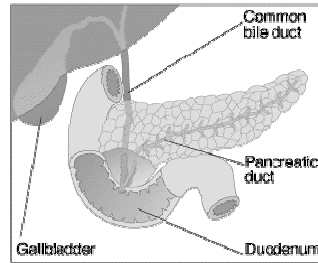


CHAPTER 31

Antidiabetic Agents

Pancreas



FUNCTIONS:

- produces enzymes that break down all categories of digestible foods (exocrine pancreas)

- secretes hormones that affect carbohydrate metabolism (endocrine pancreas).

- The Endocrine pancreas produces hormones such as insulin, glucagon and somatostatin.

Pancreas

Hormones produced in the Islets of Langerhans are secreted directly into the blood flow by (at least) four different types of cells:

- Insulin-producing Beta cells (65-80% of the islet cells)
- Glucagon-releasing alpha cells (15-20%)
- Somatostatin-producing delta cells (3-10%)
- Pancreatic polypeptide-containing PP cells (1%)

Role of Insulin

The actions of insulin on cells include:

- **Increased glycogen synthesis** – insulin forces storage of glucose in liver (and muscle) cells in the form of glycogen; **lowered levels of insulin cause liver cells to convert glycogen to glucose and excrete it into the blood.**

Role of Insulin

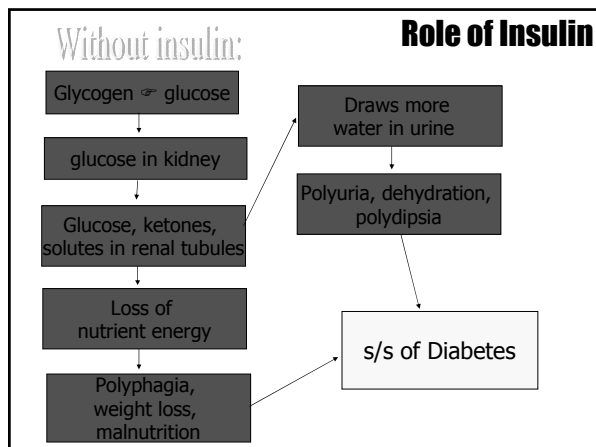
- **Increased fatty acid synthesis** – insulin forces fat cells to take in glucose which is converted to triglycerides; lack of insulin causes the reverse.
- **Increased esterification of fatty acids** – forces adipose tissue to make fats (ie, triglycerides) from fatty acid esters; lack of insulin causes the reverse.
- **Decreased proteinolysis** – forces reduction of protein degradation; lack of insulin increases protein degradation.

Role of Insulin

- **Decreased lipolysis** – forces reduction in conversion of fat cell lipid stores into blood fatty acids; lack of insulin causes the reverse.
- **Decreased gluconeogenesis** – decreases production of glucose from various substrates in liver; lack of insulin causes glucose production from assorted substrates in the liver and elsewhere.

Role of Insulin

- Increased amino acid uptake – forces cells to absorb circulating amino acids; lack of insulin inhibits absorption
- Increased potassium uptake – forces cells to absorb serum potassium; lack of insulin inhibits absorption = **hyperkalemia**
- Arterial muscle tone – forces arterial wall muscle to relax, increasing blood flow, especially in micro arteries; lack of insulin reduces flow by allowing these muscles to contract = **hypertension**



Diabetes Mellitus

- **Two types**
 - Type 1
 - Type 2
- **Hyperglycemia**
 - Fasting plasma glucose >126 mg/dL
- **Hypoglycemia**
 - Blood glucose level <50 mg/dL
- **Gestational diabetes**

TABLE 31-1

TYPE 1 AND TYPE 2 DIABETES: CHARACTERISTICS

Characteristic	Type 1 (IDDM)	Type 2 (NIDDM)
Onset	Juvenile-onset diabetes, age <20 yr	Maturity-onset diabetes, age >40 yr
Endogenous insulin	Little or none	Normal
Treatment	Insulin	Weight loss, diet and exercise, oral hypoglycemics; only 1/3 of all patients need insulin
Incidence	10% of cases	90% of cases
Insulin receptors	Normal	Decreased or defective
Body weight	Usually nonobese	Obese (80%)
Etiology	Autoimmune destruction of beta cells in the pancreas	Multifactorial genetic defects; strong association with obesity and insulin resistance resulting from a reduction in insulin receptors

IDDM, Insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus.

