Lecture 6 & 7

Use of insulin in diabetes
and
Management of diabetic ketoacidosis

Objectives:

★ **Not given**

- Additional Notes
- Important
- Explanation –Extra-

★ before starting, please check our endocrine block correction

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com

Diabetes Mellitus

1-Definition

Is a Chronic metabolic disorder characterized by **high blood glucose** level caused by **insulin deficiency** and sometimes accompanied with insulin Resistance.

2-Types

·**Type I:**

-due to autoimmune or viral diseases
-B-cells are destroyed.
-Absolute Deficiency of Insulin (Treated by Insulin)

·**Type II:**

-due to obesity, genetic factors

3-Complication

- **Cardiovascular problems:**
  –Micro-and macro-vascular complications.
- **Renal failure (nephropathy).**
- **Blindness (retinopathy).**
- **Neuropathy.**
- **Risk of foot amputation**

Fasting Blood glucose (No food for 8 h):

- **<100 mg/dl(5.6 mmol/l)= Normal**
- **100-125 mg/dl(5.6-6.9 mmol/l)= Prediabetes**
- **126 mg/dl (7 mmol/l) or higher on 2 separate tests = Diabetes**

Characteristic	Type 1	Type 2
Onset (Age)	Usually during childhood or puberty	Usually over age 40
Type of onset	Abrupt	Gradual
Prevalence	10-20%	80-90 %
Genetic predisposition	Moderate	Very strong
Defects	β-cells are destroyed	β-cells produce inadequate quantity of insulin
Endogenous insulin	Absent	Present (not enough)
Insulin resistance	absent	present
Nutritional status	Usually thin	Usually obese
Ketosis	Frequent	Usually absent
Clinical symptoms	Polydipsia, polyphagia, polyuria, Wt loss	Often asymptomatic
Related lipid abnormalities	Hypercholesterolemia frequent	Cholesterol & triglycerides often elevated
Treatment	Insulin	Oral hypoglycemics ± insulin

this part is just for reading, they will not ask about it in pharmacology

Effect of insulin

Fat

➢ **Liver:**

--Lipogenesis (+).

-Lipolysis (-).

- Inhibits conversion of fatty acids to keto acids.

➢ **Adipose Tissue:**

--Triglycerides storage (+).

--Fatty acids synthesis (+).

-Lipolysis (-).

Protein

➢ **Liver:**

-protein catabolism (-).

➢ **Muscle:**

--amino acids uptake (+)

--protein synthesis (+).

-glycogen synthesis (glycogenesis) (+).

-potassium uptake into cells (+).

Carbohydrate

➢ **Lowers of blood glucose by:**

- -↑Glucose uptake & utilization
- -↑Glycogen synthesis
- -↑Conversion of carbohydrate to fats.
- (-)Gluconeogenesis.
- ↑Glycolysis (muscle).

potassium

Increase potassium uptake into the cells

Types of insulin preparations (Insulin Analogues)

Types	• Ultra-short acting insulins	• Short acting insulins	• Intermediate acting insulin	• Long acting insulin
Characteristic	**e.g. Lispro, aspart** very fast onset of action and short duration	**e.g. regular humulin,** insulin fast onset of action and Short duration.	**e.g. NPH, lente**, Slow onset, intermediate duration of action.	**e.g. glargine, detemir** Slow onset and long duration of action.

Insulin preparations

	1-Ultra-Short acting insulins e.g. **Lispro**, **aspart**, **glulisine**	2-Short-acting (regular) insulins e.g. **Humulin R**, **Novolin R**
Physical Characteristics	❖ Clear solution at neutral pH Mimic the prandial mealtime insulin release	❖ Clear solution at neutral pH Mimic the prandial mealtime insulin release
Chemistry	Monomeric analogue	Hexameric analogue, soluble crystalline (more than 1 molecule) zinc insulin (Hexameric+crystalline zinc insulin) = The same structure of endogenous insulin So we can use it in pregnancy
Rout & time of administration	S.C.&I.V. 5-15 min (no more than 15 min) before meal , you can eat after taking it	S.C.&I.V 30 – 45 min before meal
Onset of action	5 – 15 min (S.C) (very fast onset of action)	30 – 45 min (S.C) fast action
Peak level =Maximum Effect	30 – 90 min	2 – 4 hr
Duration	3 –5hr (very short duration)	6 – 8 hr short duration

Insulin preparations

	1-Ultra-Short acting insulins e.g. **Lispro**, **aspart**, **glulisine**	2-Short-acting (regular) insulins e. g. **Humulin R**, **Novolin R**
Usual administration	2 – 3 times / day or more if the patient skip the meal, He must also skip the insulin	2 – 3 times/day or more
Indication	1-postprandial hyperglycemia (S.C) (Postprandial =after eating) 2-emergency diabetic ketoacidosis (I.V) 3-Preferred for external insulin pump (Lispro does not form hexamers)	1-postprandial hyperglycemia (S.C) (Postprandial =after eating) 2-emergency diabetic ketoacidosis (I.V) **Can be used in pregnancy**

★ Advantages of Insulin Lispro vs Regular Insulin:

1-Rapid onset of action (patients will not wait long before they eat).

