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# Hemorrhagic Syndrome in Infants

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## Abstract

Hemorrhagic syndrome is one of the actual problems of pediatrics. The development of this problem is associated with severe complications, serious health problems in infant. We review the questions of etiology, pathogenesis, clinical syndromes, differential diagnosis and treatment of hemorrhagic syndromes in infants. The authors present quantitative and qualitative differences in the system of plasma hemostasis in newborns, infants and adult patients. This text presents the basic diagnostic algorithms based on the use as routine tests for the study of plasma hemostasis. We review the modern treatment of hemorrhagic conditions in children in first months of life at children with minimal manifestations of hemorrhagic syndrome, and children with liver disease, a syndrome of cholestasis, cystic fibrosis and chronic diseases of the gastrointestinal tract. Article is illustrated by three clinical observations.

## Subject Areas

Pediatrics

## Keywords

Hemostasis, Vitamin K, Hemorrhagic Syndrome, Children

## 1. Introduction

The problem of bleeding is an important question in pediatrics, because coagulation disorders occur in children very often. This is due to the hemostatic system in children. Hemorrhagic disease develops due to the deficiency of vitamin K. The lack of prevention of the deficit vitamin K to newborns may result in the further influence of unfavorable factors of endogenous and exogenous nature to the development of hemorrhagic disease. Hemorrhagic syndrome is an increased risk of bleeding due to deficiency of coagulation factors dependent on the level

of vitamin K. Low activity of these factors in plasma is associated with functional imperfections of the liver, which is typical for children of early age. In some diseases hemostatic disorders are mixed in connection with the accession of disseminated intravascular coagulation (DIC) associated with infectious-septic, immune, destructive or neoplastic processes.

## 2. Characteristic Feature of the System of Hemostasis in Children

The synthesis of proteins of the hemostatic system starts *in utero*, but they are not able to penetrate the placental barrier. Concentrations of most plasma clotting factors can be measured after 10 weeks of fetal development. In the future their level increases. However, the activity of vitamin K-dependent factors in fetuses and newborn infants is lower than adults and becomes normal to 6 months of life. The levels of von Willebrand factor and factor XIII in plasma in newborns practically almost different from reference values for adults. The activity of V and VIII factors reduced in the early stages of gestation and increases to normal adult at the time of birth. Fibrinogen concentration in fetuses is significantly lower than in adults, and gradually increased. The level of thrombin inhibitors is most important in newborns. The concentration of protein C in plasma of newborns is much lower than in adults, and remains low during the first six months of life. The concentration of total protein S is also reduced. The activation of coagulation system does not entail a significant consumption of coagulation factors and is not the cause of low activity of a number of components of hemostasis at the moment of birth. The activity of the fibrinolytic system in neonates is mixed. On the one hand, the activation in childbirth is the increase in the level of products of fibrinolysis in plasma of newborns. The newborns and children first year of life there is a wide range of oscillation parameters in the hemostatic system.

Vitamin K very bad passes the placenta. Primary hemorrhagic disease develops as a result of the low level of vitamin K in the fetus (not more than 50% of adult levels). In breast milk vitamin K comes in small quantity after the birth. It begins to actively produce of the intestinal microflora with the 3 - 5-th day of a child's life [1].

## 3. The Biological Role of Vitamin K

Vitamin K is necessary to activate the process of $\gamma$-carboxylation of glutamic acid in prothrombin (factor II), some factor VII in here (factor VII), antihemophilic globulin (factor IX) and Stuart factor—Provera (X factor), proteins C and S in plasma. In 1929 it was first suggested the presence of a factor in blood clotting [2] [3].

The basic form of vitamin K-vitamin K1 is found in vegetables (cauliflower and Brussels sprouts, spinach, lettuce, zucchini, soy beans). Vitamin K2 is found in liver of beef and kidney of pork. Also it is contained in butter, cheese, eggs,

corn oil, oatmeal, peas. Also vitamin K2 is produced by intestinal microorganisms. Coagulation factors, dependent on the level of vitamin K in plasma, can be detected in the blood in normal quantity in the form of dysfunctional molecules-PIVKA (protein induced by vitamin K absence). These violations are due to dysfunction of carboxylation in the liver. They are not able to efficiently to provide good quality of hemostasis. This can lead to hemorrhagic disease (HD). Often this condition occurs in newborns due to the lack of prevention of vitamin K deficiency in hospitals [4]. Often hemorrhagic syndrome proceeds as hemorrhagic disease of the newborn. There are three forms of hemorrhagic disease (HD) [5]:

1) An early form—symptoms of bleeding manifest in the first day after birth. It can be as a result of taking the drugs of mother that affect neonatal production of vitamin K.

