Clinical Chemistry

Carbohydrate metabolism & Related disorders

Lecture-4

Acute(Metabolic)Complications Of Diabetes Mellitus

Patients with diabetes mellitus may develop various metabolic complications that require emergency treatment , including coma, and these include the following.

1-Hypoglycaemia

This is probably the most common cause of coma seen in diabetic patients. Hypoglycaemia is most commonly caused by accidental overadministration of insulin or sulphonylureas or meglitinides

Conversely, The Patient may have missed a meal taken or excessive exercise after the usual dose of insulin oral hypoglycaemic drugs.

Hypoglycaemia is particularly dangerous, and some patients lack awareness of this; that is to say, they lose warning signs such as sweating, dizziness and headaches. Driving is a major hazard under such circumstances. Patients should monitor their own blood glucose closely, carry glucose preparations .

2-Diabetic ketoacidosis DKA

Occurs mostly in T1DM patients **diabetic ketoacidosis may be precipitated by infection, acute MI or vomiting.**

In the absence of insulin, there is increased lipid and protein breakdown, to enhance hepatic gluconeogenesis

ketoacidosis are due to:

- **Hyperglycaemia causing plasma hyperosmolality,**
- **Metabolic acidosis ,**
- **Glycosuria**

Plasma glucose concentrations are usually in the range

20–40 mmol/L (360-700 mg/dl) but may be higher

Hyperglycaemia causes glycosuria and hence an osmotic diuresis.

Water and electrolyte loss due to vomiting, which is common in this syndrome, increases fluid depletion.

There may be haemoconcentration and reduction of GFR enough to cause uraemia due to renal circulatory insufficiency.

*It has been proposed that insulin activity is sufficient to suppress lipolysis but insufficient to to facilitate glucose transport into cells.

3-*Hyperosmolal non-ketotic (HONK) coma now may be referred to as Hyperosmolar Hyperglycaemic State (HHS) may be of sudden onset.

- **It is more common in older patients.**
- **Plasma glucose concentrations exceeds** 50 mmol/L(~1000 mg/dl)
- **The effects of glycosuria are as DKA, but hypernatraemia due to** predominant water loss that aggravates the plasma hyperosmolality ***There may also be an increased risk of thrombosis**.

Insulin Resistance Syndrome (Metabolic Syndrome)

A particular cluster is known as the metabolic syndrome, syndrome X or Reaven's syndrome and is closely linked to Insulin Resistance. By definition is the presence of three or more of the following features:

1-Abdominal obesity (waist circumference):

Male more than 102 cm (40 in),

Female more than 88 cm (35 in).

2-Fasting plasma triglycerides TG more than 1.7 mmol/L (>150 mg/dl).

3- **Fasting plasma high-density lipoprotein (HDL)** cholesterol:

– Male less than **1.0 mmol/L** (< 40 mg/dl),

– **Female less than 1.3 mmol/L (50 mg/dl),**

4- **Blood pressure ≥ 130/85** mmHg.

5- **Fasting blood glucose** more than **5.5 mmol/L** (>**100mg/dl**).

Plasma levels of insulin would be expected to be raised --------►hyperinsulinaemia

Other associated features may include polycystic ovary syndrome (PCOS), fatty liver, and dense low-density lipoprotein (LDL) particles ,which are more atherogenic .

HYPOGLYCAEMIA

By definition, hypoglycaemia is present if the plasma glucose concentration is less than 2.5 mmol/L(45mg/dl) in a specimen collected into a tube containing an inhibitor of glycolysis, for example fluoride oxalate.

Because blood cells continue to metabolize glucose *in vitro*, and low concentrations are found in a specimen collected without such inhibitor can be dangerously misleading (pseudohypoglycaemia).

Symptoms of hypoglycaemia may develop at higher concentrations if there has been

a rapid fall from a previously raised value,

When adrenaline secretion is stimulated and may cause :

- **Sweating**
- **Tachycardia &**
- **Agitation**

Cerebral metabolism depends on an adequate supply of glucose from ECF

The symptoms of hypoglycaemia may resemble those of Cerebral Hypoxia (Neuroglycopenia):

Faintness, dizziness or lethargy may progress rapidly to coma and, if untreated, Permanent Cerebral Damage or Death may occur.