2-Its duration of action is no longer than 3-4 hrs regardless of the dose.

3-Decreased risk of postprandial hypoglycemia.

4-Decreased risk of hyperinsulinemia.

Intermediate acting insulins

e.g.Isophane (NPH), Lente insulin (they are both equicalent in activity)

Isophane (NPH)	Lente insulin
	·Mixture of 30% semilente insulin + 70% ultralente insulin.
•Turbid suspension at neutral pH.	•Turbid suspension at neutral pH.
•Given S.C.only.	•Given S.C.only.
•Onset of action 1-2 h. •Peak serum level 5-7 h. •Duration of action 13-18 h.	•onset of action (1-3 h) •Peak serum level 4-8 h. •Duration of action 13-20 h.
Not used in emergencies (diabetic ketoacidosis).	Not used in emergencies (diabetic ketoacidosis).

Notes :

1-Because they turbid we can not use them I.V so we *do not* use them in emergency.

2- We do not use them in postprandial hyperglycemia because they have long onset of action.

Insulin mixtures

•75/25 - 70/30 - 50/50 (NPH/regular). **•(NPL= NPH / lispro)(NPA= NPH / aspart)**

Benefits of insulin mixture :

- **we use the insulin mixture when we want to control postprandial hyperglycemia and the normal glucose level.**
- **Use in one syringe and avoid patient mistake while mixing them.**

Long acting insulins

Insulin glargine (lantus),Insulin detemir(Levemir)

Insulin glargine (lantus)

- Clear solution
- Slow onset of action 2 h.
- Given s.c.
- once daily
- Maximum effect after 4-5 h
- produce broad plasma concentration plateau (low continuous insulin level).
- Prolonged duration of action (24 h)
- Should not be mixed with other insulin.

★ Advantages of Insulin glargine over intermediate-acting insulins:

- Constant circulating insulin over 24 hr with no pronounced peak.
- More safe than NPH & Lente insulins (reduced risk of hypoglycemia).
- Clear solution(not require resuspension before use)

What are the route of administration of insulin ?

- Can not be given orally.
- Insulin syringes (s.c., arms, abdomen, thighs).
- Portable pin injector (pre-filled).
- Continuous S.C. infusion (insulin pump).
  - More convenient
  - Eliminate multiple daily injection
  - Programmed to deliver basal rate of insulin.

How insulin is degraded ?

- Half life of circulating insulin is 3-5 min.
- 60% liver & 40% kidney (endogenous insulin)
- 60% kidney & 40% liver (exogenous insulin)
- Should be stored in refrigerators & warm up to room temp before use.
- Must be used within 30 days.

What are the complication of insulin therapy ?

★ People with diabetes should have a medical ID with them at all times
★ Hypoglycemia(life threatening occurs when blood glucose < 50 mg/dl.)
★ Overdose of insulin ,Excessive (unusual) physical exercise , A meal is missed.

How it is treated?

1. Conscious patient: Oral glucose tablets, juice or honey.
2. Unconscious patient:20-50 ml of 50% glucose solution I.V. infusion, OR Glucagon (1 mg S.C. or I.M.)

★ Weight gain
★ Lipodystrophy & Lipohypertrophy at injection site
★ Hypokalaemia

Diabetic ketoacidosis

1-Definition

- Acute emergency that requires admission to hospital.
- It develops as a result of insulin deficiency

