CLINICAL PRACTICE GUIDELINE ADULT MEDICINE

DIABETES MELLITUS TYPE 2

BACKGROUND

Diabetes is a major contributor to sickness, catastrophic health events, and premature death.

Diabetes can be classified into 4 categories:

- Type 1 diabetes (due to β-cell destruction, usually leading to absolute insulin deficiency)
- Type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin resistance)
- Other specific types of diabetes due to other causes, e.g., genetic defects in β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced (such as in the treatment of HIV/AIDS or after organ transplantation)
- Gestational diabetes mellitus (GDM) (diabetes diagnosed during pregnancy that is not clearly overt diabetes)

DIAGNOSIS[1]

- Fasting Plasma Glucose (FPG) ≥ 126 mg/dl (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.
- 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT) ≥200 mg/dl (11.1 mmol/L)
- Symptoms of hyperglycemia or hyperglycemic crises, random blood sugar ≥200 mg/dl (11.1 mmol/L)
- Hemoglobin A1C ≥6.5%)

Some individuals have higher than normal glucose levels but do not meet the criteria for diabetes. Impaired fasting glucose (IFG) is defined as FPG levels 100–125 mg/dL [5.6–6.9 mmol/L], or impaired glucose tolerance (IGT) with 2-h PG OGTT values of 140–199 mg/dL [7.8–11.0 mmol/L], or A1C levels between 5.5 and 6.5%. Impaired glucose metabolism correlates with an increased risk of the future development of diabetes.[3,4,5]

TREATMENT & GOALS

The goals for managing patients with diabetes include eliminating symptoms, and preventing or slowing disease progression, such as microvascular disease. HbA1c, also called A1C, is a measure of the amount of glucose attached to hemoglobin. The higher the glucose levels over the previous 2-3 months, the higher the A1C. The A1C test is used to monitor the glucose levels of patients who have been diagnosed with diabetes. In people who have hemoglobin variants such as HbS (sickle cell trait), some A1C tests give falsely high or low readings that can lead to the over-treatment or under-treatment of diabetes.[2]

Reduction of the A1C is correlated with decreases in microvascular disease. Lowering A1C to or below 7% is the accepted standard of practice. However, A1C must be individualized based on numerous factors, such as adherence, literacy levels, patient motivation, co-morbid conditions, age, and life expectancy. For example, it may be reasonable to lower A1C goal to less than 6.5 for when it can be achieved safely in healthy patients, without co-morbid conditions and who have minimal risk of hypoglycemia. Less stringent A1C goals (such as <8%) may be advisable for patients who are at risk for hypoglycemia, have limited life expectancy, or extensive comorbid conditions.[6]

RECOMMENDATIONS

- An appropriate DM management plan should include lifestyle practices (such as dietary and exercise modifications), weight management, medications, tools for blood glucose self-monitoring,

regular health assessments, including laboratory assessments and monitoring for complications. Management should include strategies for addressing blood sugar fluctuations, lipids, blood pressure, and kidney function. Patient education is crucial in ensuring adherence to a plan of action. Treatment goals include lowering glycemic load, managing co-morbidities, and reducing risk of complication.

- Pharmacologic intervention is helpful in lowering the A1C and managing symptoms. Optimize glucose control to slow the progression of nephropathy, and minimize adverse risk events such as hypoglycemia.

- The American Academy of Clinical Endocrinologist (AACE) recommends use of the A1C as the prompt for medication management options at the point of diagnosis.[6]

A1C≤ 7% at the time of diagnosis

Initiate monotherapy. Metformin, if no contraindications, is the preferred initial agent and is a standard part of most combination treatments. The dose of metformin should be titrated to its maximally effective dose (usually 2000 to 2500 mg per day in divided doses) over one to three months.

A1C≥ 7.5% at the time of diagnosis

Initiate dual therapy that includes Metformin and another oral agent. If noninsulin dual therapy at maximal tolerated doses does not achieve or maintain the A1C target over 3 months, add a third agent.

If noninsulin triple therapy at maximal tolerated doses does not achieve or maintain the A1C target in three months add insulin therapy

A1C≥9% at the time of diagnosis

If patient is asymptomatic initiate dual or triple therapy. If patient is symptomatic start insulin therapy with or without insulin.

