MEDICINE

432 Team

38 Complications of Diabetes

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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

Not given.

Note:

- Due to the unavailability of the lecture's PowerPoint, the contents of this file are based on the Diabetes chapters in both Kumar & Davidson's.

Diabetic patients are at risk of a wide variety of complications and have a considerably reduced life expectancy (T1DM reduces it by 11-13yrs) when compared to non-diabetics. Complications can be divided into acute and chronic.

The general pathophysiology:

Related to hyperglycemia and its consequences via the following mechanisms:

- Non-enzymatic glycosylation: accumulation of advanced glycosylated end products, causing inflammation and injury. Glucose binding to protein increases with exposure like hemoglobin A1c.
- Polyol pathway: increased glucose metabolism via aldose reductase causes the accumulation of sorbitol and fructose. Which affect vascular permeability and cellular structure. Like what happens in the eyes.

Note:

Regarding the management of hyperosmolar non-ketotic comas, the doctor emphasized giving 0.45% saline to manage they hypernatremia while the books advice starting 0.9%:
**Kumar: avoid 0.45% saline because the rapid dilution of blood may cause more cerebral damage than a few hours of hypernatremia.*
***Davidson: switch to 0.45% saline only of osmolality is increasing while giving 0.9% saline*

Acute Complications:

They are usually caused by either hypoglycemia or hyperglycemia:

A) Hypoglycemia: can lead to palpitations, confusion & loss of consciousness.

B) Hyperglycemia: can lead to:

*Type 1 diabetes: DKA & hypovolemia
*Type 2 diabetes: hyper-osmolar non ketotic coma

Chronic Complications:

Diabetics have a higher risk of developing vasculopathies, retinopathies, nephropathies & neuropathies among other systemic manifestations.

Vasculopathies:

Diabetic microangiopathy:

- Thickening of the capillary basement membrane associated increased vascular permeability throughout the body
- This form of vascular injury affects multiple systems, leading to diabetic retinopathy, nephropathy, neuropathy and accelerated atherosclerosis

Neuropathies:

Pathophysiology: Due to insulin deficiency or resistance, the Schwann cells on the neural axons are forced use the polyol pathway as their source of ATP, which processes glucose into sorbitol. The sorbitol increases the cell's viscosity. This leads to an influx of fluids into the cell (الخاصية الأسموزية), increasing its size and pressure on the axon. If the process continues, the cell might rupture. Symptoms include:

- Symmetrical sensory polyneuropathy:
  - Loss of vibration perception (usually first)
  - Numbness and paresthesia
  - Acute in lower limbs
  - Weakness and atrophy in the lower limbs may occur. Especially the interosseous muscles
- Diabetic Amyotrophy:
  - Painful muscle wasting
  - Usually asymmetrical
  - Quadriceps and shoulders are commonly affected
  - Resolves with time and proper glycemic control
- Mononeuropathies:
  - Severe and rapid with eventual recovery
  - Palsies are most likely to occur in the 3rd and 6th cranial nerves
  - Lesions in compression areas are also common
- Autonomic Neuropathy:

  The sympathetic and parasympathetic systems may be affected in one or more systems. Symptoms depend on the affected region.

  - Cardiovascular:
    - Postural hypotension
    - Resting tachycardia
    - Fixed heart rate
  - Gastrointestinal:
    - Esophageal atony (decreased motility) causing dysphagia

        - Colonic atony causing constipation
        - Nocturnal diarrhea or fecal incontinence (inability to control defecation)
        - Nausea and vomiting, feeling full, delayed gastric emptying
    - Genitourinary:
        - Urinary incontinence
        - Recurrent bladder infections due to bladder atony
        - Erectile dysfunction
    - Pupillary:
        - Delayed reflexes to light
        - Small pupil size

Nephropathies:

Pathophysiology:

- Increase in glomerular filtration rate due to hyperglycemia causes glomerular hypertrophy
- Vasodilation of afferent vessels, further increase in filtration rate
- This increase in intraglomerul pressure damages the glomerular capillaries and leads to hypertrophied mesangial cells.
- If the process continues (no glycemic control) it may lead to glomelular sclerosis
- Which causes progressive leaking of large molecules (proteins) into the urine

Retinopathies:

- Cataracts:
    - Defined as denaturation of proteins and other lens components, causing the lens to be opaque (شبه شفاف)
    - Can be acute as a result of poor control with some ketosis
- Blood glucose fluctuations can also affect the lens through osmotic changes, causing fluctuating difficulty in reading (يقرأ في الصباح بس في الليل مايقدر أو العكس)
    - Resolves with proper diabetic control
- Diabetic Retinopathy:

- Defined as damage to the retina and iris as a result of diabetes
- Most common diabetic complication
- In the peripheral retina:
  - Damage to the wall of small vessels causes microaneurysms within the retina
  - When ruptured, hemorrhage occurs as well as the leakage of proteins and lipids
  - They accumulate to form hard exudates which are eventually cleared by macrophages
  - Micro infarcts due to blocked blood vessels cause cotton-wool spots (accumulated axoplasmic debris)
  - Ischemia causes the release of growth factors and the formation of new blood vessels
  - Some new vessels might form on the surface of the retina. They are sometimes unable to withstand the normal stresses in the eye and bleed resulting in vitreous hemorrhage resulting in a sudden loss of vision.
  - Collagen tissue and fibrous bands form along the margins of these new vessels and may contract and pull the retina resulting in more bleeding and retinal detachment
- Macular area:
  - Fluid from leaking vessels is poorly cleared in this area resulting in macular edema
  - This causes distortion and thickening of the macula, affecting the central vision
  - Capillary occlusion may also affect central vision
  - Macular edema is not visible with retinal photography or the use of an ophthalmoscope

Diabetic Foot:

10-15% of diabetics develop foot ulcers, with foot issues being 50% of diabetic related hospital admissions. The main factors are neuropathy, ischemia an infection. Together, they increase the risk of tissue necrosis. Once the ulcer has developed, we should address the main threats:

- Infection:
  - Early antibiotic treatment is important

  - Drain pus and excise infected bone when needed (Rx resistant osteomyelitis)

- Ischemia:
  - In case of occlusion, perform bypass surgery or angioplasty
- Abnormal pressure:
  - Rest affected leg
  - Special shoes to reduce pressure on affected areas. Preferred to continue usage even after the ulcer is healed
- Wound environment:
  - Proper dressing is necessary to prevent contamination and absorb exudate.

Amputation is recommended when irreversible arterial insufficiency is present

- Regular checkups with the physician and a podiatrist (foot specialist) are essential in prevention and early management

Infections:

Poorly controlled diabetes increases the risks infections because the high concentrations blood glucose impair the neutrophils' superoxide generation, therefore affecting chemotaxis and phagocytosis. Diabetics are most susceptible to the following infections:

- Skin:
  - Staphylococcal infection (abscesses, boils & carbuncles)
  - Mucucutaneous candidiasis
- GIT:
  - Periodontal disease
  - Rectal and ischiorectal ascesses
- Urinary tract:
  - UTI (mostly women)
  - Pyelonephritis
  - Perinephric abscess
- Lungs:
  - Staphylococcal and pneumococcal pneumonia

Note:

Another issue is that infections can lead to loss of glycemic control; they are a common cause of ketoacidosis. Diabetics using insulin need to increase their dose by up to 25% in cases of infection.

  - Gram negative pneumonia
  - TB
- Bone:
  - Spontaneous staphylococcal spinal osteomyelitis

Joints and Skin:

- Joint contractures are a possible complication of childhood diabetes
- Thick, waxy skin on the back of fingers due to collagen glycosylation
- Type 1 diabetics may develop osteopenia in the extremities, but it rarely leads to clinical consequences

SUMMARY

1. Acute complications:
    a. Hypoglycemia
    b. Hyperglycemia
    c. Fluctuating vision acuity (poor control)
2. Chronic Complications:
    a. Vasculopathies: microangiopathy in the form of thickening basement membrane and increased permeability. This is the basic pathology of most complications
    b. Neuropathies: damage occurs due to the activation of the polyol pathway. This produces sorbitol, which causes axonal injury.
        i. Symmetrical sensory polyneuropathy
        ii. Diabetic amyotrophy
        iii. Mononeuropathies
        iv. Autonomic neuropathies
    c. Nephropathies: increased filtration rate causes injury with eventual sclerosis. This causes proteinuria
    d. Retinopathies: Vascular damage results in hemorrhage and edema, thus affecting vision. Collagen and fibrous bands may also form and contract, causing retinal detachment
3. Diabetic foot: should be properly managed to prevent tissue necrosis and maintain good arterial supply
4. Infections: diabetics are more susceptible to infection due to impaired chemotaxis and phagocytosis
5. Joint contractures and thick waxy skin may occur

Doctor's notes:

Acute complications: doctor didn't focus much on it.

