Type 2 Diabetes: New Medication Management

Geralyn R. Spollett,
MSN, C-ANP, CDE

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Objectives

- Discuss the various classes of oral diabetes medications and their action in improving glycemic control.
- Describe the concept of insulin replacement and its use in type 2 diabetes supplemental and intensive management.
- List the action and clinical use of exenatide (Byetta) in type 2 diabetes.

Type 2 Diabetes

- Dual defects
  - Insulin resistance – cells do not use insulin available effectively
  - Insulin deficit- beta cells cannot keep up with the demand for insulin production

Goals of Diabetes Management

- Avoid Long term Complications
- Microvascular (small vessel disease)
  - Eye disease (retinopathy)
  - Renal disease (nephropathy)
  - Nerve disease (both peripheral and autonomic neuropathy)

Complications….

- Macrovascular (large vessel disease)
  - Cardiovascular disease
    - MI
    - CHF
    - Cardiomyopathy
    - Elevated Blood Pressure
- **Vascular Disease is the single largest causative factor in the mortality of those with diabetes**

Maintain Medical Nutrition Therapy (MNT)

- Control portion sizes
- Aim for consistency in meal timing
- Eat well balanced meals
- Avoid excessive salt and fat
- Sugar may be used as part of a mixed meal
- Avoid fluctuations in weight

Case Study 1

- Lee, 43yo, computer programmer has a routine physical exam for work
- FBG 233 mg/dl- no S/S of hyperglycemia
- + FH-type 2 DM (mother , sister)
- BMI 32
- Active- walks 2 miles, 4 days/week

Lee

- Repeated FBG 160 mg/dl
- HbA1C 7.4 % (4-6%)
- LFTs normal
- Serum Creatinine 0.9 mg/dl (0.7- 1.2)
- 'lytes, CBC, U/A, micral all WNL

Physical Exam

- Fit appearing man
- Weight 217 lbs Ht 5'9"
- BP 122/82 2 hr pp Cap BS 2o6 mg/dl
- Thyroid- non-palpable
- CV- RRR
- Feet- DP 2+ bil, callused metatarsal heads, ecchymotic great toe nails, + monofilament

Assessment and Plan

- Lee has Type 2 DM
- Referral for MNT
  - Address healthy eating
  - Increase fruits/vegs and limit frank use of sugars (he drinks 24 oz Kool-Aid)
- Encourage current exercise program
  - Discuss footwear
  - Podiatry referral

Pharmacologic Options

To improve his glycemic control, Lee will need a

- A. TZD
- B. Biguanide
- C. SU
- D. Meglitinide

SULFONYLUREAS

- First generation-Discovered in the 1950's
- **Primary effect is to increase beta cell secretion of insulin**
- Multiple trade names- glyburide, glipizide, glimepiride- each with specific dosing
- In general, must be given BID to achieve 24 hr coverage

BIGUANIDES

- Reduces hepatic glucose output, lowering fasting glucose levels
- Metformin (GLUCOPHAGE)
  - 500, 850, 1000 mg tablets, dose efficacy achieved at 1000mg BID
  - Serum creatinine must be tested before Rx
    1.4 mg/dl -women, 1.5mg/dl- men
  - Intact liver function, no alcohol abuse, good cardiac and renal function

Biguanides, cont

- Metformin is now available in combination with glyburide- 1.25/250, 2.5/500, 5/500
- Trade name = Glucovance
- Long-acting Metformin = Glucophage XR doses: 500, 1000 mg

MEGLITINIDES

- A new class of oral agents with action similar to sulfonylureas
- Works at the pancreas to stimulate insulin production
- Drug action initiated by a rise in glucose levels occurring with food intake

Repaglinide (PRANDIN)

- Medication is taken only when a meal is eaten, reduces rise in glucose level after the meal
- Shorter duration of action than sulfonylureas
- Results in less hypoglycemia
- Dose 0.5-2.0 mg tablets
  Maximum dosage/day 12 mg

Nateglinide (STARLIX)

- Available in 120 mg only
- Action similar to repaglinide
- Limited hypoglycemic potential because of specificity to meal timing

Thiazolidinediones (TZDs)

- Increase uptake by muscle and fat
- Decrease insulin resistance
- Efficacy noted 1-4 weeks after initiating drug treatment- may continue to improve up to 12 weeks
- Rare liver toxicity
  LFTs monitored q 2 mos x 1 yr

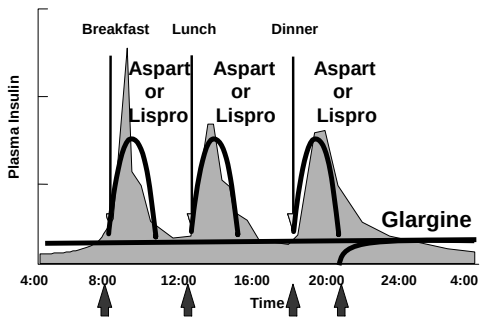
TZDs

- Pioglitazone (ACTOS)
  - 15, 30, 45mg tablets given QD
  - S/E weight gain, fluid retention
- Rosiglitazone (AVANDIA)
  - 2, 4, 8mg tablets given BID, QD
  - S/E increased lipid levels , wt gain, edema

