Complications of diabetes mellitus

Diabetes mellitus (DM) represents a heterogeneous group of chronic metabolic diseases. Their basic common manifestation is hyperglycemia resulting from a lack of insulin, its insufficient effect, or a combination of both. Complications of DM are divided into acute and chronic.

Pathophysiology of changes in DM

Hyperglycemia leading to plasma hyperosmolarity. This manifests itself as glycosuria and polyuria (osmotic diuresis) → hypovolemia and polydipsia. There is a movement of water from the cells into the interstitium and into the intravascular space → hyperosmolar coma in the brain.

Use of MK as an energy source (glucagon effect - lipolysis in adipose tissue). Fatty acids are metabolized into ketone bodies, their accumulation causes ketoacidosis (up to ketoacidotic coma). It is a metabolic acidosis that is compensated by the respiratory system (hyperventilation + tachypnea = Kussmaul breathing, acetone can be smelled in the breath), also accompanied by ketonuria.

Late complications specific to diabetes are caused by non-enzymatic glycation of proteins (with a change in their properties, AGE sare increasingly deposited in the vessel wall, thus causing microangiopathy – diabetic nephropathy and retinopathy) and intracellular edema from intracellular hyperglycemia (e.g. in neurons – diabetic neuropathy).

Acute complications

Hypoglycemic coma

Hypoglycemia with loss of consciousness. It occurs more often in DM 1. type, less in DM. 2 type. Untreated DM can have fatal consequences.

Insulin pen

Causes

The most common cause is an inadequate dose of insulin or PAD , excessive physical exertion or reduced food intake.

Clinical signs

Neuroglycopenia (rather with gradual lowering of blood glucose) – confusion, behavioural and speech disorders, convulsions, coma. Furthermore, the sympatho-adrenal system is activated (with the rapid onset of hypoglycemia) - sweating, palpitations , anxiety, hunger, tremors, pallor.

Diagnostics

History (patient treated with insulin or PAD), glucometer. Possibility of confusion with CMP (cerebrovascular accident), epileptic seizure , drunkenness or other intoxication.

In case of uncertainty, always give 50 ml of 40% glucose IV (if the patient's state of consciousness does not change, there is probably another cause of unconsciousness).

Therapy

If consciousness is sufficient with preserved reflexes, 10-20 g of carbohydrates each (a sugar cube weighs 4.5 g - i.e. at least 4) preferably in a small amount of drink. Next, glucose infusion 50–120 ml of 40% glucose – important check of the vein before application (pay attention to paravenous administration), it is always necessary to flush with physiological solution. 40% glc is strongly hyperosmolar. Also glucagon 0.5–1 mg sc, im, iv.

Glucose

Hyperglycemic states

Impairment of consciousness in hyperglycemia is relatively rare and occurs gradually, patients tend to have qualitative disturbances of consciousness (drowsiness, confusion, delirium) and the basic problem is dehydration. The term hyperglycemic coma is confusing

Glucometer

Ketoacidosis

Complications of type DM 1 with MAC in the rise of ketone bodies and hyperglycemia.

Causes:

- lack of insulin (↓ secretion, insufficient exogenous supply);
- ↑ production of counterregulatory hormones (stress factors – surgery, injury,

infection).

🔎 *For more information see Diabetic ketoacidosis.*


Glucagon hormone

Hyperosmolar nonketoacidosis

Acute complications of type 2 DM with severe hyperglycemia, dehydration and impaired consciousness, poor prognosis. **Causes:**

- dietary error, ↑ fluid loss, infection, surgery, ...

Ketoacidotic coma

Symptoms develop slowly (tens of hours to days) – polyuria , thirst, nausea , vomiting, abdominal pain (pseudoperitonitis diabetica), later dehydration , the smell of acetone from the breath, Kussmaul breathing , impaired consciousness.

Laboratory

- hyperglycemia around 20 mmol/l;
- metabolic acidosis (up to extreme with pH below 7.1);
- ↑ K + (with regard to acidosis - serum level may be normal), ↓ Na + (urine losses during osmotic diuresis).

Hyperosmolality nonketoacidotic coma

Symptoms develop gradually within 1-3 days – thirst, polyuria, dehydration, hypotension , neurological symptoms (convulsions, coma).

Laboratory

- extreme hyperglycemia (even above 50 mmol/l);
- hyperosmolarity;
- manifestations of renal failure, glycosuria.