2) Classical form develops on the 2 - 5 day of life in newborns, feeding breast milk and having dysfunction of intestinal absorption.

3) Late form—develops from 2 weeks to 6 months after birth. It develops with inadequate doses of vitamin K (low content of vitamin K in breast milk) or due to inadequate absorption of vitamin K at liver and biliary tract disease.

## 4. Clinical Manifestations

Early hemorrhagic disease of the newborn can begin even *in utero*. And can be detected the intracranial hemorrhage, cephalhematoma removed, skin hemorrhages, bleeding at birth. This violation type occurs in healthy children 5 - 7 days of life usually in the 0.25% - 0.5%. The asphyxia, birth trauma are triggers. Syndrome of hemorrhagic in cutaneous may be presented in the in the underlying parts—buttocks, bleeding under the aponeurosis. We observed the pulmonary bleeding, bleeding in the abdominal cavity (most often the liver, spleen, and adrenal glands) and melena [6] [7]. The malabsorption syndrome of more than 1 week, biliary atresia, hepatitis, cholesterics jaundice, cystic fibrosis—the aggravating factors for late hemorrhagic form. Intracranial hemorrhage, extensive skin ecchymosis, intracranial hemorrhage, melena, hematemesis, bleeding from the injection sites—are syndromes of clinical manifestations of late form [8].

## 5. Diagnosis

The diagnosis is based on the medical history, clinical syndromes and confirmed by laboratory tests: decrease in the activity of the vitamin K-dependent coagulation factors; hypocoagulation—prolonged APTT and PT; decrease of prothrombin (Quick less than 60%) [9] [10].

The level of fibrinogen, factor of von Willebrand, platelets remain within the reference intervals.

## 6. Correction of Disorders of Vitamin K

Usually recommended application vitamin K intravenously. After intravenous infusion vitamin K parameters prothrombin time and APTT normalized within

4 hours. If clinically and laboratory improvement has not occurred, it is likely that the child doesn't GBN. It can be dysfunction of liver, or some other pathology, including hereditary coagulopathy. The dose of vitamin K—1 mg/kg [10].

## 7. Prevention

Intramuscular injection vitamin K—an effective means of preventing of hemorrhagic disease of the newborn.

Premature babies are application at 0.5 mg/kg, and full term-1 mg/kg of vitamin K [9]. The oral form of vitamin K is not efficient enough in terms of prevention of late form hemorrhagic disease of the newborn. Some scientists believe that a weekly intake of 1 mg of vitamin K of all children who are breastfed, are effective in preventing late GBN [10]. The injected of vitamin K once in 5 - 7 days is better prophylactically for children receiving broad-spectrum antibiotics and prematurity.

We present clinical examples of vitamin K dependent hemorrhagic syndrome.

## 8. Clinical Example No. 1

Child, G. R., 7 month. He was observed in the surgical department with the diagnosis of obstructive mega ureter on the left, condition after surgery, urinary fistula, urinary numb. This boy of II pregnancy. He was born at 37 weeks of gestation, weight 3110 g, growth 50 cm. We observed about the megaureter on the left. At the age of 4 months-lumbotomy left, in 5 months-left perirenal abscess, urinary fistula. At the age of 6 months re-admitted to hospital hyperthermia to 39C, anxiety, reduced appetite. Diagnosis: urinary fistula, urinary numb. Therapy-antibiotic the severity of the condition caused by the phenomena: respiratory failure, hypochromic, microcytic anemia, hemorrhagic syndrome. Significant bleeding from sites of blood sampling (brush, fingers):

