بسم الله الرحمن الرحيم

كل ما شرحه الدكتور في موضوع الـ

Diabetes Mellitus

المحاضرة السابعة

Therapeutics 1

الدكتور علي اليحوي

Done by Group 2

– Diabetes Mellitus Can be Divided in to:

Type1	Type2
• Absolute insulin. • Occurs → early (≤ 30 years). • Rapid or high onset. • Symptomatic. • DKA can be occur. • Dose → 0.5-0.6 unit/kg.	• Insulin deficiency or insulin resistance. • Occurs→ in elderly (≥ 30 years). • Slow onset. • Asymptomatic. • Dose → 0.6-2.5 unit/kg → due to insulin resistance.

Screening of Type 1 Diabetes

❖ If symptomatic → (polyuria – polyphagia – polydipsia – weight loss and dyspepsia).
- In dyspepsia, we should give pro-kinetic drug →which is (Metoclopramide).

❖ في هذه الحالة نعمل ← (autoimmune-antibody test).

Screening of Type 2 Diabetes

❖ Every 3 years starting at age 45 → to prevent asymptomatic complications.
❖ Earlier if BMI ≥ 25 kg\m^2 and any of the below:
- History of CVD.
- Impaired glucose intolerance → pre-diabetes (100-125 mg\dl or impaired fructose intolerance).
- Polycystic ovary syndrome due to → ↓ovarian function and ↑LH which both cause → hyper-insulin, insulin resistance and obesity.
  - In this case, use → Metformin.
- Low HDL or elevated TG.
- Hypertension.
- History of gestational DM.
- High risk of ethnicity.
- First degree relative with DM.
- Physical inactivity.
- This means that obesity (over weight) → related to DM → due to ↑insulin resistance.

Screening for Gestational Diabetes

❖ We should be doing four tests for pregnancy:

1-D.M test → recommendations by ADA:

- 24-28 weeks of gestation (at early prenatal visit if type 2 DM risk factor present).
- 75-gram oral Glucose Tolerance Test.

2-Hypertension test → because it may happen (pre-eclampsia or eclampsia)

- Pre-eclampsia blood pressure is → ≥ 160 mmHg and has severe proteinuria.
- And Eclampsia → causes convulsion.

3- Thyroid test → because fetus needs extra thyroxine.

- في هذه الحالة نعمل فحص للـ HCG ← الذي يعتبر (as thyroxine agonist).

4- Deep vein-thromboembolism test → because it is one of the most risk factor during pregnancy period.

Type 1 and 2 DM Diagnosis

- This means for the first time.
- Fasting blood glucose (≥ 126mg/dL).
- Random blood glucose (≥ 200mg/dL).
- Elevated plasma glucose post-OGTT (≥ 200mg/dL).
- HbA1c (≥ 6.5%) → other studies (≥ 7%).

Goal of Therapy in DM

❖ يعني شخص already معه diabetes mellitus أيش الأشياء التي يجب ان اعملها له:

(Prevent acute and chronic complications)

❖ Complications can be divided in to:

Acute Complication	Chronic Complication
❖ Hypoglycemia. ❖ DKA (Diabetic Ketoacidosis).	❖ Micro-vascular. ❖ Macro-vascular.

First ⇒ Acute Complication:

❖ 1- Hypoglycemia:

- blood sugar (< 70mg/dL).
- Patient can be in → (conscious state or unconscious state).
- Symptoms of hypoglycemia:

  1- Sweeting. 2- Polyphagia. 3- Epilepsy.

  4- Shocks (hypovolemic shock or septic shock → which causes multi-organ damage).

- Treatment of hypoglycemia:

  - Give → (IV Dextrose).
  - If Dextrose is not effective → give (1mg Glucagon IM).

❖ 2- DKA:

- يحصل أكثر شيء عند مريض الـ Type 1.
- أكثر مشكلة في الـ DKA يكون المريض ← under insulin treatment for long period.
- في هذه الحالة ممكن ان يصل سكر الدم الى أكثر من 400 mg/dL .

- Symptoms of DKA:

  1- Thirst. 2- Abdominal pain. 3- Mental statues changes. 4- Fruity breath. 5- Tachycardia. 6- Hyponatremia. 7- Hyperkalemia. 8- Ketones in blood and urine.

- Treatment of DKA:

  - Give fluid replacement (IV Na % depends on serum Na).
  - Give IV insulin (0.1 unit/kg bolus) → then give (0.1 unit/kg/hr drip of insulin).

- متى اعمل holding للـ insulin؟؟ عندما يكون تركيز الـ K اقل من (3.3 mEq/L) ← as baseline .
- ممكن يحصل بعض الأحيان نقص في تركيز الـ k في الدم ← لذلك اعطي في الـ infusion بوتاسيوم ← to maintain K requirements.