1. Hypoglycemia: Patients do not usually die from the state of hypoglycemia itself but *from its consequences*. So if a patient is driving he'll crash if he's swimming he'll drown. Prolonged hypoglycemia causes brain damage.
    - Case: in which an 18 y/o male diabetic suffered from a hypoglycemic attack at school and was poorly managed. When they took him to the ER he was found to be dead and asphyxiated. Another patient became drowsy because of a hypoglycemia and was taken in by the police because they thought he was drunk. He wasn't managed and went into DKA.
    - Management: patients told to keep sugar around. Family is educated not to feed patient to prevent asphyxiation and use glucagon instead.
2. DKA: patients may lose up to 4-8L out of 12L of fluid. Most important step is **IV fluids** to restore volume. Insulin is mainly for shutting down ketogenesis. Patients are comatose due to severe hypovolemia and acidosis.
3. HONK: in elderly T2DM. Greater risk of mortality. Patients lose up to 8L. Percepitated by HF or diuretics. Severe hyponatremia (but total body sodium is normal because of dehyaration) and hyperglycemia. Demyelination and brain edema could result from mismanagement with normal saline.

- MCQ: Use normal saline for DKA, half normal for HONK.

Chronic complications:

Morbidity	Complication	Mortality
↑	Neuropathy (40%) Retinopathy (30%) Nephropathy (20%)	↓
	Vasculopathy (10)%	

- IMPORTANT: Complications in order of frequency. As you go down mortality increases. As you go up morbidity increases.

1. **Neuropathy:** Neurons are not insulin dependent. Schwann cells -that are insulin dependent switch to sorbitol pathway in its absence. Sorbitol is viscid and will drag water into the cell. The Schwann cell will swell up like a balloon and squeeze the axon causing injury resulting in severe electrical pain in the early stages - a good sign as it means the neuron at this stage is still salvageable with good control. But once sensation is lost the damage to the axon is irreversible.
    - Case: Diabetic patient tells his wife he smells something burning. She tells him she's there's nothing in the kitchen. It was winter and he was resting his feet against a warmer

and he sustained a 4th degree burn without knowing. Another finds a toy car in his shoe with toe gangrenous.

- Glove and stocking distribution: neuropathy starts distally.

2. **Retinopathy:** most active cells in the body are the rods and cones. High energy demand. In case of hyperglycemia glucose does not dissociate into the retina. Neovascularization happens as a defense mechanism. The new vessels are very delicate and are liable to rupture with the least bit of trauma like sneezing or bumping the head (real case).

    - Commonest cause of blindness.
    - Laser therapy is to prevent bleeding. We can regress it in the early proliferative changes by controlling blood glucose.
    - Hyperglycemia > Neovascularization > Rupture > Bleed > Clot > Organification > Fibrous bands > retinal detachment.

- Diabetic foot is the most common cause of non traumatic amputation. Diabetic retinopathy is the commonest cause of blindness in adults aged 30-65 y/o. Nephropathy commonest cause of ESRD.

3. **Nephropathy:** accelerated decline of number of viable nephrons/ loss of nephrons before age.

    - Hyperglycemia > increased GFR > Microalbuminuria > Proteinuria > decreased GFR > ESRD.
    - MCQ: microalbuminuria is a screening test useful for preventing nephropathy. Think of it as the rate limiting step. If not well managed, it'll proceed into nephropathy.
    - Once proteinuria is evident, glucose control does little to change the course.
    - You should start ACEIs or ARBs when the patient is at the stage of decreased GFR > increase volume of blood going to kidneys > slow progression of glomerular disease.
    - Retinopathy and nephropathy almost always present at the same time so screen.

4. **Vasculopathy:** patients often suffer three vessel CAD. But because of autonomic neuropathy and denervation of the heart patients don't feel the classic pain of MI (angina is absent).

    - spectrum of disease: CVD, CVA, PAD.
    - Most common cause of death in diabetics is coronary artery disease.

- Decreased immunity: glycation of antibodies. Higher incidence of infections.
- T1DM are more liable to complications because of more severe hyperglycemia but we see it more in T2DM because there's more of them and because they're asymptomatic initially.

Questions

1) An 18-year-old Caucasian female presents to your clinic because of a recent increase in thirst and hunger. Urinalysis demonstrates elevated glucose. The patient's BMI is 20. Which of the following is the most common cause of death in persons suffering from this patient's illness?

   a. DKA

   b. MI

   c. CVD

   d. Hypoglycemia

2) 51 y/o diabetic during the summer with severe dehydration. Patient is brought to the ER in a confused and lethargic state. BP 95/55 mmHg. Temp 37.2 and RR 20/min. 2 large bore IVs are inserted. Initial labs show: Na: 135, Cl 99, K 5.5, Bicarb 21, glucose 650, pH 7.36. What is the most likely diagnosis?

   a. ethanol intoxication

   b. HONK

   c. DKA

   d. Dehydration and heat stroke

432 Medicine Team Leaders

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Answers:

1st Questions: c

2nd Questions: b