Type 1 Diabetes Mellitus

Lecture 4

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Diagnosis (for all diabetics)

Glycemic targets are set higher for:

a. Older pts. (but strict control of BP & cholesterol, LDL: <70).

b. Comorbidities.

1. Blood glucose level:

a. Fasting (8 hours). > 120mg %.

b. 2 hours postprandial (PP) after 8 hours fast (with 75gm glucose) for earlier detection in most cases. > 180mg%.

c. Random blood glucose.

Impaired fasting glucose: fasting blood glucose 100 -120 mg%.

Impaired glucose tolerance : PP blood glucose 140 -180 mg%.

2. Glycosylated Hb (HbA1C):

It indicates mean long term blood glucose control (for the previous 3 months). Unlike blood glucose level which measures acute effects, it is not affected by other acute factors as diet, stress,….

However, it gives mean values , so, it does not diagnose fluctuations in blood glucose. Normally < 6.5%.

Impaired glucose tolerance : 5.7 - 6.4%.

3. Serum C peptide: indicates endogenous insulin (low in type 1DM).

4. Insulin.

5. HOMA-IR.

4 & 5 for insulin resistance. In type 2 DM & metabolic syndrome.

Treatment of DM

A) Life style modification

1. Diet control:

→↓HbA1c by 0.3-2% in type2.

High protein, small amount of sugar and carbohydrate mainly with high soluble fiber contents. ↓calories. Intermittent fasting.

Glycemic index: The lower glycemic index, the less postprandial hyperglycemia.

< 55%: vegetables, some fruits, grainy breads & legumes.

> 70%: some fruits, white bread, rice & simple sugar.

Glycemic load: according to glycemic index & food quantity.

Insulin index & Insulin load.

2. Reduction of body weight:

Body mass index (**BMI**) = body wt. (Kg)/ length (meter) square.

In normal adults = 20 - 25 kg/m2.

Overweight & obesity: BMI > 25 & 30 kg/m2 respectively.

BMI>40 = loss of 10 years of life.

3. Exercise:

a. ↓insulin requirements. Exercising muscles need no insulin for glucose uptake.
b. ↓visceral fat and ↓liver production of glucose.

c. Releases endorphins. d. Improves blood flow,… e. If….↓ Wt.

Effect persists for 1-3 days.

Exercise should be gradual, mild to moderate, short of exertion, at least 30 minutes daily for 5 days weekly (150 minutes weekly).

4. Avoid emotions. Stress → ↑cortisol. Psychotropic drugs may be given.

5. ttt of periodontitis, intestinal dysbiosis and vitamin & mineral deficiency.

50 of type 2DM patients can be controlled by these 5 items without drugs.

Even in inadequate response, they are also added to drug therapy.

Otherwise, obesity and 2ry failure may occur early.

Indications of insulin

1. Type 1 DM.
2. When there is ↑insulin requirements in (stress) as in:

a. Thyrotoxicosis. b. Surgery. c. Trauma.
d. Infections. e. Fever. f. Ketoacidosis.

3. DM with pregnancy and lactation.
4. Pts. with rapid onset of symptoms as ↓ weight.
5. Pts. >40 years old with severe DM manifestations.
6. Severe liver or renal diseases, to avoid hypoglycemia
7. Bedtime insulin (insulin glargine or....) may be combined with oral therapy in type II diabetes if HbA1c > 8.5.
8. Pts. not controlled by oral antidiabetics and diet (2ry failure).

2nd & 3rd uses are temporary uses. Others are permanent.

Insulin preparations

Route: SC injection (100 units/ml).

For food timing, onset, peak and duration are considered.

Soluble insulin, rapid & long acting analogs are clear. Others are turbid.

A) Rapid acting insulin analogs: by specific amino acids substitution in human insulin → monomer → rapid SC absorption → rapid onset (10 minutes) & short duration (4 hours). This → more post prandial (PP) glycemic control and less hypoglycemic risk respectively.

More predictable. By all methods except IV.

e.g. insulin lispro, insulin aspart and insulin glulisine.

Given 20 minutes before meals. Other insulin preparations are given 60….

Time is in hours.