  - If K concentration reaches to less than (3.3 mEq/L) → must be given (KCl) as treatment.

- DKA Treatment Goals:

  - Serum glucose < 200 mg /dl (as goal target) and at least 2 of the following:
  - PH > 7.3 →this means changes from acidosis to alkalosis.
  - Serum bicarbonate ≥ 15mEq/L →due to deficiency of bicarbonate leads to ↑acidosis.
  - Anion gap ≤ 12 mEq/L.
  - Convert IV drips to subcutaneous insulin.

Second ⇒ Chronic Complications:

❖ 1- Micro-vascular:

- Retinopathy → must be taken (ophthalmic examination every year) especially in Type 2 DM.
- Neuropathy → which may be cause gangrene.
- Treatment of neuropathy → give Gabapentin → to reduce pain, also give low dose of TCAS (tri-cyclic antidepressant).
- Nephropathy:

  - The most risk factor due to → proteinuria → renal failure → death.
  - 40% of end stage chronic renal failure formed by DM.

- لذلك في هذه الحالة لازم اعمل فحص للبروتين في البول.

Normal proteinuria	E2 or Micro-albumin	Macro-albumin
<30 mg/g	30-300 mg/g	≥300 mg/g

- Treatment of nephropathy:

  - Protein restriction → 0.8 g/kg.
  - Give ACEIs or ARBs drugs → if both (ACEIs and ARBs) are not effective → give non-dihydropyridines (Verapamil-Diltiazem) to stabilize nephron.

❖ 2- Macro-vascular:

- Which are (cardiovascular –peripheral vascular disease – stroke – carotinosis).
  - مريض السكر بسب الـ resistance يعتبر مخزن للكولسترول ← حتى إذا فحصنا المريض وكانت النتيجة normal ← there are small particles of LDL which are more atherogenic.
  - وهذه الـ small particles ← لا تظهر الا عن طريق جهاز الـ (Electrophoresis).
- So give Statins regardless lipid profile in baseline.

ADA'S Glycemic Goals

- ❖ Fasting blood glucose → (70-130 mg/dL) (9-12hr).
- ❖ HbA1c → (< 7 % or <6.5 %):
  - Obtained every 3 months if uncontrolled.
  - Obtained every 6 months if at goal.
- ❖ Post-prandial → (< 180mg /dL).
- ❖ Glycemic goals in gestational DM are much more aggressive.

Other Goals of Therapy

- ❖ To prevent (micro and macro) vascular complications.
- ❖ Blood pressure → (< 180/85 mm Hg according to JNC 8).
- ❖ LDL-C → (< 100mg /dl) (ADA)
  - <70 mg/dl an option with CVD.
  - بسبب ان بعض الدراسات قالت إذا قل الـ LDL عن الـ (70mg/dL) فذلك يقلل من الـ ← risk factor of CVD.
- ❖ Triglyceride → < 150 mg /dl.
- ❖ HDL → ≥ 50(women), ≥40(men).
- ❖ HDL which attracts LDL from blood and deliver it to liver.
- ❖ Things maybe lead to ↑HDL:

  - 1- Exercise. 2- Fibrates. 3- Niacin. 4- Statins.
  - Statins can lead to →↑ (15-30% of HDL).

- اما في حالة إذا قل الـ HDL بشكل كبير الى 30mg/dL او الى 20mg/dl اعطي المريض Fibrates او Niacin عشان ← HDL↑.
- ما الفرق بين الـ Niacin والـ Fibrates والـ Statins ؟

Niacin	Fibrates	Statins
• ↓LDL, ↓Triglyceride. • Not used with DM due to it causes → hyperuricemia and hyperglycemia.	• ↑HDL, ↓Triglyceride. • High drug –drug interactions and cause myopathy.	• ↓cholesterol syntheses. • Cause myopathy (rhabdomyolysis) and ↑blood glucose (5-6mg/dL) so caution → with prediabetes.

Benefits of Good DM Control

- Glycemic control:
  - Reduces micro-vascular complications.
- Cholesterol control:
  - Reduces macro-vascular complications.
- Blood pressure control:
  - Reduces both micro-vascular and macro-vascular complications.

Treatment of Diabetes Mellitus

- لما اعالج مريض السكري لازم اعطي الدواء المناسب لحالته ← هل هو thin or obese ← هل هو young or elderly حيث الـ elderly أكثر عرضه للـ hypoglycemia.
- أيضا يتم تصنيف الادوية على أساس ← (hypoglycemic effect or non-hypoglycemic effect).