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Table 31-1 Type 1 and Type 2 Diabetes: Characteristics

Type 1 Diabetes Mellitus

- **Lack of insulin production or**
- **Production of defective insulin**
- **Affected patients need exogenous insulin**
- **Complications**
 - Retinopathy, nephropathy, neuropathy
- **Diabetic ketoacidosis (DKA)**
- **Oral antidiabetic agents not effective**

Type 2 Diabetes Mellitus

- **Most common type**
- **Caused by insulin deficiency and insulin resistance**
- **Many tissues are resistant to insulin**
 - Reduced number insulin receptors
 - Insulin receptors less responsive

Type 2 Diabetes Mellitus (cont'd)

- **Several comorbid conditions**
 - Glucose intolerance
 - Obesity
 - Dyslipidemia
 - Hypertension
 - Insulin resistance

Type 2 Diabetes Mellitus (cont'd)

- **Several comorbid conditions**
 - Hyperinsulinemia
 - Microalbuminuria (protein in the urine)
 - Enhanced conditions for embolic events (blood clots)
 - Heart disease

Types of Antidiabetic Agents

- **Insulins**
- **Oral hypoglycemic agents**

Both aim to produce normal blood glucose states

Insulins

- **Function as a substitute for the endogenous hormone**
- **Effects are the same as normal endogenous insulin**
- **Restores the diabetic patient's ability to:**
 - Metabolize carbohydrates, fats, and proteins
 - Store glucose in the liver
 - Convert glycogen to fat stores

Human-Based Insulins

- **Rapid acting**
 - Most rapid onset of action (15 minutes)
 - Shorter duration
 - Insulin aspart (NovoLog)
 - Insulin lispro (Humalog)
- Get complete information at**
http://www.novolog.com/consumer/assets/NovoLog_Prescribing_Info.pdf

Human-Based Insulins (cont'd)

- **Short acting**
 - Regular insulin (Humulin R, Novolin R)
 - The only insulin product that can be given by IV bolus, IV infusion, or even IM

Human-Based Insulins (cont'd)

- **Intermediate acting**
 - Isophane insulin suspension (also called NPH) (Humulin N, Novolin N)
 - Insulin zinc suspension (also called Lente) (Humulin L, Novolin L)
 - Both have a cloudy appearance
 - Slower in onset and more prolonged duration than endogenous insulin

Human-Based Insulins (cont'd)

- **Long acting**
 - Glargine (Lantus)
 - Clear, colorless solution
 - Extended insulin zinc suspension (Ultralente, Humulin U)
 - White, opaque solution

Human-Based Insulins (cont'd)

- **Combination Insulin products**
 - NPH 70% and regular insulin 30% (Humulin 70/30, Novolin 70/30)
 - NPH 50% and regular insulin 50% (Humulin 50/50)
 - Insulin lispro protamine suspension 75% and insulin lispro 25% (Humalog Mix 75/25)

Sliding-Scale Insulin Dosing

- SC regular insulin doses adjusted according to blood glucose test results
- Typically used in hospitalized diabetic patients
- Subcutaneous regular insulin is ordered in an amount that increases as the blood glucose increases
- See example on p 522

TABLE 31-2
COMPARISON ACTIONS OF HUMAN INSULINS AND ANALOGS

Insulin Preparation	Onset of Action	Peak Action	Duration of Action
lispro*/aspart*	5-15 min	1-2 hr	4-6 hr
human regular	30-60 min	2-4 hr	6-10 hr
human NPH/Lente	1-2 hr	4-8 hr	10-18 hr
Ultralente	2-4 hr	8-14 hr	18-24 hr
glargine*	1-2 hr	Flat	24 hr

From Colwell JA: *Diabetes: hot topics*, Philadelphia, 2003, Hanley & Belfus.