A1C ≤7%	A1C≥7.5%	A1C≥7.5%	Not at goal on Triple Therapy	A1C≥ 9% Newly Diagnosed	
				Asymptomatic	Symptomatic
Monotherapy	Dual Therapy with Metformin or other first line agent	Triple Therapy	Intensify treatment with insulin therapy ± other agents	Dual or triple therapy	Insulin ± other agents
Metformin GLP-1RA DPP4-i AG-i	GLP-1 RA DPP4-1 Colesevelam Bromocriptine QR AG-i	GLP-1 RA DPP4-1 Colesevelam Bromocriptine QR AG-i			
Use with caution	Use with caution	Use with caution			
SGLT-2 TZD SU-GLN	TGD SGLT-2 Basal Insulin SU/GLN	TGD SGLT-2 Basal Insulin SU/GLN			

- Monitor metabolic profiles, including serum creatinine, glomerular filtration rates, lipids and urine microalbumin. The lipid and urine microalbumin monitoring is to be at least annually.
- If there is evidence of microalbuminuria, even in the absence of hypertension, the evidence supports the use of an angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB).

- Maintain the blood pressure less than 140/90.[7] If treatment for hypertension is indicated, evidence supports the initiation of an angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB). If monotherapy is insufficient, refer to hypertension guidelines for appropriate guidance.[9]
- Manage lipid disorders and maintain within acceptable parameters (LDL cholesterol <100 mg/dL, HDL cholesterol >50 mg/dL, and triglycerides <150 mg/dL.
- For those patients at increased cardiovascular risk (10-year risk >10%), add an antiplatelet agent, such as aspirin therapy (75–162 mg/day) as a primary prevention strategy. In cases of documented aspirin allergy, clopidogrel (75 mg/day) should be used.
- Morbidly obese patients may benefit from bariatric surgery, which has been shown to improve glycemic control. This should be discussed as a reasonable alternative with carefully selected patients.
- Advise patients not to smoke or use tobacco products. Tobacco cessation counseling and smoking cessation products are advisable.
- Psychosocial screening and refer for treatment if underlying mental health problems.
- Immunizations
  - Hep B series, if non-immune status
  - Annual influenza vaccine
  - Pneumococcal polysaccharide vaccine as recommended:
    - Administer pneumococcal polysaccharide vaccine 23 (PPSV23) to all patients with diabetes ≥2 years of age.
    - Adults ≥65 years of age, if **not** previously vaccinated, should receive pneumococcal conjugate vaccine 13 (PCV13), followed by PPSV23 6–12 months after initial vaccination.
    - Adults ≥65 years of age, if **previously** vaccinated with PPSV23, should receive a follow-up ≥12 months with PCV13.

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- Annual specialty evaluations, more often if clinically indicated
  - Podiatry evaluation, including screening for neuropathy
  - Ophthalmology, including dilated retinal examination
  - Nutrition assessment by nutritionist, registered dietician, or diabetes educator
  - Oral/dental

Diabetes Drug Categories (This list is not all inclusive, refer to current information)

Category	Action
Biguanide	Enhance insulin sensitivity
Glucagon-like peptide-1 (GLP-1)	Stimulate receptors to increase insulin production, inhibits post-prandial glucagon release
Incretin mimetics (GLP-1) receptor analogues	Increase production of insulin and decrease production of glucagon
Alpha-glucosidase inhibitors (AG-i)	Slow digestion of carbohydrates in the small intestine
Thiazolidinedione/ Glitazones (TZD)	Improve insulin sensitivity and reduce triglyceride levels
Dipeptidyl peptidase-4 (DPP-4) inhibitors Gliptins (DPP4 Inhibitors)	Stimulate production of insulin and reduce production of glucagon particularly during digestion. Prevent the protein dipeptidyl peptidase-4 from destroying incretin hormones
Amylin analogues	Pancreatic hormone helps to suppress glucagon release
Sodium-glucose cotransporter 2 inhibitor (SGLT2)	Reduces reabsorption of filtered glucose, increases urinary glucose excretion

Sulfonylurea-first generation	Stimulates pancreatic insulin secretion *Not preferred by either ADA or AACE*
Sulfonylurea-second generation	Stimulates pancreatic insulin secretion *Glyburide not recommended by ADA*
Sulfonylurea-third generation	Stimulates pancreatic insulin secretion
Bile acid sequestrants	Reduces hepatic insulin resistance
Dopamine agonist	May reverse metabolic changes associated with insulin resistance
Injectable Insulin	Additional insulin to overcome insulin resistance

SOURCES

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All web-based sources were accessed on 10/15/15.