Diabetic Emergencies

DG van Zyl

3 Emergency Presentations

- Hypoglycaemia
- Diabetic keto-acidosis
- Hyperglycaemic hyperosmolar state

Hypoglycaemia

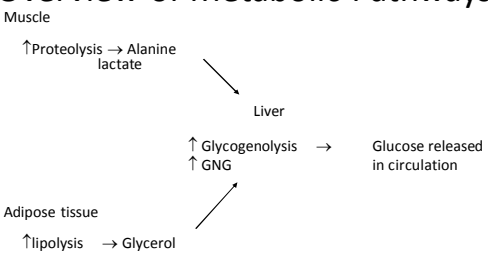
Normal Blood Glucose

3.9 – 5.8 mmol/l

Incidence

- Probably the most common endocrine emergency
- Frequently occurs in diabetic patients receiving insulin treatment with tight control
- In DCCT
  - 10-30% of type 1 diabetics per year
  - Of those, 10% required 3rd party intervention

Overview of Metabolic Pathways



Hormonal Responses

- ↓Insulin
- ↑Glucagon
- ↑Adrenalin
- ↑Cortisol
- ↑Growth hormone

Hypoglycaemia – Causes (1)

- Drugs
  - Too much insulin
  - Too much Sulphonylurea
  - Alcohol
- Too little food
- Exercise
- Critical illnesses
  - Hepatic, renal, or cardiac failure
  - Sepsis (including malaria)
- Autonomic neuropathy

Hypoglycaemia – Causes (2)

- Hormone deficiency
  - Cortisol
  - Glucagon
  - Epinephrine
- Endogenous hyperinsulinism
  - Insulinoma
  - Functional -cell disorders (nesidioblastosis)
  - Noninsulinoma pancreatogenous hypoglycaemia
  - Post gastric bypass hypoglycaemia

Symptoms Consistent With Hypoglycaemia

Neuroglycopenic responses

- Behavioral changes
- Confusion
- Fatigue
- Seizure
- Loss of consciousness
- Death

These responses are directly due to CNS glucose deprivation

Autonomic response

- **Adrenergic symptoms**
  - Palpitations
  - Tremor
  - Anxiety
- **Cholinergic symptoms**
  - Sweating
  - Hunger
  - Paraesthesia

Signs of hypoglycaemia

- Pallor
- Diaphoresis
- ↑ Heart rate
- ↑ Systolic blood pressure

Diagnosis:

Whipple's triad

1. Symptoms consistent with hypoglycaemia.
2. A low plasma glucose concentration.
3. Relief symptoms after plasma glucose level is raised

Classification of Hypoglycaemic Disorders (1)

A) Symptomatic fasting hypoglycaemia with hyperinsulinism

1. Insulin reaction → insulin treated diabetes
2. Sulfonylurea overdose
3. Factitious hypoglycaemia
4. Autoimmune hypoglycaemia → AB to insulin
5. Pentamidine inuced → Used for pneumocystis
6. Pancreatic ß- cell tumours → insulinoma

Classification of Hypoglycaemic Disorders (2)

B) Symptomatic fasting hypoglycaemia without hyperinsulinism

1. Ethanol induced
2. Liver disease with low hepatic glucose output
3. Non-pancreatic tumours
   - Utilization of glucose by large tumours
   - Production of IGF-2 by tumour → insulin receptor

Classification of Hypoglycaemic Disorders (3)

C) Nonfasting hypoglycaemia

1. Postgastrectomy
   →Rapid gastric emptying ↑ vagal stimulation with ↑ in GIP release
2. Post gastric bypass
3. Late hypoglycaemia → Reactive hypoglycaemia
   - Occult diabetes
   - Delayed insulin release → Hyperglycaemia → Exaggerated / reactive insulin response

Insulinoma

- Insulin producing tumour of the pancreatic ß –cell
  - 80% of these tumours are single and benign
  - 10% malignant
  - 10% multiple micro and macroadenomas
- Inability of insulinoma cells to suppress insulin secretion during low glucose states

Leading to severe hypoglycaemia

Insulinoma

- Whipple triad before workup commence
- Neuroglycopenic response dominate
  - Leads to delayed diagnosis
  - Often psychiatric symptoms / seizures / TIA
- Patient may be overweight (50%)
  - Frequent feeding prevents symptoms