Insulin Therapy

- Safe- no cross reaction with any medications, no allergic reactions, natural substance
- Must be given by injection
  - Ease of use with pen device
  - Inhaled insulin available
- Many different types
- Individually designed insulin program

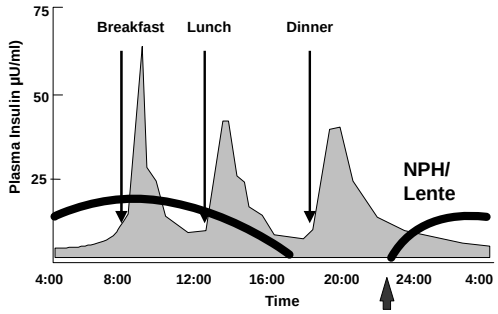
Basal + Meal-Related Regimen
Glargine + Aspart/Lispro



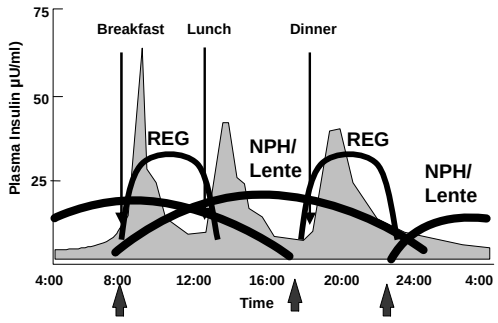
Types of Insulin

- Rapid-acting- Humalog (lispro) or Novalog(Aspart), Apidra (glulysine)
  - Used before meals or when ill
- Fast- acting- Regular insulin
  - May be used for meal coverage
- Intermediate- NPH, Lente (Humulin N , Novolin N)
  - Can be used to give 12-18 hr coverage

Intermediate-Acting Insulin
Bedtime Only



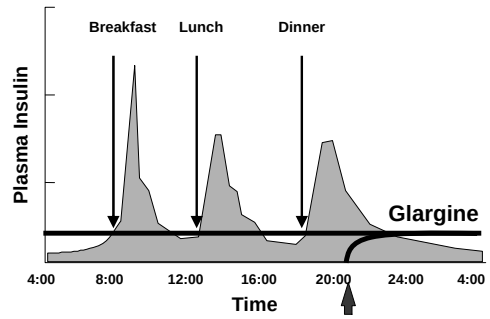
Split-Mixed Regimen
Bedtime Intermediate Insulin



Glargine (LANTUS)

- 22-24 hr and provides a base of insulin to improve glucose levels
- Can be used with either rapid-acting insulin or short-acting oral meds (Starlix, Prandin) to help with meal glucose levels

Long-Acting Insulin Glargine Bedtime Only



Detemir (Levemir)

- QD or BID dosing
- Available in a pen device
- Use with a rapid-acting insulin for basal bolus therapy

Mrs R M

- 78 year old with Type 2 DM
- 12 years duration, previously well-controlled on glyburide 5 mg bid and glucophage 850 mg tid
- She develops CHF and creatinine increases to 1.7 mg/dl
- Glucophage must be discontinued

Mrs RM 2

- With glyburide alone, glucose levels rise.
- A1C increases to 8.2%
  - Fasting glucose levels 122-167 mg/dL
  - Presupper glucose levels 118-220 mg/dL
- Therapy changes are necessary to regain control

Insulin Choices

- Choices:
  - Evening intermediate insulin
  - Humalog Mix 75/25 or 70/30 Novolog presupper or bid
  - Glargine once daily
- Considerations:
  - Hypoglycemia
  - Ease of use
  - Best effect for patient's glucose needs

Lifestyle Issues Influence Decision

- Delivery method
  - Vial/syringe
  - Pen device
- Timing of Injection
  - Meal schedule