One useful approach is to divide hypoglycaemia into:

I-(Inappropriate) hyperinsulinaemic hypoglycemia,

II-(Appropriate) hypoinsulinaemic hypoglycemia and

III- Reactive hypoglycaemia

I-Hypoinsulinaemic hypoglycaemia

Non-pancreatic tumours (non-islet cell tumours)

Although carcinomas (especially of the liver) and sarcomas have been reported to cause hypoglycaemia,

leukaemia :**Hypoglycaemia may be the presenting feature**.

Endocrine causes

Hypoglycaemia may occur in hypothyroidism, pituitary or adrenal insufficiency.

However, it is rarely the presenting manifestation of these conditions.

Impaired Liver Function

The functional reserve of the liver is so great that, despite its central role in the maintenance of plasma glucose concentrations, hypoglycaemia is a rare complication of liver disease.

It may complicate very severe hepatitis, hypoxic liver disease associated with congestive cardiac failure or liver necrosis if the whole liver is affected..

Renal failure

Renal failure can result in hypoglycaemia as the kidney, like the liver, is a gluconeogenic organ.

II-Hyperinsulinaemic hypoglycaemia

- **Insulin or other drugs are probably the most common causes.**
- **It is most important to take a careful drug history.**

Hypoglycaemia in a diabetic patient may be caused by: -

Accidental Insulin Overdosage:-

- **By changing insulin requirements, or by failure to eat after insulin has been given.**
- **Sulphonylureas or meglitinides may also induce hypoglycaemia, especially in the elderly.**

Hypoglycaemia due to exogenous insulin suppresses insulin and C-peptide secretion.

Measurement of plasma C-peptide concentrations may help to differentiate exogenous insulin administration;Where C-peptide secretion is inhibited,
If plasma C-peptide is raised;either :

- **It is from an insulinoma or**
- **Following pancreatic stimulation by sulphonylurea drugs.**

An insulinoma is usually a small, histologically benign primary tumour of the islet cells of the pancreas .

III-Reactive (Functional) hypoglycaemia(uncommon)

Some people develop **symptomatic hypoglycaemia between 2 and 4 h after a meal or a glucose load** (Loss of consciousness is very rare).

Similar symptoms may follow a gastrectomy or **bariatric gastric banding,** when rapid passage of glucose into the intestine, and rapid absorption, may stimulate **excessive insulin secretion**

('late dumping syndrome').

Alcohol-induced Hypoglycaemia

Hypoglycaemia may develop between 2 and 10 h after the ingestion of large amounts of alcohol.

It is found most often in undernourished subjects and chronic alcoholics but may occur in young subjects when they first drink alcohol.

Hypoglycaemia is probably caused by the suppression of gluconeogenesis during the metabolism of alcohol.

Box 12.1 Some causes of hypoglycaemia in adults

Hyperinsulinaemic hypoglycaemia

Inappropriately high insulin concentrations due to:

- Pancreatic tumour — insulinoma
- Hyperplasia of the pancreatic islet cells
- Insulin receptor antibodies
- Autoimmune insulin syndrome
- Exogenous insulin
- Sulphonylureas, meglitinides

Hypoinsulinaemic hypoglycaemia

Endocrine

- Glucocorticoid deficiency/adrenal insufficiency
- Severe hypothyroidism
- Hypopituitarism

Organ failure

- Severe liver disease
- End-stage renal disease
- Severe congestive cardiac failure
- Malaria (particularly if taking quinine)

Some non-pancreatic islet cell tumours

- Insulin-like growth factor (IGF)-2-secreting tumours, e.g. liver, adrenal, breast, mesenchymal, haemangiopericytomas
- Leukaemias, lymphomas, myeloma
- Widespread metastases

Reactive hypoglycaemia

Idiopathic

Post-gastric surgery

Alcohol induced

Miscellaneous causes

Von Gierke's disease (type 1 glycogen storage disease)

Drugs, e.g. salicylates, quinine, haloperidol, pentamidine, sulphonamides