Insulinoma: Diagnosis

- Blood glucose < 2.5mmol/L, with concommitant insulin level > 6µU/mL
- Confirm diagnosis with prolonged fast, up to 72 hours
  - P-glucose ↓
  - S- insulin and c-peptide ↑
- Localization can be problematic
  - Endoscopic ultrasonography / CT / MRI / Ocreotide scan
  - Selective angiography and venous sampling, with calcium stimulation

Insulinoma: Treatment

- Emergency hypoglycaemic treatment
- Surgical resection
- Medical therapy if patient inoperable
  - Diazoxide
  - Ocreotide
- 10% 20 year occurence

Hypoglycaemia in Diabetes

- Mostly in diabetic patients on treatment attempting to reach normal or near normal blood glucose
- Most commonly in type 1 diabetic patients on Insulin, although it does occur in type 2 diabetic patients on insulin or sulphonylureas

Problem: Hypoglycaemia unawareness

Hypoglycaemic Unawareness

- Repeated episodes of hypoglycemia →blunted response of the sympathetic nervous system to hypoglycemia with absence of symptoms
- This can be improved by relaxing strict glucose control for a few weeks

Prevention

- Patient education
- Hypoglycemia causes harm
- Carry glucose
- Diabetic card may help others to help them

Any person with diabetes treated with sulphonylureas or insulin who behaves oddly in any way whatsoever is hypoglycemic until proven otherwise

Emergency Treatment

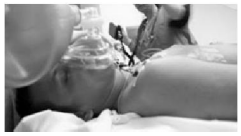
Remember ABC's in unconscious patients!

- A = Airway
- B = Breathing
- C = Circulation
- D = Drugs

Emergency treatment

1. Dextrose 50%: 50ml bolus – Orally/IV
   Followed by 10% glucose infusion
2. Glucagon:
   Especially useful if IV access is problematic
   1 – 2 mg IV/IM/SC
   Ineffective during states of starvation

Diabetic keto-acidosis



Background:

Diabetic Ketoacidosis

- State of uncontrolled catabolism associated with insulin deficiency
- Results from
  - grossly deficient insulin availability
  - increase in counter regulatory hormones such as glucagon, cortisol, catecholamines and growth hormone

Background:

- One of the most serious acute metabolic complications of diabetes
- Occurs more commonly in patients with Type 1 diabetes
- Common cause of death in diabetic patients, especially children
- Mortality rate was 100% in 1922 but has since come down to 5% with improvements in health care

Diagnostic Criteria

- Blood glucose: > 13.9 mmol/l
- pH: < 7.3
- S Bicarbonate: < 15 mmol/l
- U Ketones: > 3+ (Nitroprusside reaction method)
- S Ketones: Positive at 1:2 dilutions
- S Osmol: Variable

Diagnostic criteria for DKA

	Mild	Moderate	Severe
Plasma glucose (mmol/L)	>13.9	>13.9	>13.9
Arterial pH	7.25-7.30	7.00-7.24	<7.00
Serum bicarbonate (mmol/L)	15-18	10-14	<10
Urine ketones	Positive	Positive	Positive
Serum ketones	Positive	Positive	Positive
Anion gap	>10	>12	>12
Alteration in sensorium	Alert	Alert/ Drowsy	Stupor/ Coma

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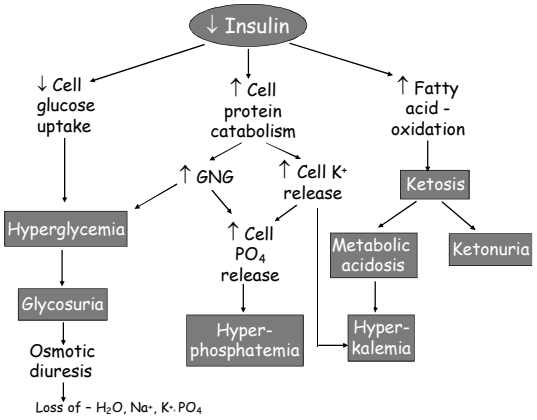
Pathogenesis: Alterations in metabolism

Caused by

- Ineffectiveness/ absence of insulin
- Elevations in glucagon, catecholamines & cortisol