2-Characters

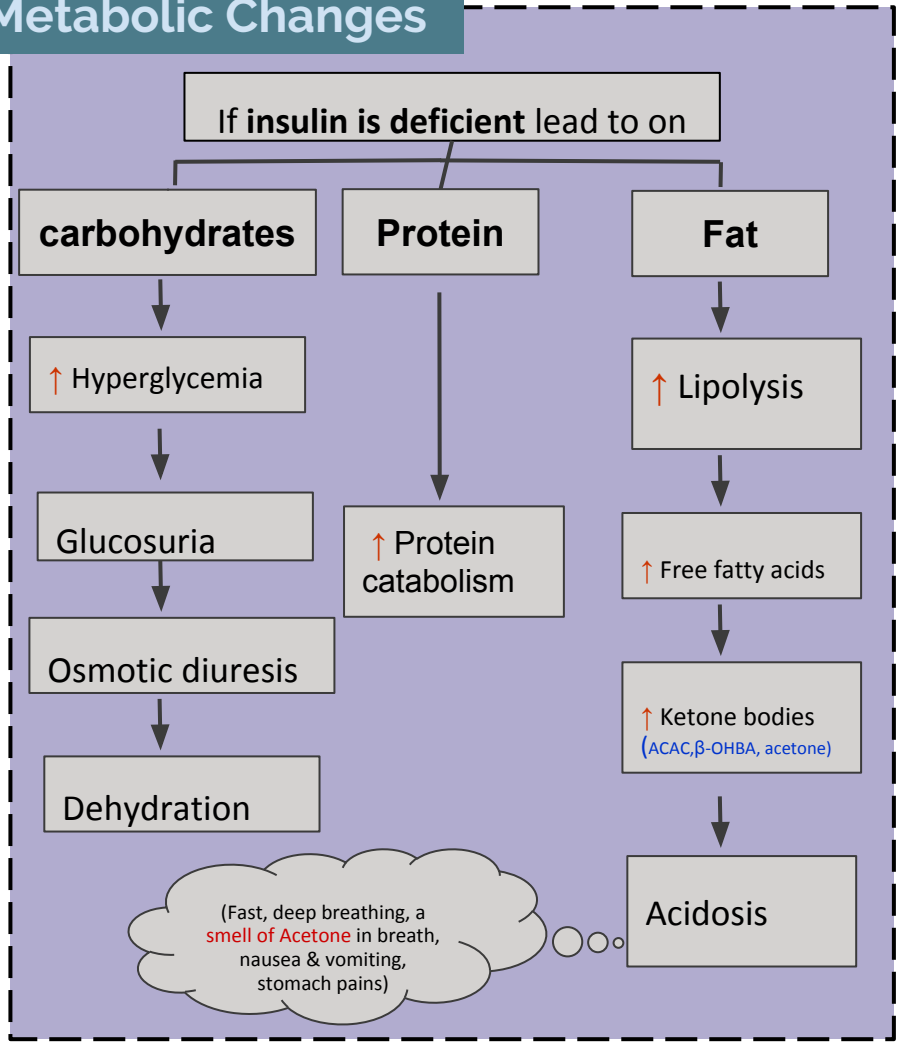
- Hyperglycemia
- Ketogenesis (Hyperketonemia)
- Metabolic acidosis → hyperventilation
- Glucosuria
- Polyuria
- Dehydration
- Electrolyte imbalance
- Thirst
- Polydipsia (increased drinking).

3-Treatment

Adequate correction of :

- Hyperglycemia *(insulin)*
- Dehydration *(fluid therapy)*
- Electrolyte deficits *(potassium therapy)*
- Ketoacidosis *(bicarbonate therapy)*

Metabolic Changes



Treatment of diabetic ketoacidosis

Insulin therapy	❑ Short acting insulins → Regular insulin, continuous IV infusion in small doses through an infusion pump. ❑ Insulin stops lipolysis and promotes degradation of ketone bodies.
Fluid therapy (Rehydration)	❑ Restore blood volume and perfusion of tissues. ❑ Infusion of isotonic saline (0.9% sodium chloride) at a rate of 15–20 mL/kg/hr
Potassium therapy	❑ potassium replacement must be initiated. ❑ potassium replacement is added to the infusion fluid to correct the serum potassium concentration.
Bicarbonate therapy	❑ Correct for metabolic acidosis ❑ Only if the arterial pH < 7.0 after 1 hour of hydration, bicarbonate therapy should be used *(sodium bicarbonate should be administered every 2 hr until pH is at least 7.0).*

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	Hypoglycemic coma (Excess insulin)	Hyperglycemic coma Diabetic ketoacidosis (Too little insulin)
Onset	Rapid	Slow - Over several days
Acidosis & dehydration	No	Ketoacidosis
B.P.	Normal	Subnormal or in shock
Respiration	Normal or shallow	air hunger
Skin	Pale & Sweating	Hot & dry
CNS	Tremors, mental confusion, sometimes convulsions	General depression
Blood sugar	Lower than 70 mg/100cc	Elevated above 200 mg/100cc
Ketones	Normal	Elevated

MCQs

1-Which one of the following is an intermediate acting insulins ?

A-lispro
B-regular humulin
C-NPH
D-lente insulin

2-Mohammed had diabetes type1 his friends surprised him with graduation party , the party start with cakes and drinks which of the following drugs is the best choice for mohammed ?

A-glulisine
B-isophane
C-novolin R
D-insulin glargine

3-Which one of the following drugs can be used in pregnancy?

A- humulin R
B-lispro
C-glulisine
D-insulin glargine

4-Which one of the following drugs can be used in emergency?

A-NPH
B-lente insulin
C-aspart
D-insulin detemir

5-Which of the following is true about Insulin therapy in treatment of diabetic ketoacidosis?

A-stop lipolysis
B-correct metabolic acidosis
C-correct the serum potassium concentration
D-restore blood volume and perfusion of tissues

6-In treatment of diabetic ketoacidosis sodium bicarbonate should be administered until pH is at least:

A-5.0
B-6.0
C-7.0
D-8.0

1-C&D
2-A
3-A
4-C
5-A
6-C

Good luck!

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