*Insulin analog.

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TABLE 31-3
INSULIN MIXING COMPATIBILITIES

Type of Insulin	Compatible With
regular (Humulin R, Novolin R, Velosulin BR)	All insulins except glargine, Lente, and Ultralente (see below)
regular regular	Lente or Ultralente* NPH; may use mixture immediately or store for future use
insulin lispro (Humalog), insulin aspart (NovoLog)	Regular, NPH, Lente, and Ultralente; inject mixture 15 min before meal†
insulin glargine (Lantus)	Must give alone due to low pH of diluent
NPH 70% and regular insulin 30% (Humulin 70/30, Novolin 70/30)	Already premixed; do not mix with other insulins
NPH 50% and regular insulin 50% (Humulin 50/50)	
insulin lispro protamine suspension 75% and insulin lispro 25% (Humalog Mix 75/25)	

Table 31-3 Insulin Mixing Compatibilities
p. 519

*These combinations are not normally recommended unless patient is already adequately controlled on this mixture. If so, patient should standardize the length of time between mixing and injection because of chemical interactions that delay the onset of action of the regular insulin. For this reason this mixture must be used soon after preparation; it is not suitable for storage for future use. †Normally used as an alternative to regular insulin and therefore not usually given with it. NPH, Isophane insulin suspension.

Oral Antidiabetic Agents

- **Used for type 2 diabetes**
- **Treatment for type 2 diabetes includes lifestyle modifications**
 - Diet, exercise, smoking cessation, weight loss
- **Oral antidiabetic agents may not be effective unless the patient also makes behavioral or lifestyle changes**

Oral Antidiabetic Agents (cont'd)

- **Sulfonylureas**
 - Chlorpropamide (Diabinese), tolazamide (Tolinase), tolbutamide (Orinase)
 - Glimepiride (Amaryl), glipizide (Glucotrol), glyburide (DiaBeta)
- **Biguanides**
 - Metformin (Glucophage)

Oral Antidiabetic Agents (cont'd)

- **Alpha-glucosidase inhibitors**
 - Acarbose (Precose), miglitol (Glyset)
- **Thiazolidinediones**
 - Pioglitazone (Actos), rosiglitazone (Avandia)
 - Also known as "glitazones"

Oral Antidiabetic Agents: Mechanism of Action

- **Sulfonylureas**
 - Stimulate insulin secretion from the beta cells of the pancreas, thus increasing insulin levels
 - Beta cell function must be present
 - Improve sensitivity to insulin in tissues
 - Result: lower blood glucose levels

Oral Antidiabetic Agents: Mechanism of Action (cont'd)

- **Biguanides**
 - Decrease production of glucose
 - Increase uptake of glucose by tissues
 - Do not increase insulin secretion from the pancreas = does not cause hypoglycemia

Oral Antidiabetic Agents: Mechanism of Action (cont'd)

- **Alpha-glucosidase inhibitors**
 - Reversibly inhibit the enzyme alpha-glucosidase in the small intestine
 - Result: delayed absorption of glucose
 - Must be taken with meals to prevent excessive postprandial blood glucose elevations

Oral Antidiabetic Agents: Mechanism of Action (cont'd)

- **Thiazolidinediones**
 - Decrease insulin resistance
 - “Insulin sensitizing agents”
 - Increase glucose uptake and use in skeletal muscle
 - Inhibit glucose and triglyceride production in the liver

Oral Antidiabetic Agents: Indications

Used alone or in combination with other agents and/or diet and lifestyle changes to lower the blood glucose levels in patients with type 2 diabetes