Treatment of ketoacidotic/hyperosmolar coma

Replenishment of fluid volume is primary:

1. Physiological solution - 1000 ml for the first hour, then 500 ml/hour for 2-3 hours, then during control of diuresis and clinical picture. Despite the total deficit of 5-10 l, increased caution is required in patients with circulatory, lung and kidney diseases. This is where CVP monitoring is required.
2. Checking blood glucose every hour.
3. When the glycemia drops to 15 mmol/l, we give 5% glucose to cover the deficit of pure water and as an energy substrate.
4. Insulin iv continuously 6 I/hour so that the maximum drop is 4 mmol/hour (otherwise brain edema will occur).
5. Potassium supplementation – when treating acidosis, ↓ potassium – administration of 7.5% KCl (1 mmol K + = 1 ml of solution) at a rate of 20–40 mmol/hour. ECG monitoring and alkalinization only at pH below 7.1 – bicarbonate worsens tissue acidity and causes a significant decrease in K + .
6. Prophylaxis of TEN (heparinization) and administration of ATB in case of infectious complications.

Lactic acid coma

In type 2 DM treated with biguanides - it was common after phenformin in combination with alcohol, or with kidney , heart , or liver insufficiency .

Clinical signs

Fatigue, weakness, somnolence, lethargy, tendency to hypotension, severe acidosis with pH up to 6.8, blood glucose slightly increased, lactate above 10 mmol/l.

Therapy

Intravenous access, for ↑ lactate immediately hemodialysis , despite intensive therapy, most severe cases end fatally.

Chronic Complications

In order to prevent chronic complications, it is necessary to normalize glycemia. To reduce the risk of macroangiopathy, other risk factors for cardiovascular disease must be minimized. It is therefore important to treat arterial hypertension (in the first line, usually with angiotensin-converting enzyme inhibitors - ACEI) and treat

dyslipidemia (fibrates for retinopathy, statins for nephropathy). Efforts to adjust lifestyle, i.e. not smoking, sufficient physical activity and weight adjustment, should be a matter of course.

Non-specific

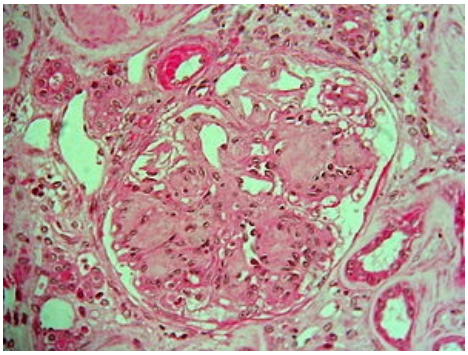
- macroangiopathy (atherosclerosis in diabetics – CHD, ICHDK, CMP),
- increased susceptibility to infections (skin inflammations - mycoses , Mycobacterial inflammations ...),
- renal papilla necrosis,
- cataract.

Specific

- diabetic microangiopathy (retinopathy, nephropathy – glomerulosclerosis KW),
- neuropathy (visceral, somatic),
- diabetic foot syndrome as a complication of neuropathy and microangiopathy.

Diabetic nephropathy

It is characterized by albuminuria, arterial hypertension and progressive renal failure. Diabetic intercapillary glomerulosclerosis is one of the most serious microangiopathic complications of DM.


Microscopic picture of diabetic nephropathy

Etiology

Hyperglycemia → non-enzymatic glycation of proteins of the basement membrane and mesangial matrix → thickening of the basement membrane

Hypertension → ↑ glomerular plasma flow , hyperfiltration, microalbuminuria → subsequent glomerulosclerosis.

The course of the disease

1. ***latent stage, early*** – clinically asymptomatic, ↑flow, ↑filtration, kidneys usually enlarged,
2. ***incipient stage*** – microalbuminuria 20–200 µg/ min , changes in basal membranes, expansion of mesangium, disappearance of some glomeruli,
3. ***manifest stage*** – albuminuria greater than 200 µg/ min , fully developed nephrotic syndrome with hypertension, development of renal insufficiency ,
4. ***stadium chronické renální insuficience***.

Therapy

- Diabetes compensation, ACE inhibitors (they reduce intraglomerular pressure and reduce both microalbuminuria and proteinuria).
- low-protein diet - proteins max. 0.8 g/kg/24 h;
- intermittent fasting.