	Onset	Peak	Duration
B. Short acting:			
1. Crystalline insulin (regular, soluble)	1/2	3	6
2. Semilente insulin (ins. zinc suspens.)			
C. Intermediate acting:			
1. Isophane insulin (NPH)	2	4	12
2. Lente insulin (ins. zinc suspens.)			
D. Long acting* :			
1. PZI.	3	12	24
2. Ultralente insulin (ins. zinc suspens.).			
E. Long acting analog:			
1. Insulin glargine	6	no	<24
2. Insulin detemir			
3. Insulin degludec			

Soluble insulin:

1. Rapid onset (but short duration).
2. The only preparation which can also be given by IV injection or infusion (better, dilution changes hexameric into monomers) or IM injection in emergencies as diabetic ketoacidosis and stress.
3. Used also (SC) combined with intermediate insulin.

PZI (protamine zinc insulin) and ultralente insulin are not preferred due to delayed onset (no control of PP hyperglycemia) and long duration (→ hypoglycemia).

Long acting insulin analogs

1. Insulin glargine is acid, not mixed with other insulins in the same container (separate syringes are used).

Used once daily at bed time. Its action is more predictable & physiological. It causes less hypoglycemia (plasma concentration gives plateau flat curve).

2. Insulin detemir is similar but onset of action is 2 hours instead of 6 hours and may be given once or twice daily to obtain a smooth background insulin level.

3. Insulin degludec can be mixed with other insulins and is more potent with less hypoglycemic risk. Longer t1/2, more flat curve, with less variability. 1/ day or 3/ week.

Insulin regimens

A) Conventional insulin therapy:

1. Single morning dose before breakfast SC. : in mild cases, old patients and honey moon period.

2. Two daily doses: in moderate & severe cases (>50 units/day). 2/3 of total dose is given before breakfast and 1/3 in the evening. A mixture of intermediate (for intermediate duration) and rapid or short acting insulin (for rapid onset) are given (biphasic insulin = premixed insulin).

B) Intensive insulin therapy: in pregnancy & renal transplantation (fine control):

- 1 - Multiple SC insulin: 50% of dose as intermediate insulin (or better long acting analogs) at night for basal coverage.

The rest of dose as regular (or better rapid) insulin before each meal.

2 - Portable external infusion pump (SC).

Insulin delivery systems

A) Insulin syringes & needles

Insulin is supplied in vials, stored at 2-8 C.

Use any part of body covered by loose skin as abdomen, thighs, upper arms, flanks & upper buttocks, with rotation of sites.

B) Portable pen injectors

Less painful, allow more accurate dosing and achieve pt. compliance.

C) Continuous SC insulin infusion device (insulin pump)

They produce less fluctuations in blood glucose level. They deliver individualized basal insulin + bolus insulin replacement doses based on blood glucose. Via SC injection by glucose sensor measuring glucose in interstitial fluid. Rapid (mainly) & short acting insulin are used.

Used in:

1. Inadequate ttt by...
2. Frequent hypoglycemia, dawn phenomenon & brittle diabetes.
3. If intensive insulin therapy is required: in pregnancy & renal transplantation (fine control).

D) Inhaled insulin

Adverse effects of insulin

1. Hypoglycemia:

Causes:

a- ↑insulin dose.

b- ↓diet .

c- Exercise.

d- Use of hypoglycemic drugs.

e- Renal & liver failure (insulinase is present in liver & kidney), → ↑ t1/2. :

Manifestations:

a- ↓cerebral blood glucose→ impaired mental function, hunger, confusion & coma.

b- ↑sympathetic activity → tremors, anxiety, palpitation, tachycardia, sweating…

ttt:

a. IV glucose rapidly (or oral glucose if conscious): 25ml of 25% of glucose solution.

b. Glucagon IM: 1mg.

:Insulin resistanc .2 •

Patient needs >120 units daily in absence of stress..

3. Insulin allergy:

Immediate reactions as anaphylaxis: ttt by corticosteroids or desensitization.

Local skin reactions: ttt by antihistaminics.

4. Lipodystrophy: SC injection causes atrophy and hypertrophy of SC tissue (→ ↓absoption) by scarring and ↑fatty tissue respectively.

5. Hypokalemia.

6. ↑Body weight.

7. Somogi or dawn,s phenomenon:

Post hypoglycemic hyperglycemic mainly in children due to release of hormone antagonists due to ↑insulin (night hypoglycemia →reactive fasting hyperglycemia). ttt : ↓ evening dose.