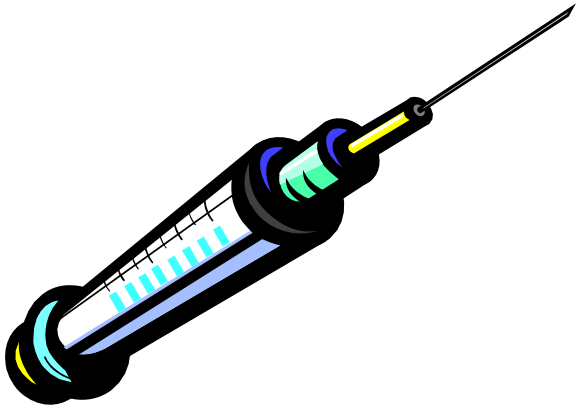
Treating Patients with Type 2 Diabetes Mellitus –Office setting



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- **What are the three criteria for making a diagnosis of Type 2 diabetes mellitus?**

Criteria - Diagnosis Type 2 Diabetes Mellitus

- **Any random glucose value ≥ 200 mg/dL and classic symptoms**
- **Fasting glucose levels ≥ 126 mg/dL on two separate days**
- **2 hour value ≥ 200 mg/dL after 75 gm of anhydrous glucose dissolved in water**

In the absence of overt hyperglycemia, testing should be repeated a 2nd day

Hemoglobin A1c

- What is hemoglobin A1c?
- How is it utilized to diagnosis or treat diabetes?

Hemoglobin A1c

- Glucose binds irreversibly to red cells to form hemoglobin A1c for life span of that red cell
- Value weighted to the previous 30 days (~50%), 30-60 days & 90 days (~25%)
  - Do not have to wait 90 days to see meaningful change if significant change in glucose
- ADA guidelines
  - A1C should not be used to screen for diabetes
  - Should not be used to make the diagnosis!

Initial & Ongoing Treatment

- Diet and weight loss if overweight
  - Give newly diagnosed patients 4 weeks of diet and exercise, unless FPG > 250 mg/dL
  - Many experts now recommend starting medication at the same time regardless of the FPG
- Exercise to help lose weight

- What dietary instructions will you give your patients this week?

Dietary Instructions

- Eat 6-8 fruits or vegetables a day
- Eat two servings fiber (cereals, whole grain breads, etc) every day
- Use only low fat (skim) dairy products
  - Milk, cheese, yogurt, ice cream
- Moderation for less nutritious food items

Dietary Instructions

- Tell patients what to add to their diet first
- Avoid telling patients just what not to eat
- Consistency of diet is the most important guideline!
  - Consistency on a weekly basis

Natural History of Disease

- Once a patient has the disease, it will progress no matter what the therapy
  - No evidence treatment alters the natural history of diabetes
  - Evidence tight control reduces risk of microvascular complications (but not mortality)

Natural History of Disease

- Patients will require more & more medication to control their glucose
  - Exception could be patients with dramatic weight loss from surgery

Pharmacologic treatment options

- Once the decision is made to start medication, what classes of medications are available?

Diabetic Medications

- Sulfonylureas
- Biguanide
- Thiazolidinediones
- Alpha-glucosidase inhibitors
- Sort-acting secretagogues
- DPP-4 inhibitors
- Incretin mimic
- Amylin analog
- Insulin
  - Short acting
  - Long acting
  - Basal (peakless)

Sulfonylurea

- Increase insulin secretion
  - Need some beta cell function to be effective
- Weight gain is a common side effect

Biguanide - Metformin

- Suppresses hepatic gluconeogenesis
- No associated weight gain
- Contraindicated:
  - With renal insufficiency (male creatinine >1.5; women >1.4)
  - With cardiac or pulmonary disease
- No risk of hypoglycemia if used alone
- Can cause lactic acidosis

Thiazolidinediones

- Reduce insulin resistance
- Associated with fluid retention
- May take 6-14 weeks to exert full hypoglycemic effect

Alpha-Glucosidase Inhibitors

- Acarbose (Precose) Glyset (Miglitol)
- Taken with first bite of meal interferes with hydrolysis of dietary disaccharides and complex carbohydrates- delays absorption
- Helps control post prandial glucose

Secretagogue – short acting

- Repaglinide (Prandin); nateglinide (Starlix)
- Stimulate insulin secretion from B-cells
- Quick onset (< 1 hr), short duration of action (≤ 4 hrs)
- Reduces post prandial hyperglycemia
  - Responds to meals – reduced response with no meal

Adjunctive Injection

- Exenatide (Byetta)
  - Synthetic peptide GLP-1 agonist (incretin mimic)
  - Potentiates insulin secretion
  - Injected subq am & pm (fixed dose)
  - No weight gain & usually weight loss
  - Endogenous incretins broken down in minutes by DPP-4 enzyme – not Byetta
- NOT FDA approved for patients using insulin

DPP-4 Inhibitor

- Sitagliptin (Januvia) 1st of new class approved
- Blocks DPP-4 from destroying endogenous incretin
- Minimal side effects
- Does not lower A1c as much as older less expensive medications

Under which clinical conditions would you use insulin for patients with type 2 diabetes?

