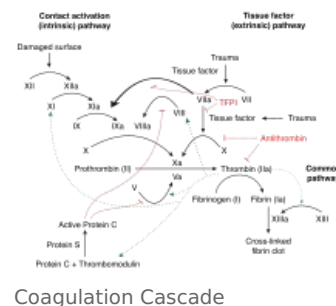


Haemorrhagic disease of the newborn

Haemorrhagic disease of the newborn (*morbus hemorrhagicus neonatorum*) is a vitamin K deficiency disease that causes spontaneous bleeding. Due to vitamin K deficiency, **the activity of vitamin K-dependent coagulation factors II, VII, IX, X, protein C and S is reduced.** Vitamin K is crucial for the activation (γ -carboxylation) of these proteins. The level of these factors in the newborn reaches 30% of the adult level. Vitamin K crosses the placenta poorly, its supply is insufficient after birth. Breast milk contains low levels of vitamin K and the production of vitamin K by intestinal bacteria is missing in newborns.^{[1][2][3]} In the absence of vitamin K, ineffective precursors of coagulation factors, so-called PIVKA (proteins induced by the absence of vitamin K), with impaired coagulation function are formed in hepatocytes.^[4]



Risk factors for bleeding disorders

- exclusive breastfeeding (breast milk contains significantly less vitamin K than cow's milk, the intestinal flora of breastfed babies produce less vitamin K);
- drugs given to the mother before childbirth (anticonvulsants, etc.);
- prematurity (due to liver immaturity they are more prone to bleeding);
- liver damage (hepatitis), bile duct atresia, malabsorption, cystic fibrosis, diarrhea, celiac disease, alpha1-antitrypsin deficiency, short bowel syndrome, bacterial overgrowth syndrome, chronic exposure to broad-spectrum antibiotics.^{[1][2][5]}

Sources of vitamin K

- External: food - the presence of fats and bile acids is necessary for resorption,
- Internal: synthesis by intestinal bacteria (synthesis decreases with ATB administration).^[2]

Clinical signs

Bleeding into the GIT, skin, navel, punctures, nose, hematuria, later bleeding into the CNS.

Forms:

- according to O. Hrodek and J. Vavřinec, Pediatrics (2002):
 - **early** (0-24 hours) - the least common form, severe bleeding including gastrointestinal bleeding and intracranial bleeding, occurs in severe vitamin K deficiency in utero, for example due to drugs administered to the mother before delivery (antiepileptics (phenobarbital, phenytoin), antituberculotics (eg rifampicin, baronuridates) salicylates, coumarin preparations, ATB, CHT), vitamin K can be given prophylactically to the mother at the end of pregnancy;
 - **classic** (2nd-7th day) - in newborns who were not prophylactically given vitamin K after birth, it manifests as bleeding from the navel, gastrointestinal tract (melena), skin, nose, surgical sites (eg after circumcision), there is usually no bleeding into CNS;^[6]
 - **late** (1st-6th month) - most often between the 2nd and 8th week of life, the first manifestation is sudden bleeding into the CNS in an otherwise healthy breastfed fullborn or in children with liver disease (eg biliary atresia) or malabsorption, can have fatal consequences.^{[2][3]}
- according to A. C. Muntau, Pediatrics (2009):
 - **early form** (2nd-5th day of life): hematemesis, melena, nose and navel bleeding;
 - **late form** (3rd-7th day of life): acute life-threatening CNS bleeding in fully breastfed infants - 20% lethality.^[1]

Diagnosis

Coagulation parameters: **prolonged prothrombin time** (Quick, INR) with normal platelet levels and fibrinogen, in severe cases also prolongation of aPTT. The diagnosis is confirmed by normalization of PT after administration of vitamin K. Alternatively, the diagnosis can be confirmed by examining the levels of vitamin K-dependent factors and PIVKA II, an inactive form of factor II (decarboxyprothrombin).^{[1][3]}

Therapy

According to the severity of the bleeding. Vitamin K (Kanavit inj.) - 1 mg i.v. or i.m.- the level of active vitamin-K dependent factors is adjusted in the order of hours. In case of severe bleeding, fresh frozen plasma is given together with vitamin K.^[3]

Risk of nuclear jaundice due to reduced albumin binding capacity for bilirubin.^[1]

Prevention

In full-term newborns:

- 1 mg i.m. (*Kanavit*® 1 mg = 0,1 ml) or
- 2 mg p.o. (1 drop = 1 mg), in fully breastfed it is necessary to repeat 1 mg p.o. once a week up to 10-12 weeks of age.^[7]

Vitamin K

Vitamin K is a group of lipophilic and hydrophobic vitamins. The name vitamin K is derived from the German term *koagulations-vitamin*.

There are 3 known forms of vitamin K:

- K1 (phylloquinone) is found in green leafy vegetables, legumes, soybeans, vegetable oils and dairy products. Vitamin K administered to newborns prophylactically after birth is vitamin K1.
- K2 (menaquinone) is formed by the intestinal flora (especially *Bacteroides* species; on the contrary, *Lactobacilli*, which colonize the intestine of breastfed children, do not form vitamin K).
- K3 (menadione) is a synthetic, water-soluble form that is no longer used in medicine due to the potential risk of hemolytic anemia.

Vitamin K is an essential cofactor of γ -glutamyl carboxylase enzymatic activity, which catalyzes the γ -carboxylation of some proteins (so-called Gla-proteins) - coagulation factors II, VII, IX and X, protein C, protein S, protein Z.

In vitamin K deficiency, the level of abnormal prothrombin is increased (so-called PIVKA II), which does not contribute to the formation of blood clots. It is a dysfunctional protein (des-carboxylated prothrombin) that is unable to bind calcium and phospholipids.^[5]

Sources

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