General Principles of Use of Insulin in Diabetes

Which Patients need Insulin

- All patients with type 1 diabetes
- Secondary diabetes due to pancreatic insufficiency
- Type 2 diabetes with persistent hyperglycemia
- Clinical features in a patient with diabetes at any age
  - Marked unexplained recent weight loss
  - Short history with severe symptoms
  - Presence of moderate to heavy ketonuria
- Hyperglycemic emergencies

Insulin Preparations

- Biosynthetic human insulin - NPH, regular
- Synthetic insulin analog - glargine, lispro
- Animal-sourced insulins - pancreas of cows, pigs

Human versus Analogs

- Human insulin preparation:
  - Time to peak, duration of action do not replicate endogenous insulin
- Very rapid-acting insulin analogs:
  - Faster, shorter duration of action than regular insulin (premeal)
- Long-acting analogs
  - Longer, flatter profile than NPH (basal)

Rapid Acting Insulins

- Include:
  - Lispro
  - Aspart
  - Glulisine
- Faster onset (5 -15 min)
- Peak action within 45 – 75 min
- Shorter duration of action (2 – 4 hours)
- Reduction in hexamer formation

Long Acting Insulin

- Neutral protamine lispro:
  - Protamine-based suspension lispro
  - Activity similar to NPH
- Insulin glargine:
  - Precipitates in tissue, forming hexamers
  - Duration of action of 24 hours
  - Cannot be mixed with rapid-acting insulins

Long Acting Insulin

- Insulin detemir:
  - Acylated insulin
  - Less potent
  - Twice daily administration
  - Cannot be mixed with rapid-acting insulins
- Insulin degludec:
  - Long duration of action (>40 hours)
  - Can be mixed with rapid-acting insulins

Basal versus Bolus

- Basal:
  - Suppress hepatic glucose production
  - Maintain near normoglycemia in fasting state
- Prandial (premeal) bolus:
  - Cover extra requirements after food is absorbed

Basal

- Intermediate to long-acting preparations
- Administered OD, BD
- Can also be achieved by continuous infusion of a short, rapid-acting insulin via insulin pump

Bolus

- Short-acting, rapid-acting
- Provided as a premeal bolus

Insulin type	Onset of action	Peak effect	Duration of action
Lispro, aspart, glulisine	5 to 15 minutes	45 to 75 minutes	Two to four hours
Regular	About 30 minutes	Two to four hours	Five to eight hours
NPH	About two hours	4 to 12 hours	18 to 28 hours
Insulin glargine	About two hours	No peak	20 to >24 hours
Insulin detemir	About two hours	Three to nine hours	6 to 24 hours*
NPL	About two hours	Six hours	15 hours
Insulin degludec	About two hours	No peak	>40 hours

Insulin Therapy

- Conventional insulin therapy:
  - Simpler insulin regimens
    - Single or two daily injections of regular and NPH insulin
    - Mixed together
    - Fixed amounts before breakfast, dinner
  - Unlikely to achieve target A1C levels

Insulin Therapy

- Intensive insulin therapy:
  - More complex regimens:
    - Separate basal insulin delivery
    - Superimposed doses of insulin bolus

Determinants of Insulin Efficacy

Type of Insulin

- Due to variable absorption of insulin

Size of Subcutaneous Depot

- Variability in absorption is increased and net absorption is reduced with increasing size of subcutaneous depot

Injection Technique

- Same with insulin syringes and pen injectors
- Angle / depth of penetration
  - Very shallow insertion can cause painful intradermal injection that is not well absorbed
  - Perpendicular injection in a lean area may result in intramuscular injection

Sites of Injection

Sites of Injection

- Include:
  - Upper arms
  - Abdominal wall
  - Upper legs
  - Buttocks
- Absorbed fastest from abdominal wall, slowest from leg, buttock
  - Pre-meal bolus to be injected in abdominal wall
  - Night dose on leg to ensure duration of action through the night

Alterations in Subcutaneous Blood Flow

- Insulin absorption is reduced by smoking
- Increased by any increases in skin temperature
  - Exercise
  - Saunas or hot baths
  - Local massage
- More marked with regular and rapid-acting insulins

Disadvantages

- Weight gain
  - Result in noncompliance
  - Average weight gain after 10 years of therapy was 7 kg
  - Greater with prandial than basal insulin
- Hypoglycemia
  - Less hypoglycemia than type 1
  - Basal insulin is associated with less hypoglycemia