Endocrine Emergencies

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Endocrine Emergencies

Topics for Discussion

- Hypoglycemia
- Diabetic Ketoacidosis (DKA)
- Hyperglycemic Hyperosmolar Nonketotic Coma (HHNC)
- Thyroid Storm
- Myxedema Coma
- Adrenal Crisis

Hypoglycemia

Hypoglycaemia

- Defined as fall in blood glucose concentrations that elicits symptoms of glucose deprivation in the central nervous system, usually blood glucose below 50 mg/dl
- "Whipple's triad"
  - low plasma glucose
  - Neuroglycopenia
  - Corrected by glucose

Hypoglycaemia : Classification

- **Fasting hypoglycemia**
  - **underproduction**
  - **overutilization**
- **Post prandial hypoglycemia**

Underproduction of glucose

- Insufficient intake of carbohydrate.
- Delay or omission of a snack or main meal
- Hormone deficiency
- Enzyme defect
- Substrate deficiency
- Acquired liver disease
- Drug : alcohol, propanolol, salicylate,quinine etc.

Overutilization of glucose

Hyperinsulinism

- **Insulinoma**
- **Exogenous insulin**
- **Sulfonylurea**

Appropriate insulin

- **Extrapancreatic tumor**
- **Carnitine deficiency**

Symptoms of Hypoglycemia

- **Adrenergic**
  - sweating
  - anxiety
  - tremor
  - nausea
  - palpitations
  - tachycardia
- **Neuroglycopenic**
  - dizziness
  - headache
  - visual disturbances
  - difficulty speaking
  - inability to concentrate
  - loss of memory
  - confusion or coma
  - seizures

Treatment of Hypoglycemia

- Mild to moderate hypoglycemia in conscious patient:

  Fast-acting carbs (glucose tablets, juice) usually 15-30g followed by long acting carbohydrate to prevent recurrent hypoglycemia

  Repeat BG in 15-30 min
- Severe hypoglycemia/unconscious patient:

  25-50g of 50% glucose (1/2-1 amp D50W) IV

  0.5-1.0 mg glucagon sc/IM if no IV access, (children < 25kg, give 0.5 mg or 0.02 mg/kg body weight)

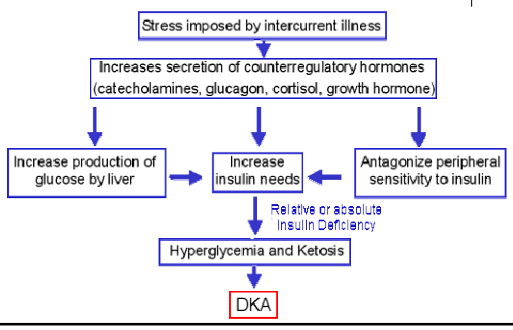
Diabetic Ketoacidosis

Diabetic Ketoacidosis

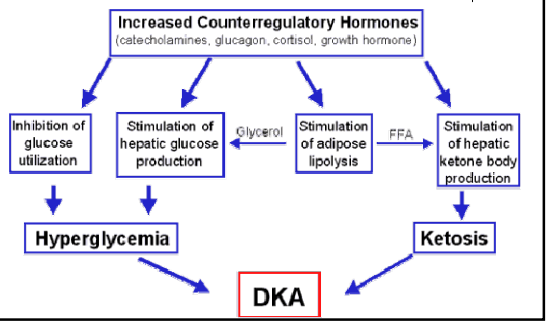
Introduction

- DKA is a medical emergency that results from a combination of both a relative lack of insulin *and* an excess of the stress hormones (catecholamines, cortisol, glucagon, etc.)
- Most often occurs in type 1 DM
- Sometimes be the presenting condition with newly diagnosed type 2 DM
- Often there are precipitating factors that lead to the development of DKA.
- Overall mortality is 5-15%.

DKA: Pathophysiology



DKA: Pathophysiology



Factors associated with development of DKA

Factor	Approximate frequency (%)
Infection	35
Omission of insulin or inadequate insulin	30
Initial presentation of diabetes mellitus	20
Medical illness	10
Unknown	5

Diagnostic Triad

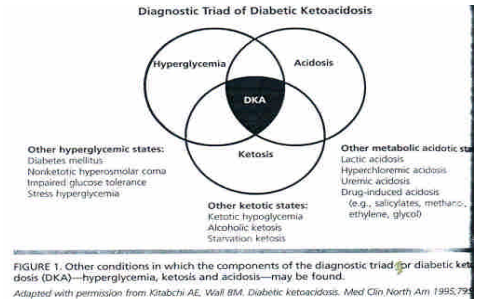


FIGURE 1. Other conditions in which the components of the diagnostic triad for diabetic ketoacidosis (DKA)—hyperglycemia, ketosis and acidosis—may be found.

