DIAGNOSTIC PROCEDURES, THERAPY AND COMPLICATIONS OF HAEMOPHILIA (CASE STUDY)

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ABSTRACT

Introduction: Defects in blood coagulation can be congenital or acquired. Haemophilia belongs to the congenital (hereditary) coagulopathies.It is inherited recessively by a mutant gene located on the X-chromosome, therefore it affects only men. There are two common types of haemophilia, A and B.

Aim of this researche is to trace the representation of haemophilia in the general population, to follow the clinical course, diagnostic procedures, necessary therapy, complications, the role of the laboratory analyst in constructing precise and proper analysis.

Results: We are followed three cases of haemophilia, recorded in transfusion department at the Clinical Center in Macedonia.

For the purpose of this paper work are allocated three people, two with haemophilia A, one child and one adult person and one person with haemophilia B, all male. In all these cases, therapy is preventive and receive appropriate according to age and needs. Their dose increases in case of injuries or extensive bleeding.

Conclusion: Early prophylactic use of clotting factors with severe haemophilia is gaining acceptance as a way to prevent pain and morbidity associated with bleeding disorders. Treatment of severe haemophilia A or B consists of administration of plasma-derived or recombinant clotting factor concentrates.

Keywords: *hematologic diseases, haemophilia, prevention, health*

Introduction: Haemophilia is a rare genetic disorder that limits the blood's ability to clot. This condition can cause prolonged or excessive bleeding, which may occur spontaneously or following an injury or medical or dental procedure. Haemophilia is one of several disorders of the blood clotting process that greatly prolong coagulation (clotting) time. Defects in blood coagulation can be congenital or acquired. Haemophilia belongs to the congenital (hereditary) coagulopathies. It is inherited recessively by a mutant gene located on the X-chromosome, therefore it affects only men. Women are carriers of the pathological gene. There are two common types of haemophilia, one associated with the F VIII deficiency or haemophilia A, and the other with the F IX deficiency or haemophilia B. The genes for both factors are located on the long arm of X-chromosome. Even in the ancient times people recognized haemophilia as a disease even though it was not officially given a name. It is often called "the royal disease ". Platelets are small cells that circulate in the blood. One litre of normal blood has about 150-400 billion platelets. They play an important role in stopping bleeding by clumping together and forming a plug, thus beginning the repair of injured blood vessels. Factors VIII and IX are necessary to fix the plug on the spot and form the cover.

Coagulation, or clotting, is the body's mechanism to halt bleeding. It involves at least 14 sequential steps, each requiring a specific plasma protein or "factor" normally found in the blood. In haemophilia, one of the factors required for the clotting sequence is deficient or absent. The condition known as haemophilia has been recognized for thousands of years. The two most common forms of haemophilia are haemophilia A and haemophilia B. Haemophilia A and B have similar symptoms and were not recognized as separate disorders until 1952. Haemophilia A (classic haemophilia), is caused by the deficiency of Factor VIII. Haemophilia B (also called Christmas

disease, for the name of the family the disorder was first observed in), is caused by the deficiency of factor IX.

Haemophilia A is four times as common, with an estimated incidence of 1 in 10,000 males, while haemophilia B is estimated to occur in one in 40,000 males. Approximately 1 woman in 5,000 is a carrier for haemophilia A, and 1 in 20,000 is a carrier of haemophilia B. Haemophilia is typically divided into three classes: severe, moderate and mild, based on the level of clotting factor in the blood. In severe haemophilia, there is less than 1 percent of normal clotting factor. The degree of severity tends to be consistent from generation to generation. The main treatment for haemophilia is called replacement therapy. Concentrates of clotting factor VIII (for haemophilia A) or clotting factor IX (for haemophilia B) are slowly dripped or injected into a vein. These infusions help replace the clotting factor that's missing or low. Clotting factor concentrates can be made from human blood. The blood is treated to prevent the spread of diseases, such as hepatitis. With the current methods of screening and treating donated blood, the risk of getting an infectious disease from human clotting factors is very small. Approximately 30% of people with severe haemophilia. A develop antibodies to transfused factor VIII, usually shortly after their first few treatments. These antibodies (also called inhibitors) prevent the factor VIIII treatment working properly. It is often the case that, after a while, the inhibitors disappear and only about 10% or less of people with severe haemophilia A will suffer from long term inhibitors. In recent years it has become possible to prevent inhibitors becoming persistent through immune tolerance induction therapy.