Laboratory: hemoglobin 66 g/l (120 - 150 g/l), erythrocytes 3.66*10*12/l, (4 - 6*10*12/l) platelets 388*10*9/L (150 - 550*10*9/L), prothrombin Quick 0% (70% - 120%), prothrombin time of more than 240 sec (11 - 15 sec), INR 0 (0.86 - 1.22); thrombin time of 18.3 sec (14 - 21 sec); fibrinogen of 2.23 g/l (0.8 - 3.8 g/l); APTT 77.9 sec (29 - 35 sec); D-dimer 0.22 μg/ml (0.11 - 0.42 μg/ml). The coagulation factor VIII—168% (50% - 120%), coagulation factor IX 5% (50% - 120%); coagulation factor II—4% (50% - 120%); coagulation factor VII is 4% (50% - 120%); coagulation factor X—2% (50% - 120%),

Therapy: erythrocytemass, vitamin K-5 mg/day. We observed normalization of coagulation parameters after one day: prothrombin Quick 90%, prothrombin of 13.9 seconds, INR was 1.06; thrombin time was 17.3 sec; fibrinogen 1.59 g/l; APTT 29 sec; D-dimer 0.37 mcg/ml; plasminogen 75%; protein with 47%. The coagulation factor IX—65%; coagulation Factor II 64%; the coagulation Factor VII—74%; coagulation Factor X—82%.

## 9. Clinical Example No. 2

Patient M, girl, 7 months. Cystic fibrosis (combined form). Chronic Pseudomo-

nas aeruginosa infection.

The girl from the third pregnancy of 36 weeks from caesarean section, weight-2500 kg, growth 47 cm. Breast milk received 2 months. On the third day after birth, with a diagnosis—enterocolitis. At the time of observation (7 months of life)—physical development was low, disharmonious due to the deficit of body weight. The child was observed respiratory failure in the background of cystic fibrosis

Skin was pale, slightly cyanotic tinge in the region of nasolabial triangle. We observed participation of auxiliary muscles during respiration with retraction of compliant places of a thorax. Heart tones are muffled, rhythmic. Breathing with oxygen via mask. Bleeding from injection sites, nasal bleeding was noted. The acid-base balance and blood gases: pH of 7.3, $pCO_2$—44, $pO_2$—153. In the blood was detected hypochromic anemia, hypokalemia is of 2.76 mmol/l, hyponatremia—123 mmol/l, WBC—15 × $10^9$/l, hemoglobin—70 g/l, prothrombin Quick 48%, PT—35 sec, APTT—70, factor von Willebrand 130%, IX factor—11%, VII—7%, II factor—10%, X factor—14%.

Treatment: vitamin K—1 mg /kg. We observed positive dynamics on the second day after vitamin K injections. Hemorrhagic syndrome was stopped. PT—14 sec, APTT—38 sec, IX factor 9% - 42%; VII factor—48%.

## 10. Clinical Example No. 3

Girl, 1 month. The child was born on time by caesarean section, weight—3130 g. She was observed from 6 days after born. During the examination was revealed a tongue-tie. Upon inspection of surgeon at the age of 1 month were bleeding from the mouth which gradually increased over 3 days. During this time, there was dark brown feces, ecchymosis on the chest and back. On examination—an isolated bruises on the skin of the trunk, petechial.

PT > 240 sec, APTT > 128 sec, factor von Willebrand—157%, IX factor—2%. Treatment: introduction of a 1% solution of vitamin K—1 mg/kg twice with an interval of 12 hours. At inspection the next day—no bleeding was noted. The coagulogram indices were within the reference intervals PT—13.1 sec (11.5 - 15.3 sec), APTT—37.1 sec (29.1 - 35.5). The patient was treated of vitamin K a daily dose of 2 during the next 7 days. Hemorrhagic syndrome was stopped within 1 day. After 2 weeks we observed of the child's condition was normal, no bleeding was observed, the skin was clean.

## 11. Conclusion

It is necessary to examine children with minimal manifestations of hemorrhagic syndrome, inject a preventive dose of vitamin K to the children undergoing long-term antibiotic treatment, especially the children with cystic fibrosis, as well as to the risk group children. Periodic monitoring of children with hepatic diseases, cholestasis syndrome and/or chronic gastrointestinal diseases involves additional examination of the cholestasis system in order to timely diagnose and

correct hemorrhagic conditions.

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