Adapted with permission from Kitabchi AE, Wall BM. Diabetic ketoacidosis. Med Clin North Am 1995;79:9

Diagnostic Criteria

- Blood glucose: >250 mg/dL
- pH: <7.3
- Serum bicarbonate: <15 mEq/L
- Urinary ketone: >=3+
- Serum ketone: positive at 1:2 dilutions
- Serum osmolality: variable
- Metabolic acidosis with an elevated anion gap
- Not all patients will meet all diagnostic criteria

Clinical features

- Nausea and Vomiting
- Polyuria
- Polydipsia
- Dehydration
  - decreased skin turgor, dry mucous membranes, tachycardia
- Vaguely localized abdominal pain
  - Gastric stasis/ delayed gastric emptying
  - Intestinal ileus
- Hyperventilation and respiratory distress
- Tachycardia
- Shock
- Altered mental status / lethargy / Coma

Therapy of Diabetic Ketoacidosis

- Main therapeutic goals are:
  - Improving circulatory volume and tissue perfusion => Hydration
  - Reducing blood glucose and Clearing ketones => Replace insulin
  - Correction of electrolyte abnormalities
  - Treat any precipitating factors

Therapy of Diabetic Ketoacidosis

- **Correction of hypovolemia is a critical first step**
  - Normal Saline is the initial fluid of choice
  - present with massive total-body water deficits, up to 6-10 L
  - standard to administer one liter of saline within the first 30 to 60 minutes, followed by a continuous infusion of 250 to 500 mL/hour as guided by clinical and laboratory parameters
  - Add glucose to IV fluids when glucose falls below 250 mg/dl, to minimize the risks of cerebral edema and hypoglycemia

Therapy of Diabetic Ketoacidosis

- **Insulin is required to reverse ketoacidosis**
  - IV bolus of 0.15 U/kg of regular insulin, followed by a continuous insulin infusion of 0.1 U/kg/hour in adults
  - Continuous infusion of 0.1 unit/kg/hr in children is recommended

Fluid/insulin Supply

- While glucose = 250 mg/dL
  - Continuous/hourly insulin = 0.05u/kg/hour
  - IVF: D5W + 0.45% saline keep 100-200 ml/hr
  - Keep glucose = 150-200 mg/dl (FS q4h)
- Should achieve 2 parameters
  - Serum bicarbonate > 18 mEq/L
  - Venous pH > 7.3 and anion gap < 14 mEq/L .

=> subcutaneous (SQ) insulin therapy can be initiated.

Complications of Insulin Therapy

- Too rapid correction: cerebral edema
  - 1 percent of children with diabetic ketoacidosis
  - onset of headache and decreased mental status occurring several hours after the start of treatment
  - mortality rate of up to 70 percent
- Treated by 1-2 g/kg mannitol over 15 minutes

Therapy of Diabetic Ketoacidosis

- Correct all electrolyte abnormalities
  - Initial hypokalemia may worsen as acidosis is corrected due to shift of H+ and K+ in intracellular/extracellular fluid
  - Na+ is falsely lowered in a predictable manner in the face of hyperglycemia

  Corrected Na =

  Measured Na + 1.6 x (glucose –100)/100

Potassium Therapy

- Usually hyperkalemic at the time of diagnosis
- Potassium will fall during therapy:
  - Move into cells resulting from insulin, correction of acidosis, and restoration of volume
  - Haemodilution
  - Urinary loss
- Typical potassium deficit in diabetic ketoacidosis is 500 to 700 mEq (500 to 700 mmol)
  - $K^+ < 3.3$ mEq/L, hold insulin and give K^+ at 40 mEq/L, (1/3 KCl, 2/3 K_3PO_4), until $K^+ > 3.3$ mEq/L
  - $K^+ > 5.5$ mEq/L initially, hold K^+ supply and recheck q2h
  - $3.3 < K^+ < 5.5$, give K^+ **20-30** mEq/L.

Therapy of Diabetic Ketoacidosis

- Bicarbonate (alkali therapy) for DKA is usually not recommended
- Bicarbonate (alkali therapy) for DKA
  - slowly and in small doses 1 amp over 1 hour for pH less than 7.0
  - 1 to 2 amps may be used if pH is less than 6.9

Hyperglycemic Hyperosmolar Nonketotic Coma (HHNC)

Hyperglycemic Hyperosmolar Nonketotic Coma (HHNC)

Introduction

- Typically affects elderly, debilitated patients with a history of Type II Diabetes
- It is characterized by the development of profound dehydration, hyperglycemia, and hyperosmolarity ***without ketoacidosis***
- There is often an underlying concomitant illness that may be precipitating or worsening the HHNC
- Develops over a period of weeks
- When compared with DKA, it has:
  - Higher mortality
  - Higher hyperglycemia
  - More severe dehydration

Diagnosis of HHNC

- The physical exam may show:
  - Alteration of mental status, ranging from confusion to coma
  - *Focal* neurologic signs
  - Evidence of dehydration including hypotension, tachycardia, dry mucous membranes, and prolonged capillary refill.