Effects of insulin deficiency

- Alterations in metabolism
  - Carbohydrates, protein and lipids affected
- Fluid and electrolytes
- Hepatic gluconeogenesis, glycogenolysis, and lipolysis are affected
- Fat, liver and muscle can survive without glucose
- Brain must maintain use of glucose for starvation



Typical Deficits

- Water: 6 L (100 ml/kg)
- Na^+: 7 – 10 mmol/kg
- K^+: 3 – 5 mmol/kg
- PO_4^-: ± 1 mmol/kg

Diabetic keto-acidosis

Symptoms

- Nausea / vomiting
- Thirst
- Polyuria
- Abdominal pain
- Shortness of breath

Diabetic keto-acidosis

Signs

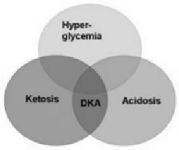
- Lethargia / confusion / obtundation / coma
- Tachycardia / hypotension
- Dehydration / dry mucous membranes
- Tachypnoea / Kussmaul breathing
- Abdominal tenderness

DKA

With progressive dehydration, acidosis, hyperosmolality, and diminished cerebral oxygen utilization, consciousness becomes impaired, and the patient ultimately becomes comatose

Laboratory findings:

- Diagnosis dependent on
  - Hyperglycemia
  - Ketonuria
  - Acidosis
- Leucocytosis is common
- S- Amylase may be elevated



Differential diagnosis:

Differentiate from acidosis and coma due to other causes:

- hypoglycemia
- uremia
- gastroenteritis with metabolic acidosis
- lactic acidosis
- salicylate intoxication
- encephalitis

Precipitating factors

- Infection 40%
- Omission/inadequate insulin 25%
- Initial presentation of DM 15%
- Other medical/surgical illness (CVA / AMI/ Pancreatitis / GIT Bleeds / Trauma) 15%
- Unknown 5%

Management goals

- High care / ICU
- Insulin
- Water and Sodium replacement
- Potassium replacement
- Correction of acidosis
- Phosphate and Magnesium replacement
- Monitoring
- Post hyperglycemic care

Insulin

Initial IV bolus of 0,15 U regular insulin per kg (± 10 -12 U)

Continuous infusion of regular insulin 0,1 U/kg/h (5-8 U/h)

20 U Actrapid in 200 ml saline
or
50 U Actrapid in 500 ml saline

Insulin

- Be careful to start insulin before s-K^+ result is available
  - If initial K < 3.0 mmol/l, first correct.
- Increase insulin infusion if glucose does not decrease by at least 5mmol/l after first hour
- When glucose < 14mmol/l, decrease infusion rate by half

Insulin Adjustment

THEN

Adjust insulin infusion rate based on blood glucose 2 hrly

- <5.6 mmol/l - ↓ by 10 ml/h and give 25 ml 5%DW
- 5.6 – 8.9 mmol/l - ↓ by 10 ml/h
- 9 – 12.2 mmol/l – no change
- 12.3 – 15.6 mmol/l - ↑ 10 ml/h
- >15.6 mmol/h - ↑ 10 ml/h and add 8 U Actrapid bolus

Water and Sodium Replacement

S Na^+ (mmol/l)	Infusion solution
> 165	2,5% DW
145 – 165	0,45% NaCl
< 145	0,9% NaCl

- Fluid deficit = [0.6 x kg x (sNa/140)] – [0.6 x kg]
- Average deficit for
  - DKA is 4 – 6 L
  - HHS 8 – 10 L

Water and Sodium Replacement

Infusion rate

1st hour	- 1 L
2nd – 7th hour	- 0,5L/h
After 8th hour	- 0,2 L/h

Water and Sodium Replacement

Infusion rate in patients with cardiac failure or older than 65 years according to CVP

CVP (cm H_2O)	Infusion rate (l/h)
< 3	1
3 – 8	0,5 – 1
9 – 12	0,5
>12	0,25

Water and Sodium Replacement

- The total amount of fluids in the first 12h should not exceed 10% of the total body weight
- If hypovolemia persists after 6 L of fluid, administer colloid containing solutions
- If blood glucose ≤ 14 mmol/l
  → Change IV fluids to 5% Dextrose, rate as above
- Continue with Insulin infusion until ketone free

Potassium

S-K+ (mmol/L)	Amount of K+ (mmol/h)
>5.0 mmol/l	No K+, check K+ in 2h
3.0 – 5.0 mmol/l	Add 20 mmol in each litre of fluid administered
< 3 mmol/l	Add 40 mmol/l to initial fluid, withhold insulin until K+ > 3.0 mmol/l