  Activity level

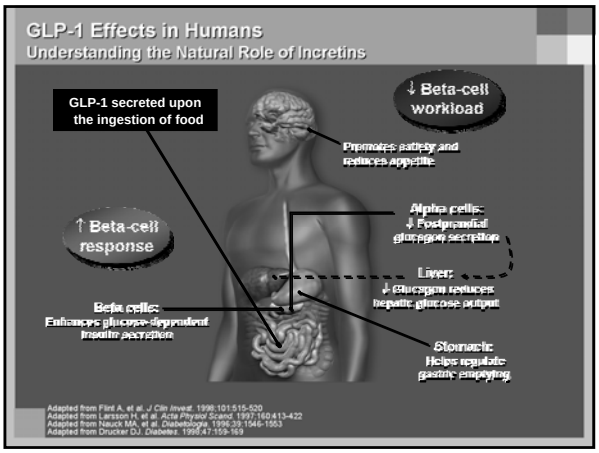
  Other medications

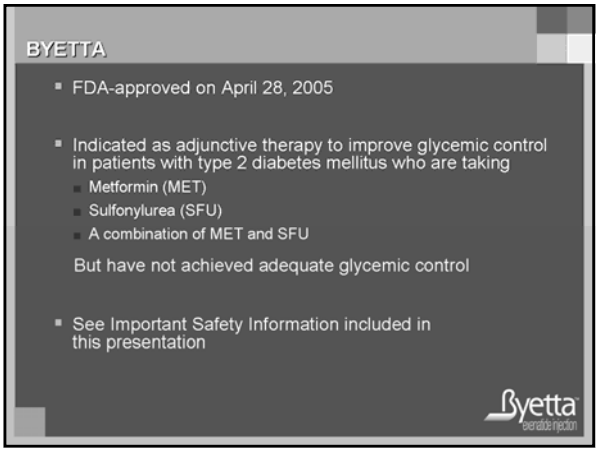
The Decision

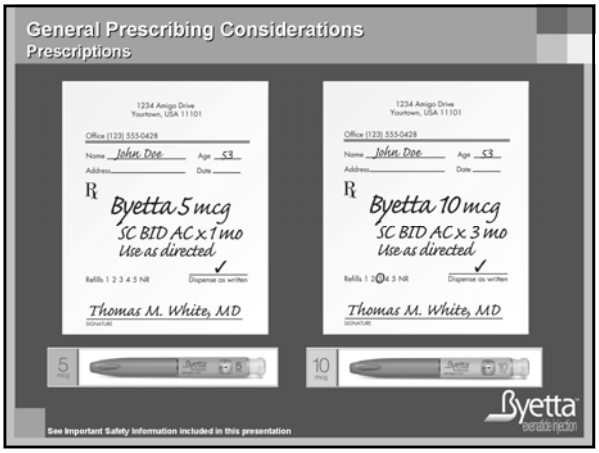
- Start Lantus
- Reduce or stop glyburide
- Monitor fasting glucose level
- Goal – Less than 130 mg/dl at fasting

Byetta

- Injectable hormone to improve glucose control
- Given within an hour prior to breakfast and supper
- Side effect : Nausea, usually subsides within the first 7-14 days
- Pen delivery
  - Start at 5 mcg then advance to 10 mcg as tolerated


GLP-1 Effects in Humans
Understanding the Natural Role of Incretins
GLP-1 secreted upon the ingestion of food
↓ Beta-cell workload
Promotes satiety and reduces appetite
↑ Beta-cell response
Alpha cells: ↓ Postprandial glucagon secretion
Liver: ↓ glucagon reduces hepatic glucose output
Beta cells: Enhances glucose-dependent insulin secretion
Stomach: Helps regulate gastric emptying
Adapted from Flint A, et al. J Clin Invest. 1998;101:515-520
Adapted from Larsson H, et al. Acta Physiol Scand. 1997;160:413-422
Adapted from Nauck MA, et al. Diabetologia. 1996;39:1546-1553
Adapted from Drucker DJ. Diabetes. 1998;47:159-169


BYETTA
FDA-approved on April 28, 2005
Indicated as adjunctive therapy to improve glycemic control in patients with type 2 diabetes mellitus who are taking
Metformin (MET)
Sulfonylurea (SFU)
A combination of MET and SFU
But have not achieved adequate glycemic control
See Important Safety Information included in this presentation
Byetta
exenatide injection


General Prescribing Considerations
Prescriptions
1234 Amigo Drive
Yourtown, USA 11101
Office (123) 555-0428
Name John Doe Age 53
Address Date
℞ Byetta 5 mcg
SC BID AC x 1 mo
Use as directed
✓
Refills 1 2 3 4 5 NR Dispense as written
Thomas M. White, MD
SIGNATURE
1234 Amigo Drive
Yourtown, USA 11101
Office (123) 555-0428
Name John Doe Age 53
Address Date
℞ Byetta 10 mcg
SC BID AC x 3 mo
Use as directed
✓
Refills 1 2 3 4 5 NR Dispense as written
Thomas M. White, MD
SIGNATURE
5 mcg
10 mcg
See Important Safety Information included in this presentation
Byetta
exenatide injection

Byetta Case Study

- Mary age 45, type 2 diabetes x 12 years
- Medications: Glipide ER 10 mg BID, Metformin 1000 mg BID
- Has edema with Actos (pipglitazone) stopped 2 years ago
- Glucose control deteriorating- A1C now 7.6%
- Overweight and has not been able to lose more than 10 lbs

Steps to Initiation

- Education re: use of pen, timing of medication, possible side effects
- Diet reviewed with patient
- Monitoring glucose control with SMBG
- Hypoglycemia: may need to reduce the dosage of glipizide ER

Sitagliptin (Januvia)

- Works to inhibit the chemical that breaks down GLP-1
  - May be used with metformin, 'glitazones or alone
- Classified as a DPP4 inhibitor
- Weight neutral

How to use Sitagliptin (Januvia)

- Given as an oral medication- 100 mg QD
  - Lower doses used if creatinine clearance is impaired (25, 50 mg)
- Side effects-nasopharyngitis, URI, headache
- Monitor digoxin as Januvia may increase concentration