Oral Antidiabetic Agents: Side Effects

- **Sulfonylureas**
 - Hypoglycemia, hematologic effects, nausea, epigastric fullness, heartburn, many others
- **Metformin (biguanide)**
 - Abdominal bloating, nausea, cramping, diarrhea, metallic taste, reduced vitamin B12 levels

Oral Antidiabetic Agents: Side Effects (cont'd)

- **Alpha-glucosidase inhibitors (Precose, Glyset)**
 - Flatulence, diarrhea, abdominal pain
- **Thiazolidinediones (Actos, Avandia)**
 - Moderate weight gain, edema, mild anemia, hepatic toxicity

Antidiabetic Agents: Nursing Implications

- **Before giving any drugs that alter glucose levels, obtain and document:**
 - A thorough history
 - Vital signs
 - Blood glucose level
 - Potential complications and drug interactions

Nursing Implications

- **Before giving any drugs that alter glucose levels:**
 - Assess the patient’s ability to consume food
 - Assess for nausea or vomiting
 - Hypoglycemia may be a problem if antidiabetic agents are given and the patient does not eat
 - If a patient is NPO for a test or procedure, consult physician to clarify orders for antidiabetic drug therapy

Nursing Implications

- **Keep in mind that overall concerns for any diabetic patient increase when the patient:**
 - Is under stress
 - Has an infection
 - Has an illness or trauma
 - Is pregnant

Nursing Implications

- **Thorough patient education is essential regarding:**
 - Disease process
 - Diet and exercise recommendations
 - Self-administration of insulin or oral agents
 - Potential complications

Nursing Implications

- **When insulin is ordered, ensure:**
 - Correct route
 - Correct type of insulin
 - Timing of the dose
 - Correct dosage
- **Insulin order and prepared dosages are second-checked with another nurse**

Nursing Implications

- **Insulin**
 - Check blood glucose level before giving insulin
 - Roll vials between hands instead of shaking them to mix suspensions
 - Ensure correct storage of insulin vials
 - **ONLY** insulin syringes, calibrated in units, are to be used to measure and give insulin
 - Ensure correct timing of insulin dose with meals

Nursing Implications

- **Insulin (cont'd)**
 - When drawing up two types of insulin in one syringe, always withdraw the regular insulin first
 - Provide thorough patient education regarding self-administration of insulin injections, including timing of doses, monitoring blood glucoses, and injection site rotations

Nursing Implications

- **Oral antidiabetic agents**
 - Always check blood glucose levels before giving
 - Usually given 30 minutes before meals
 - Alpha-glucosidase inhibitors are given with the first bite of each main meal
 - metformin is taken with meals to reduce GI effects

Nursing Implications

- **Assess for signs of hypoglycemia**
- **If hypoglycemia occurs:**
 - Give glucagon
 - Have the patient eat glucose tablets or gel, corn syrup, honey, fruit juice or nondiet soft drink
 - Or have the patient eat a small snack such as crackers or half a sandwich
 - Monitor blood glucose levels

Nursing Implications

- **Monitor for therapeutic response**
 - Decrease in blood glucose levels to the level prescribed by physician
 - Watch for hypoglycemia and hyperglycemia
 - Measure hemoglobin A_{1c} to monitor long-term compliance to diet and drug therapy
 - The A1C value is an index of mean blood glucose over the past 2-3 months but is weighted to the most recent glucose values.
 - Diabetes Association (ADA) recommends A1C as the best test to find out if a patient's blood sugar is under control over time. The test should be performed every 3 months for insulin-treated patients, during treatment changes, or when blood glucose is elevated. For stable patients on oral agents the recommended frequency is at least twice per year.

Hemoglobin A1C

HbA1c %	Mean Blood Glucose (mg/dL)	Average Plasma Glucose (mg/dL)	Interpretation
4	61	65	Non-Diabetic Range
5	92	100	
6	124	135	
7	156	170	Target for Diabetes in Control
8	188	205	Action Suggested according ADA guidelines
9	219	240	
10	251	275	
11	283	310	
12	314	345	