Correction of Acidosis

- Only in DKA if pH < 7.0
- If pH 6.9-7
  Bicarbonate 50 mmol in 200 ml
  0.45% saline over 1h
- If pH < 6.9
  Bicarbonate 100 mmol in 200 ml
  0.45% saline over 1h
- Repeat 2 hrly till pH >7.0

Phosphate and Magnesium

- If s-PO_4^- < 0.5 mmol/l
  - Oral phosphate solution 15 ml 8 hrly
- If s-Mg^{++} < 0.6 mmol/l
  - Infuse 20 – 40 mmol $MgSO_4$ over 8h

Monitoring of serum parameters

- Capillary blood glucose:
  →1 hly, till BG<14 mmol/l, then 2 hourly
- Na^+, K^+, urea, pH, u ketones:
  → 2 hly for first 12 hrs, then 4 hourly
- PO_4^-, Mg^{++}:
  → 6 – 12 hly
- U- output, BP and heart rate:
  → 4 hrly for at least the first 12 hrs
- CVP:
  →1hrly for first 12 hrs

Other:

- Urine MCS
- Blood cultures if pyrexial
- CXR
- ECG
- NG tube if comatose
- Subcut heparin
- U - catheter

Treatment after blood glucose decreased below 14 mmol/l

- Continue with Insulin infusion until ketone free
- Change IV fluids to 5% Dextrose, rate as above

Resolution of DKA:

- With correct regimen, DKA usually is usually fully corrected in 36 to 48 hours
- Criteria for resolution:
  - serum bicarbonate > 18 mmol/L
  - venous pH > 7.30
  - glucose level <11 mmol/l

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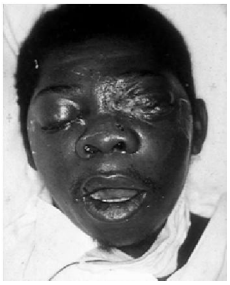
As Soon As Ketone Free

- Injection of subcutaneous insulin
  - 0.6 – 0.7 U/kg/day (for new diabetic patient)
  - Previous insulin regimen for previously diagnosed diabetic patients
- Monitor blood glucose 4 hly
- Patient must be able to eat

Complications of DKA

- Cerebral edema
- ARDS
- Thrombo-embolic events due to hypercoagulable state
- Hypokalaemia
- Myocardial infarction
- Acute gastric dilatation
- Late hypoglycemia
- Erosive gastritis
- Hypophosphatemia
- Mucor mycosis



Prognosis

- DKA accounts for 14% of all hospital admissions for diabetes and for 16% of diabetic related fatalities
- Overall mortality is about 2%

Beware:
Patients with DKA and pneumonia are unable to compensate for metabolic acidosis and are at high risk of dying – admit to ICU

Hyperglycaemic Hyperosmolar State (HHS)

Previously: Hyperosmolar Non-Ketotic Coma(HONC)

Diagnostic Criteria

- Blood glucose > 33 mmol/L
- Osmolarity > 320 mOsmol/L
- Arterial pH > 7,3
- S bicarbonate > 15 mmol/L
- U- Ketones <2+

Pathophysiology

- Concomitant disease
- Osmotic diuresis and shift with intracellular dehydration
- Exact reason for not developing ketosis is not known

Precipitating Factors

- Preceding illness that result in several days of dehydration
- Oral hydration is usually impaired by concurrent illness or chronic co morbidity (dementia, immobility, vomiting)
- Pneumonia and UTI is the most common concurrent illness

Treatment

- Treatment is the same as for DKA although fluid resuscitation should be more aggressive

- First hour: 1,5 L of 0,9% saline
- h 2 and 3: 1L of 0,9% saline
- h 4 onwards: 0,5 – 0,75L of 0,45% saline

Complications

- Same as for DKA
- A wide variety of neurological complications may be present, this can be focal or global

Prognosis

- Mortality of HHS is high even in the best hands between 10 and 20 %
- Early recognition and aggressive therapy is essential
- Do not neglect the precipitating illness

Conclusion

- All acute diabetes complications are potentially lethal and the urgency of treatment should not be underestimated
- All patients should know about these complications and should be instructed to seek help early