compared to insulin NPH and should be the choice for her basal insulin. Rapid-acting insulin analogues would be an appropriate choice for her bolus prandial dose. Her basal insulin dose would need to be simultaneously decreased as her prandial dose is added. The glyburide
should be discontinued at this point as it can contribute to hypoglycemia and does not appear to add any further A1C reduction benefits once prandial insulin has been started.

References


CASE 7

Mr. Fontello is an overweight, Caucasian 63-year old patient who comes in for a 6-month check-up. He has a 12-year history of type 2 diabetes. He was diagnosed at age 33 with high blood pressure, but had never really done much about it as it was “too much of a hassle” and he felt “just fine.” At the time his diabetes was diagnosed, he was referred to a diabetes education program and was started on metformin, lovastatin, losartan and aspirin. He has an individualized A1C goal of 7%.

Four years after diagnosis, pioglitazone was added to Mr. Fontello’s diabetes regimen. Three years ago, he came in for an appointment complaining of polyuria, polydipsia and fatigue with an office A1C of 9.3%. At that time he was started nightly basal insulin detemir. Since that time, he has made concerted efforts to eat a healthy diet and get to the gym.

Today, he reports his SBGM fasting plasma glucose levels are on target (FPG<130mg/dL). He also states that his feet always feel a little bit swollen. BP 128/78, HR 73, RR 19. Physical exam is remarkable for peripheral edema and mildly decreased pedal pulses. Current medications: metformin, pioglitazone, insulin detemir, lovastatin, losartan, aspirin. At today’s visit, his office A1C is 8.1%.

70. What changes would you recommend for his antihyperglycemic regimen?

A. Add a premixed insulin to all three meals of the day
B. Increase his detemir dose
C. Add a sulfonylurea to his regimen
D. Add a rapid-acting insulin analogue to his largest meal of the day

CORRECT ANSWER: D

Rationale

When FPG is at target, but postprandial glucose levels are above target (generally reflected in an A1C higher than target), consideration should be given to the addition of a preprandial insulin
dose to the management plan. This can be achieved through either (a) addition of premixed insulin before the morning and evening meals (titrated to the correct dose), or (b) the titrated and graduated addition of rapid-acting insulin bolus dose to meals, starting with the largest meal (highest carbohydrate content) of the day, followed by the next largest meal and finally the smallest meal, based upon individualized glycemic goals. Increasing his detemir dose would not achieve the goal of blunting daytime postprandial glucose elevations and could lead to an increased risk of hypoglycemia. Adding glyburide at this point would not be a realistic option, as secretagogues do not seem to provide any additional benefit once insulin has been started.

Reference

71. Labs taken last year show Mr. Fontello had a serum creatinine 1.2mg/dL with an eGFR 61mL/min. Today, his serum creatinine is 1.6 mg/dL and his eGFR is 44 mL/min. Because guidelines indicate when a patient’s eGFR falls below 60mL/min, dose reduction of medications should be considered, you decide to adjust Mr. Fontello’s medication. In type 2 diabetes, which one of the following medications does not need to be considered for dose reduction?

A. Glyburide
B. Metformin
C. Insulin
D. Pioglitazone
E. Exenatide

CORRECT ANSWER: D

Rationale
20-30% of patients with type 2 diabetes develop moderate-severe renal disease (GFR<60mL/min). Pioglitazone does not undergo renal elimination and can therefore be used without restriction in chronic kidney disease. Metformin undergoes renal elimination and current U.S. guidelines suggest caution using in individuals with creatine ≥1.5 mg/dL (males) and creatine ≥1.4 mg/dL (females) as its use has been associated with lactic acidosis in patients with CKD. U.K. guidelines advise dose reduction of metformin at GFR of 45 ml/min and cessation with GFR of 30 ml/min. Exenatide is renally eliminated and its use should be discontinued at GFR<30 ml/min. In CKD, elimination of insulins are impaired and dose reduction should be
Glyburide should be avoided in CKD due to renal clearance as well as prolonged duration of action and active metabolites.

Reference


72. The list below indicates the ethnicities of the patients whose cases you have just reviewed. Please choose the correct order showing the relative risk of developing diabetes for each ethnicity in adults > 20 years.

A. Non-Hispanic blacks > Hispanic > non-Hispanic whites > Asian American
B. Hispanic > Non-Hispanic blacks > non-Hispanic whites > Asian American
C. Non-Hispanic blacks > Hispanic > Asian American > non-Hispanic whites
D. Hispanic > Non-Hispanic blacks > Asian American > non-Hispanic whites

CORRECT ANSWER: C

Rationale

After adjusting for population age differences, 2007-2009 national survey data for people diagnosed with diabetes, aged 20 years or older include the following prevalence by race/ethnicity:

- 7.1% of non-Hispanic whites
- 8.4% of Asian Americans
- 12.6% of non-Hispanic blacks
- 11.8% of Hispanics

Compared with non-Hispanic white adults, the risk of diagnosed diabetes was 18 % higher among Asian Americans, 66 % higher among Hispanics/Latinos, and 77 % higher among non-Hispanic blacks. Among Hispanics/Latinos compared with non-Hispanic white adults, the risk of diagnosed diabetes was about the same for Cuban Americans and for Central and South Americans, 87 % higher for Mexican Americans, and 94 percent higher for Puerto Ricans

Reference