Diagnosis of HHNC

- Laboratory findings:
  - Glucose levels in excess of 600 mg/dl
  - Serum osmolarity in excess of 350 mOsm/L
  - Absence of significant serum ketones
  - Potassium depletion
  - Lack of acidosis, but the acid base disturbances can range from a contraction alkalosis to a wide anion gap metabolic acidosis
  - Presence of azotemia

Therapy of HHNC

- Priorities of treatment include:
  - fluid replacement
  - electrolyte management
  - correction of hyperosmolarity
  - management of the underlying disease that precipitated the decompensation

Therapy of HHNC

- Volume deficit is often 8-12 liters
- Fluid replacement should initially be with normal saline
- The goal is to replace one half of the volume deficit in the first 8-12 hours
- The remaining fluid correction occurs over the remaining 12-24 hours

Therapy of HHNC

- Electrolyte replacement should be anticipated, with potassium being the most important
- Magnesium and phosphorus should be replaced as needed

Therapy of HHNC

- Insulin replacement via continuous infusion at 0.05-0.1 units/kg/hr
  - Note: very little insulin is often needed
- Stop insulin when blood glucose reaches 300 mg/dl
- When the plasma glucose level reaches 250 mg/dl, glucose should be added to the IV fluids

Thyroid Storm

Thyroid Storm

Introduction

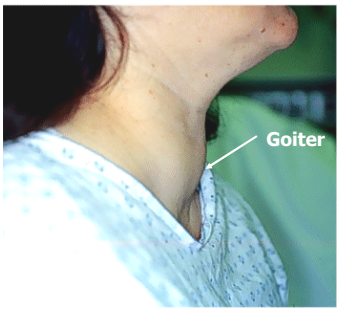
- Thyrotoxicosis refers to the clinical, physiologic, and biochemical findings that result when the peripheral tissues are exposed and respond to an excess of thyroid hormone
- The most devastating complication of hyperthyroidism is the development of thyroid storm. Also may be termed **Thyrotoxic Crisis**
- Usually precipitated by a physiologic stressor
- 20% mortality if left untreated

Diagnosis of Thyroid Storm

- The diagnosis is *clinical*; do not wait for laboratory confirmation prior to initiating treatment
- Laboratory findings will usually demonstrate an elevated free thyroxin (T4) level and a suppressed TSH level

Diagnosis of Thyroid Storm

- Diagnosis is difficult! General clues include:
  - Hx of Thyrotoxicosis
  - Graves disease (or proptosis)
  - Palpable goiter
  - Widened pulse pressure
- Classic symptoms associated with thyrotoxicosis include:
  - sweating
  - palpitations
  - diarrhea, weight loss
  - increased appetite
  - menstrual changes
  - tremor
- Temperature > 37.8 C (100 F)
- Tachycardia (classically out of proportion to fever), arrhythmia (eg. Atrial fibrilation)
- CNS changes (early – excitation, late - depression)



Thyroid Storm: Clinical Presentation

- **Temperature**
  Hyperpyrexia
- **Cardiovascular**
  accelerated tachycardia, atrial dysrhythmia, systolic hypertension, congestive heart failure
- **Respiratory**
  Dyspnea, tachypnea
- **Gastrointestinal**
  nausea, vomiting, diarrhea, abdominal pain, jaundice
- **Central Nervous System**
  anxiety, agitation, delirium, psychosis, confusion, seizure, stupor, coma
- **Skin and soft tissue**
  warm, moist skin, sweating

Precipitating events

- Infection
- Surgery
- Radioactive iodine
- Withdrawal of anti-thyroid drugs
- Amiodarone, thyroid hormone ingestion
- DKA, CHF, Hypoglycemia
- Toxemia of pregnancy, parturition
- Trauma
- Emotional Stress
- Vigorous palpation of the thyroid gland

Treatment of Thyroid Storm

(1) Supportive therapy
(2) Blocking TH synthesis and release (and peripheral TH conversion)
(3) Blocking the peripheral effects of TH
(4) Identifying and treating the precipitating event.