First ⇒ Treatment of Type 2 DM:

Metformin
• Mechanism of action → ↑uptake of glucose in peripheral. ↑sensitivity of receptor to insulin. ↓insulin resistance. • Properties → (cheap – safety issue – weight loss 2-3kg). • Adverse effect → (lactic acidosis →↓ oxygen in heart failure (stage c)). • Contraindication→ (GFR < 30 ml/min or serum creatinine (> 0.4 or > 0.5)).
Sulfonylureas
• Mechanism of action → acts directly on β cell to ↑ insulin secretion. • Long time use can lead to → β cell damage. • Adverse effects → weight gain and hypoglycemia.
Meglitinide
• Short acting is given as bolus. • Used in post-prandial → (take meal take pill). • Mechanism of action → ↑insulin secretion. • Adverse effects→ weight gain and hypoglycemia.
DPP-4 Inhibitors
• Mechanism of action → ↑ insulin secretion by indirectly way and ↑ GLP-1. • Adverse effects → pancreatitis.
GLP-1 Agonist
• Like → (DDP-4 inhibitors).

Thiazolidinediones
• Mechanism of action → ↑ sensitivity of receptor to insulin. ↓ insulin resistance. ↑ glucose degradation. • Adverse effects → fluid retention. - Pioglitazone→ can lead to bladder cancer. - Rosiglitazone →↑heart fatality, ↑LDL →↑atherosclerosis. • Contraindication → with heart failure especially (stage C).
SGLT-2 Inhibitors
• Used as diuresis. • Mechanism of action → ↓glucose reabsorption. • Adverse effects → block glucose reabsorption → urinary tract infection. → block Na reabsorption→ diuresis.
α-Glucosidase Inhibitor
• Mechanism of action → ↓absorption of glucose in intestine. • Adverse effects → abdominal cramps.

Second ⇒ Treatment of Type 1 DM:

❖ Treatment by insulin as (basal–bolus) technique or a broach to mimic physiological or mimic nature → يحاكي جسم الانسان.

❖ طبعا افضل طريقة من اجل إعطاء الانسولين لمريض type 1 هي الـ multiple injections.

❖ **Insulin can be divided in to:**

Bolus insulin	Basal insulin
- Used during meals (breakfast-lunch-dinner).	- Used for fasting state.

❖ طبعا كيف يفرز الـ bolus insulin ؟

- When we eat foods containing glucose → food reaches to enterochromaffin cell in GIT → which releases incretin hormone→ which stimulates β-cell to produce bolus insulin.

❖ **Types of insulin:**

1- Rapid-acting	Aspart – lispro – Glulisine	Bolus insulin
2- Short-acting	Regular	Bolus insulin
3- Intermediate-acting	NPH	Basal insulin
4- Intermediate-long acting	Deter	Basal insulin
5- Long-acting	Glargine	Basal insulin

❖ **Initial treatment often weight base estimate:**

- E.g. 0.6 unit/kg/day = total daily insulin (TDI) needs.
- Basal is 50% of total daily insulin needs.
- Bolus is 50% of total daily insulin needs.

- مثال ١← إذا كان وزن شخص ما 50kg وكان يأخذ (insulin= 0.6 unit/kg) فكم بيكون الـ Total daily insulin؟

- Total insulin daily = 0.6 ×50 = 30 units.
- So 50% → basal= 15 units → use as once 15 units (long acting) or as twice 7.5units (intermediate acting).
- 50 %→ bolus= 15 units → use as 5 units for (breakfast), 5 units for (lunch) and 5 units for (dinner).

- في حالة المريض الذي يأخذ انسولين يجب علية ان يعمل exercise وكذلك diet control عشان يتجنب الـ hypoglycemia.

- Correctional Dosing= 1800/TDI= #mg/dL.

- مثال ٢← مريض تناول وجبة الـ breakfast وهو يأخذ انسولين بجرعة 5 unit/kg وعمل فحص للسكر ووجد ان الـ(blood sugar= 300mg/dL) بينما كان الـ (target goal= 180mg/dL) هل تنفع هذه الجرعة من الانسولين؟

- طبعا لا بنزيد جرعة الانسولين على أساس الـ (Correctional Dosing).

- So correctional dosing= 1800/TDI=1800/30= 60mg/dl.
- This means every unit of insulin →↓60 mg/dl of blood sugar.
- Blood sugar after breakfast= 300 mg/dl and target goal= 180 mg/dl.

- So additional→ insulin dose = $\frac{blood\ sugar\ after\ breakfast - target\ goal}{corretional\ Dosing}$

- Additional→ insulin dose = $\frac{٣٠٠ - ١٨٠}{٦٠} = ٢\ units$

- So appropriate insulin dose = 5+2= 7 units.

- إذا صحي مريض السكر وحقة الـ blood sugar <60mg/dL أيش اعمل؟
أنقص من جرعة الـ basal insulin.