Diabetic retinopathy

It is caused by the involvement of the capillary bed of the eye fundus. There is a change in the ratio of the number of pericytes to endothelial cells, as pericytes decrease, thereby changing the cytoskeleton and capillary contractility. There are three typical abnormalities: capillary occlusion, vascular dilatation, and neovascularization. Diabetic retinopathy is investigated using fluorescence angiography .

- Animation showing the progression of diabetic retinopathy (https://commons.wikimedia.org/wiki/File:Diabetic_retinopathy-NIE.gif)

Clinical stages and forms

- ***Nonproliferative retinopathy*** – microaneurysms , focal bleeding (intraretinal hemorrhage), hard exudates.
- ***Advanced non-proliferative retinopathy*** (preproliferative diabetic retinopathy) – soft (cotton-like) exudates on the basis of small infarcts during occlusion or decrease in arteriolar flow.
- ***Proliferative retinopathy*** – characterized by neovascularization (on the basis of VEGF - vascular endothelial growth factor produced by hypoxic areas) with fibrotization and subsequent hemorrhages and detachment of the retina (traction amocia).
- ***Diabetic maculopathy*** – arises in connection with microangiopathy , the collapse of the hemato-ocular barrier in the central landscape of the retina. Macular edema occurswith deposits of hard exudates . Visual acuity decreases.

Therapy

- Achieving normoglycemia and normotension, drugs to reduce fragility and improve vascular permeability,
- laser therapy – panretinal laser photocoagulation (panlaser photocoagulation), laser coagulation of the macula,
- in advanced proliferative form – PPV,
- anti VEGF treatment (injection treatment directly into the eye, prevents blood vessel proliferation).

Normal visus

Visus in diabetic retinopathy

Panretinal laser photocoagulation (PRP)

Diabetic polyneuropathy

The cause of diabetic neuropathy is long-term hyperglycemia , during which there is a disturbance of the membrane potential, loss of myelinated and demyelinated axons , and thickening and puckering of the myelin sheath. Nerves show signs of axonal degeneration .

Somatic neuropathy

Somatic or peripheral neuropathy is divided into symmetrical distal (sensory and motor), symmetrical proximal (motor) and further into focal and multifocal neuropathies .

- Distal neuropathy – the most common complication that causes sensitivity disorders in the hands and feet, causes unbearable night pains mainly in the lower limbs, often leads to trophic changes.
- Focal neuropathy – proximal amyotrophy affecting the muscles of the pelvic girdle and thighs. There are gait disturbances, weakness and myalgia . Another group is mononeuropathies and radiculopathy - this also includes cranial neuropathy with clinical manifestations of diplopia, strabismus and eyelid ptosis.

Vegetative

Vegetative or autonomic neuropathy manifests itself mainly in the cardiovascular system, GIT and urogenital system.

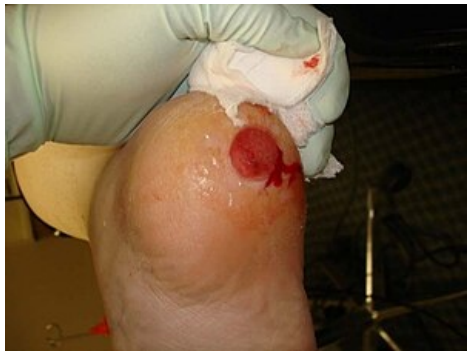
- in the cardiovascular area: faster heart rate, loss of physiological heart rate fluctuations during inspiration and expiration, orthostatic hypotension ,
- in the GIT: swallowing disorders, gastric emptying disorders, diabetic constipation, diabetic diarrhea ,
- in the urogenital system: there is a neurogenic bladder with urinary residue, erectile dysfunction , profuse sweating or anhydria of body areas.

Therapy – metabolic compensation of diabetes.

Diabetic foot

🔎 *For more information see Diabetic foot.*

Diabetic foot is a condition located distal to the ankle , which is manifested by ulcerations or deformities. The disease is complicated by the polymorbidity of the patient, poor blood circulation and frequent infections. The result can be gangrene and hard-to-manage infections that end in limb amputation. The pathogenesis of the diabetic foot is complex and involves neuropathy (sensory, motor and autonomic), angiopathy (macropathy), reduced joint mobility (cheiroarthropathy), infection and smoking.