Supportive therapy

- Provide general support
  - Treatment of precipitating event
  - IV Fluids
  - Temperature control
    - cooling blankets, acetaminophen not aspirin
  - Oxygen therapy or mechanical ventilation
  - Benzodiazepines and barbiturates

Block Synthesis & Release of TH

- Inhibit hormone synthesis
  - Prophlthiouracil (PTU): loading dose 600-1000 mg, then 200-250 mg q4hr
  - Methimazole: loading dose 60 to 100 mg, 20 to 30 mg q6hr
- Block hormone release
  - Sodium iodide 1gm IV qd only after the synthetic pathway has been blocked or more hormone will be made
  - Inorganic iodine only after carbimazole. Orally or nasogastric.
  - Lugol's iodine 30 drops daily, 4-8drops q6hr
  - Ipodate (Oragrafin) 0.5 to 1.0 g q12hr. Also inhibit T4 conversion
  - Lithium only if allergic to iodine, 1200mg/day, po q6hr

Prevent Peripheral effect of TH

- Prevent peripheral conversion of T4 to T3
  - PTU 400mg po/nasogastric q8h
  - Propanolol
  - Corticosteroids: hydrocortisone 100 mg iv q8h
  - Ipodate
- Block the peripheral effects of thyroid hormone
  - B-Blockade
    - Propanolol: 0.5 to 1.0 mg, IV, Q 2 to 3 hr / 40 to 80 mg, po, Q4 to 8hr
    - Esmolol: 250 to 500 μg/kg, IV load, then 50 to 100 μg/kg/min IV
  - Glucocorticoids
  - Guanethidine: 30 to 40 mg q6hr

Myxedema Coma

Myxedema Coma

Introduction

- Hypothyroidism is a chronic systemic disorder characterized by the progressive slowing of body functions due to the lack of thyroid hormone
- The most feared complication of hypothyroidism is myxedema coma, which represents a form of decompensated hypothyroidism
- Mortality rate : 30-40% if untreated

Myxedema Coma

Etiology

- Likely due to a stressful event
  - CHF or pulmonary infection
  - Exposure to cold
  - Drugs, eg anesthetics, sedatives, narcotics, diuretics and β-blockers
  - Trauma, burns, surgery
  - CVA
  - Sepsis and severe infections

Myxedema Coma

Diagnosis

- Hypothermia (80% of cases)
- Respiratory failure
  - Depressed ventilatory drive, hypoventilation, hypoxia, hypercapnea
- Hyponatremia
- Hypotension
- Bradycardia
- History or physical evidence of hypothyroidism

Myxedema Coma

Evidence of Hypothyroidism

- History
  - progressive mental deterioration
  - depression
  - cold intolerance
  - fatigue
  - memory deficit
- Physical findings:
  - dry, rough skin
  - yellow skin discoloration
  - puffy eyelids
  - loss of the outer one third of the eyelids
  - goiter or a scar on the neck from thyroid surgery
  - prolonged recovery phase of the reflexes

Myxedema Coma

Diagnosis

- Laboratory Findings:
  - TFT's should be ordered but will not likely impact on emergency management
  - Low (or undetectable) levels of T4(total and free) and T3, TSH levels are usually elevated
  - Low PO2 and high PCO2 (respiratory failure)
  - Low Na+ and Cl+
  - Normal or low glucose
  - Normal or elevated WBC with left shift

Therapy of Myxedema Coma

- Supportive measures
- Active and passive rewarming
- Thyroid hormone replacement
  - IV Thyroxine
- Hydrocortisone, 50 to 100 mg IV q6-8 hr
- Antibiotics as indicated

Adrenal Crisis

Adrenal Crisis

Introduction

- Adrenal insufficiency (Addison's Disease) occurs when there is absent or inadequate production of adrenal hormones
- Any stressful event may lead to an acute decompensation characterized by altered mental status, electrolyte abnormalities, gastrointestinal disturbances, and even circulatory collapse

Adrenal Crisis

Pathophysiology of Adrenal Insufficiency

- Decreased secretion of hormones by the adrenal medulla
  - Cortisol – glucocorticoid
  - Aldosterone – mineralocorticoid
- Primary causes effect the adrenal gland directly
- Secondary causes result from dysfunction or destruction of the pituitary gland and subsequent lack of ACTH

Adrenal Crisis

Diagnosis

- Weakness, lethargy, easy fatigability
- Hypotension
- Fever is common
- GI upset including nausea, vomiting, and abdominal pain
- Altered mental status or seizures
- Circulatory compromise or even frank collapse

Adrenal Crisis

Diagnosis

- Lab findings:
  - Normal or low sodium
  - Normal or slightly increased potassium
  - Low blood glucose

Adrenal Crisis

Therapy

- Supportive care
- IV fluids with D5/NS with 1 liter given over first hour
- Correct both mineralocorticoid and glucocorticoid deficit with hydrocortisone sodium succinate 100mg IV push plus 100mg added to first IV bag

THANK YOU!