Insulin Indications

- Significant hyperglycemia at presentation
- If decompensation occurs due to:
  - Acute injury, infection
- $A1_c$ not controlled despite 2 (or 3) oral drugs
- Surgery or pregnancy
- Allergy or serious reaction to oral agents

Every patient will eventually use insulin if they live long enough

Insulin – Risks

- Hypoglycemia
- Weight gain
  - Less if combined with metformin

Insulins

Insulin	Onset	Peak	Duration
Lispro	5 – 15 min	1 – 2 h	3 – 5 h
Aspart	5 – 15 min	1 – 2 h	3 – 5 h
Glulisine	5 – 15 min	1 – 2 h	3 – 5 h
Regular	30- 60 min	2 – 4 h	8 – 10 h
Inhaled	10- 20min	1 – 2 h	6 h
NPH	1 – 3 h	5-7 h	13 – 18 h
Glargine	1 – 2 h	Min peak	Up to 24 h
Detemir	1 – 2 h	Min peak	Up to 24 h

Insulin Dosage

- No maximum allowable dosage
  - Whatever amount it takes to control A1C
- When starting or increasing insulin be aggressive
  - Go up quickly – weeks not months to get control

Inhaled Insulin (Exubera)

- Short-acting bolus insulin
- Smoking is a contraindication
  - Increases rate & extent of absorption
  - Passive smoking reduces rate & extent – use with caution
- Use in asthma or COPD not recommended

Inhaled Insulin (Exubera)

- Spirometry prior to initiation
  - If FEV1 < 70% not to be used
- Dosage 0.05 mg/kg
  - Comes as 1 mg & 3 mg blister
    - Equivalent to 3 & 8 unit of insulin
- If need 3 mg dosage cannot substitute 3 - 1mg blisters
  - Get 30-40% higher insulin exposure
- Spirometry again at 6 months & annually
  - If FEV1 decreases >20% or 500 ml from baseline – discontinue indefinitely

Inhaled Insulin (Exubera)

- Use mainly in patients absolutely afraid of injections or severe problems at injection site
- Since may require multiple inhalations
  - And increased cost
  - Risk of hypoglycemia
  - Unknown risk to long term lung function

Adjunctive Injection

- Pramlintide (Symlin) subq TID ac
  - Synthetic analog of human amylin
  - Amylin is co-secreted with insulin
- Indicated in patients who use rapid acting insulin with meals & need more reduction in post prandial glucose
  - Reduce dosage of rapid acting insulin 50%
- Nausea common side effect

Diabetic Medications

- Patients will eventually be on 2-3 of these medications
- You can combine them in any way
  - But the thiazolidinediones less likely to be single initial medication
- Keep adding medication until $A1_C$ is controlled

Monitoring patients with diabetes

- What clinical or laboratory findings should be regularly monitored in patients with Type 2diabetes?

Monitoring Diabetics

- Measure $\underline{A1_C}$ at least twice a year
  - More often if change therapy
  - Goal < 7.0% in patients in general
    - In an individual patient the goal is an A1C as close to normal (<6%) as possible without significant hypoglycemia

Monitoring Diabetics

- Measure BP every visit
  - Goal < 130/80

Neuropathy - Complication

- Annually screen for neuropathy
  - Sensory exam using nylon monofilament pressed to point of buckling
  - High risk if abnormal (positive)
- Patient advice
  - Never go barefoot
  - Inspect feet daily
  - Changes shoes twice daily
  - Before any tub bath test water temperature with their hands

Retinopathy - Complication

- Refer for annual screening by qualified eye professional

Nephropathy - Complication

- Measure microalbuminuria at least annually
  - Spot urine adequate if normal
  - Goal < 30 mg
- Measure creatinine annually and calculate estimated GFR

Cardiovascular Disease (MI & CVA)

- Measure lipids at least annually
  - Goal LDL < 100 mg/dL
- If LDL > 100 mg/dL
  - Treat with statin medication
  - Consider statin even if LDL is < 100 mg/dL
  - If patient has overt CAD goal is < 70 mg/dL

What other interventions have been proven to reduce mortality in type 2 diabetics?

Other Interventions

- Daily dose aspirin
- ACE inhibitor
- Eliminate tobacco use

Diabetes Mellitus

- Patient involvement can be extremely helpful in reaching therapeutic goals
  - A1C < 7.0 %
  - LDL < 100 mg/dL
  - BP < 130/80
  - Microalbuminuria < 30 mg
- Write them down for patients on a prescription pad to take with them

Summary Office Visit

- Ask about symptoms of complications
  - Cardiac, vascular, visual
- Review goals (A1C, LDL, BP, microalbuminuria)
- Exam should include fundi, cardiac, vascular, feet each visit
- Determine goal of next visit, be aggressive in the care of diabetes

Rules of dating!

- Never continue dating anyone who is rude to the waiter.
- If he or she says that you are too good for them - believe it.
- Everyone seems normal until you get to know them.

Rules of Dating!

- Being miserable because of a bad or former relationship just proves that the other person was right about you.
- Being happy doesn’t mean everything’s perfect; it just means you’ve decided to see beyond the imperfections.