The purpose of this research is to trace the representation of haemophilia in the general population, to follow the clinical course, diagnostic procedures, necessary therapy, complications arising as a result of this syndrome, the role of the laboratory analyst in constructing precise and proper analysis by monitoring three cases of haemophilia recorded in the transfusion service in Macedonia.

Matherial and methods: Diagnosis of haemophilia is treat with blood tests to determine the effectiveness of clotting and the levels of clotting factors will be abnormal. We are followed three cases of haemophilia, recorded in transfusion department in Macedonia. For the purpose of this paper work are allocated three people, two with haemophilia A, one child and adult person and one person with haemophilia B, all male. In all these cases, therapy is preventive andreceive, appropriate according to age and needs. Their dose increases in case of injuries or extensive bleeding.

Factor concentrates should usually be stored in a refrigerator but are stable at room temperature for quite long periods. They should not be frozen as this may damage the vials or syringes. Some may be taken out for travel but should ideally be kept in a cool bag.

Item number	Type of haemophilia	Lack factor	Age	Therapy
1.	Haemophilia A	VIII	Child	Koate F VIII 250 I.E
2.	Haemophilia A	VIII	Adult	Koate F VIII 500 I.E
3.	Haemophilia B	IX	Adult	Aimafix 500 IE

Results: Previously, patients were given factor VIII concentrates pooled from thousands of plasma donations. Kogenate is made using baby hamster kidney cells that have been altered by recombinant DNA technology to produce factor VIII. The resulting factor is highly purified, eliminating any possibility of transmission of virus from plasma. Haemophilia B is managed with factor IX concentrates. Factor VIII concentrates are ineffectual in this type of haemophilia. The use of Factor IX concentrate are to maintain a patient through a major surgical procedure. Factor levels should be measured to ensure that expected levels are achieved and that an inhibitor is not present. Factor IX concentrates contain a number of other proteins, including activated coagulating factors that appear to contribute to a risk of thrombosis with recurrent usage of factor IX concentrates. Because of the risk of thrombosis, more care is needed in deciding to use these concentrates.

Case 1

In this case it is a patient aged 23 years, who has been diagnosed with haemophilia B as a baby at 3 months old when the first bruises while bathing. The anamnestic data sets that it is a disease with family history and has his uncle, and this patient had inherited from his mother. The patient in this review appears in the transfusion service, where the blood tests established that it is a type of haemophilia B, which is administered therapy with plasma of 250ml. This patient had a normal childhood without major injuries and bleeding and preventive received plasma and appeared in control examinations in children's clinic and the department of hematology. In the period of puberty, not very often had bleeding from the nose to know that last up to 1 hour, but are regulated by receiving plasma.

After a certain period of treatment with plasma appeared and allergic reactions that manifest the rash on the body, choking and coughing. So as a result of his treatment with plasma is replaced with a concentrate of factor IX or drug Aimafix 500IE.

At age 17, the patient received a blow on the head during sleep the subject located in the immediate vicinity, where there is bleeding in the head above the membrane. This injury is manifested by pain in the head and abundantly discharge in the ears. Therapy that applied patient after this injury is 1000IE concentrate factor IX. For this injury the patient does not appear consequences, he's continued with preventive application of factor IX, often alone when you feel the need, and tingling in the body at a dose of 500 IE from Aimafix.

He lives a normal life like any young man rides a bicycle, doing exercises to strengthen muscles, improve tone, motor skills, coordination and endurance, which would protect the joints alone would have improved the quality of their life. At 22 years old in summer patient collapse it hurts his back and bleeding occurs in the area of first toracal disc, and first and secund lumbal disc. Receiving therapy factor of 1000 IE. In this period occurred no complications until october when patient began to feel severe pain in the lumbar region, pain which lead to hallucinations. Patient occurs the hematology clinic where the doctor determines the inability to move and lost sensation in the lower limbs. Two days before this admission patient received plasma and analgesics. Because progressive symptoms during this admission the patient was hospitalized for further investigations and a decision about treatment. By objective findings have noticed that the patient was subfebril of receipt, conscious and oriented to time, space and people, passively movable and espousing aspect of many severely ill, with moderate nutrition. Skin and mucosa pale colored, without signs of hemorrhagic syndrome. After treatment we obtained the following results:

- Hb-143 g/L
- Le-8,0 x 10^9L
- Tr-388 x10^9L
- Kaolin time -40 secunds
- Chrsitmas factor (IX)-16%

- Total proteins - 86g/L
- Glykemia-5,1 mmol/L
- Kreatinin-49 mmol/L
- Total bilirubin-14 mmol/L
- ALP – 65 U/l
- AST – 23 IJ/I
- ALT – 2 IJ/I
- LDH - 228

Case 2

In this case it is a male patient at 3 years old, who suffers from haemophilia A and it passed him his mother is a carrier. His diagnosis is set at 2 years of age when hospitalized for persistent bleeding from the gums, which has suffered bleeding before 24 hours. When reception is noted that bleeds from lacerokontuzna wound over the teeth and the treatment kauterizator, bleeding never stopped, but after long compression bleedingstopped.

Due to no proportionate injury and bleeding, particularly because the duration of bleeding, doctors suspected of coagulopathy. After treatment we obtained the following results:

- Protrombin time - 75%
- Partial thromboplastin time - 72%
- Fibrinogen - 2,8g/L
- factor VIII - 70%

Thus diagnosed haemophilia type A, so this patient was given a treatment of 250 IE of factor VIII of the drug Koate, preemptively if necessary. In this patient to date has no impact of this disease as a result of prevention.

Case 3

The third case is a person of 29 years who has a lack of factor VIII, which means he is diagnosed with haemophilia A. In this case it is a hereditary disease that the patient receives from his mother. With the diagnosis of 1 year old starts his therapy with factor VIII drug Koate of 500 IE. Childhood passes with minimal bleeding obtained from the children's games, no major injuries, while all the while applying preventive dose of therapy. After administering the drug over a period of about 45 minutes, until it is transported through all the body parts he needs to rest, and then it is recommended that a small movement. Every 6 months or 2 times a year makes analysis of hepatitis C because it has the ability to transmit through blood products. At 9 years of age is surgery of inguinal hernia. This operation does not cause patient complications. Before surgery the patient receives a greater dose of factor VIII and plazma. That he will apply:

-Koate and eight vials, or 4,000IE and after surgery
-Koate- x 2000 I.E /2days
-x1000I.E/4days.

For 22 years there is bleeding, which is indicated by the extraction of two teeth. By analyzing the blood during this bleeding following results were obtained:

- Protrombin time - 87%
- Partial thromboplastin time–48%"(26-36)
- Trombin time -15 "
- Fibrinogen - 3 g/L
- Factor VIII - 20%

Treatment which is applied because this bleeding is:

- Koate-
- x5000IE/2days
- x2000I.E/5days
- x1000 I.E/4days
- and plasma

Three months after injury the wound is completely recover and the patient continues with prevention. So to this day the application of factor VIII when necessary. After administering the drug over a period of about 45 minutes, until it is transported through all the body parts he needs to rest, and then it is recommended that a small movement. Every 6 months or 2 times a year makes analysis of hepatitis C because it has the ability to transmit through blood products.

Conclusion: Contrary to popular belief, minor cuts and wounds do not usually present a threat to haemophiliacs. Rather, the greatest danger comes from spontaneous bleeding that may occur in joints and muscles. This is most prone to occur during years of rapid growth, typically between the ages of 5 and 15 years. Early prophylactic use of clotting factors with severe haemophilia is gaining acceptance as a way to prevent pain and morbidity associated with bleeding disorders. Treatment of severe haemophilia A or B consists of administration of plasma-derived or recombinant clotting factor concentrates. Repeated spontaneous bleeding in joints may cause arthritis, and adjacent muscles become weakened. Pressure on nerves caused by the accumulation of blood may result in pain, numbness, and temporary inability to move the affected area. In the past, this led to permanent crippling disability by adulthood. Haemophilia treatment will mainly depend on its severity and for patients with Haemophilia A or B involves clotting factor replacement therapy.

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