Periferal neuropathy

Classification

- ***according to Wagner***:

  st. 0: intact skin cover but increased risk of ulceration.
  st. 1: superficial ulceration in the dermis, mainly under the head of the 1st metatarsal.
  st. 2: deeper ulceration without bone disorder.
  st. 3: deep ulceration, phlegmon, abscess, osteomyelitis.
  st. 4: localized gangrene, on the heel or toes.
  st. 5: gangrene of the whole leg..

Clinical picture

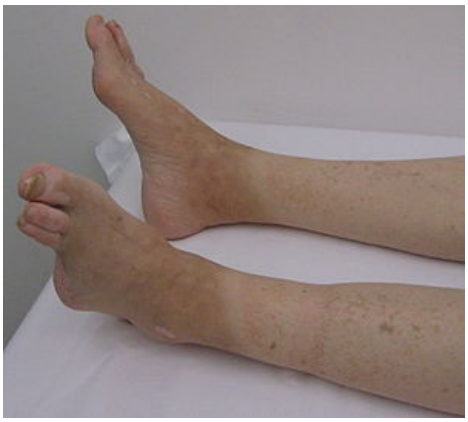
A distinction is made between neuropathic, angiopathic and neuroischemic (mixed) diabetic foot. Osteoarthropathy (Charcot's arthropathy) is characterized by progressive destruction of the leg bones in neuropathy, which contributes to hypercirculation and microtraumas or microfractures. With vascular occlusion, the leg is livid, cold, peripheral pulsations are palpable or weakened, the lesions are usually painful and are localized on acres.

Diagnostics

- anamnesis – usually smoking, hypertension, hyperlipoproteinemia, or claudication;
- physical examination – leg is pink, warm, peripheral pulsations are palpable, lesions are painless;
- X- ray demonstrable osteolysis or osteomyelitis and mediocalcinosis.

Therapy

The principles of treatment of neuropathic ulcerations include the requirement of good compensation of diabetes and other deviations, relief of the foot with removal of pressure at the site of ulceration, systematic locomotion therapy and long-term and effective treatment of infection. Local treatment – cleaning the wound, supporting granulation and epithelization. Antibiotics – oxacillin, clindamycin, amoxicillin, macrolides. Treatment of angiopathic leg requires reconstructive procedures. Amputation is the last solution in conservatively unmanageable progression of gangrene, sepsis or pain at rest without the possibility of reconstructive surgery.



Amputation of toes due to diabetic complications

Gastrointestinal complications of DM

- esophageal motility disorder, deterioration of relaxation of the lower esophageal sphincter during swallowing, repeated contractions of the lower esophageal sphincter;
- slowing of gastric emptying → anorexia, abdominal pain; extreme to paresis of the stomach;
- contractions of the duodenum and jejunum that impair gastric emptying;
- postprandial syndromes: nausea, belching, vomiting, rapid satiety, anorexia;
- impaired contractility of the gallbladder - cholecystolithiasis occurs more easily;
- motility disorders of the small and large intestines → diarrhea or constipation;
- hepatic steatosis; increased tendency to cirrhosis of the liver.

Cardiovascular autonomic neuropathy

🔎 *For more information see Cardiovascular autonomous neuropathy.*

- specific and functional changes of the myocardium
- heart rate control abnormalities
- dysfunction of the left ventricle of the heart
- resting and fixed tachycardia - fixed tachycardia without response when the load changes
- exercise intolerance

Links

Related articles

- Diabetes mellitus ■ Diabetes mellitus type 1 ■ Diabetes mellitus type 2 ■ Gestational diabetes mellitus ■ Pancreas transplantation
- Selected biochemical examinations in patients with diabetes mellitus
- Diabetes and tumors
- Transplantation in diabetology
- Diabetic glomerulosclerosis (preparation)
- Cardiovascular autonomnic neuropathies (https://www.wikiskripta.eu/w/Kardiovaskuláarn%C3%AD_autonomn%C3%AD_neuropatie_(KAN)?veaction=edit#Auton.C3.B3mna_neuropatia_.28AN.29)
- Perioperative care of a patient with diabetes

External links

- FORBES, J. M. – COOPER, M. E.. Mechanisms of diabetic complications. *Physiol Rev.* [online]. 2013, y. 93, vol. 1, p. 137-88, Available from <https://www.physiology.org/doi/pdf/10.1152/physrev.00045.2011>. ISSN 1522-1210.

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- ROZSÍVAL,, et al. *Oční lékařství.* 1. edition. Galén, Karolinum, 2006. ISBN 80-7262-404-0, 80-246-1213-5.

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