Journal of Advanced Drug Delivery (JADD)
Volume 3, Issue 2 March- April -2016
ISSN NO: 2348-3278
ISRA IMPACT FACTOR: 0.46

Introduction and Guidelines for the Management of Hemophilia: A Review

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Abstract: Hemophilia is an inherited bleeding disorder where one of the bloods clotting proteins is absent or present in a reduced amount. It is an unfortunately a less attracted disease for researchers compared to other life threatening diseases. A diagnosis of hemophilia in you or your child can be a traumatic experience as your knowledge of hemophilia may be very limited or rooted in a past reality where adequate and safe treatment was no available. There is obviously a need to establish facilities and treatment options that will help the patient with hemophilia to manage their life with ease. Current state of the art treatment for hemophilia is available in Ireland. The life expectancy of a child born with hemophilia now in Ireland is essentially normal and their quality of life will be excellent. As this is a genetic disorder no complete cure is possible as of now. The only available treatment option is the infusion of factors and some adjuvant therapies depending upon the bleeding conditions. This article present an review of hemophilia, in order to produce the attention of medical as well as pharmacy professionals for the management of millions of hemophilic patients .

Keywords: Hemophilia, Chromosomes, Clotting factor, Hemostasis.

HEMOPHILIA:

Hemophilia is a group of inherited blood disorders in which the blood does not clot properly. It is a genetic condition that causes people to keep on bleeding for a long time unless treated. People with hemophilia do not bleed faster than anyone else; but will bleed continuously at the normal rate until they are treated. This is because the blood is unable to clot without any therapy. Internal bleeding is the major concern in hemophilia. Bleeding is common into joints such as knees, ankles and elbows. This may be caused by injury, but in severe hemophilia, can begin spontaneously.[1,2] Hemophilia is the standard international spelling, also known as haemophilia in the UK, other translations include: hémophilie, hemofilie, hemofili, hemofilia, hämophilie, emofilia. We will use the standard international spelling for the purpose of this section. Bleeding disorders are due to defects in the blood vessels, the coagulation mechanism, or the blood platelets. An affected individual may bleed spontaneously or for longer than a healthy person after injury or surgery.

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The blood coagulation mechanism is a process which transforms the blood from a liquid into a solid, and involves several different clotting factors.

The mechanism generates fibrin when it is activated, which together with the platelet plug, stops the bleeding. When coagulation factors are missing or deficient the blood does not clot properly and bleeding continues. Patients with Hemophilia A or B have a genetic defect which results in a deficiency in one of the blood clotting factors. [1,3.] The first medical professional to describe a disease was Abulcasis. In the tenth century he described families whose males died of bleeding after only minor traumas [1,2]. While many other such descriptive and practical references to the disease appear throughout historical writings, scientific analysis did not begin until the start of the nineteenth century.

In 1803, Dr. John Conrad Otto, a Philadelphian physician, wrote an account about "a hemorrhagic disposition existing in certain families" in which he called the affected males "bleeders".[18]He recognised that the disorder was hereditary and that it affected mostly males and was passed down by healthy females. His paper was the second paper to describe important characteristics of an X-linked genetic disorder (the first paper being a description of colour blindness by John Dalton who studied his own family). Otto was able to trace the disease back to a woman who settled near

Plymouth in 1720. The idea that affected males could pass the trait onto their unaffected daughters was not described until 1813 when John Hay published an account in The New England Journal of Medicine.[2] In 1924, a Finnish doctor discovered a hereditary bleeding disorder similar to Haemophilia localised in a group of islands (called the "Åland Islands") which are located to the southwest of Finland. This bleeding disorder is called "Von Willebrand Disease".

The term "haemophilia" is derived from the term "haemorrhaphilia" which was used in a description of the condition written by Friedrich Hopff in 1828, while he was a student at the University of Zurich. In 1937, Patek and Taylor, two doctors from Harvard, discovered anti-haemophilic globulin. In 1947, Pavlosky, a doctor from Buenos Aires, found haemophilia A and haemophilia B to be separate diseases by doing a lab test. This test was done by transferring the blood of one haemophiliac to another haemophiliac. The fact that this corrected the clotting problem showed that there was more than one form of haemophilia.

European royalty

Haemophilia has featured prominently in European royalty and thus is sometimes known as 'the royal disease'. Queen Victoria passed the mutation for Haemophilia B to her son Leopold and, through some of her daughters, to various royals across the continent, including the royal families of Spain, Germany, and Russia. In Russia, Tsarevich Alexei Nikolaevich, son of Nicholas II, was a descendant of Queen Victoria through his mother Empress Alexandra and suffered from haemophilia. It was claimed that Rasputin was successful at treating Tsarevich's haemophilia. At the time, a common treatment administered by professional doctors was to use aspirin, which worsened rather than lessened the problem. It is believed that, by simply advising against the medical treatment, Rasputin could bring visible and significant improvement to the condition of Tsarevich. In Spain, Queen Victoria's youngest daughter, Princess Beatrice, had a daughter Victoria Eugenie of Battenberg, who later became Queen of Spain. Two of her sons were haemophiliac sand both died from minor car accidents. Her eldest son, Prince Alfonso of Spain, Prince of Asturias, died at the age of 31 from internal bleeding after his car hit a telephone booth. Her youngest son, Infante Gonzalo, died at age 19 from abdominal bleeding following a minor car accident where he and his sister hit a wall while avoiding a cyclist. Neither appeared injured or sought immediate medical care and Gonzalo died two days later from internal bleeding.

Blood contamination issues

Ryan White was an American haemophiliac who became infected with HIV/AIDS through contaminated blood products. Prior to 1985, there were no laws enacted within the U.S. to screen blood. As a result, many haemophilia patients who received untested and unscreened clotting factor prior to 1992 were at an extreme risk for contracting HIV and hepatitis C via these blood products. It is estimated that more than 50% of the haemophilia population, i.e. over 10,000 people, contracted HIV from the tainted blood supply in the United States alone. As a direct result of the contamination of the blood supply in the late 1970s and early/mid-1980s with viruses such as hepatitis and HIV, new methods were developed in the production of clotting factor products. The initial response was to heat-treat (pasteurise) plasma-derived factor concentrate, followed by the development of monoclonal factor concentrates, which use a combination of heat treatment and affinity chromatography to inactivate any viral agents in the pooled plasma from which the factor concentrate is derived. The Lindsay Tribunal in Ireland investigated, among other things, the slow adoption of the new methods.

MOST COMMON TYPES OF HEMOPHILIA

Hemophilia-A (Classic hemophilia)

It is otherwise called as the classic hemophilia. It is "X" linked recessive disorder occurred due to the absence or deficiency of clotting factor VIII (FVIII). Hence it affects only males. Females are said to be carriers. Carrier females usually are asymptomatic but can have bleeding symptoms (e.g., are easily bruised or have menorrhagia or excess bleeding after trauma) when they have significant reductions in factor VIII levels, which are caused by the greater (extreme) inactivation of the normal FVIII gene, compared with the hemophilic FVIII gene, during early embryogenesis. The occurrence of hemophilia –A is 1:5000-10000. [1,2,3,4]

Hemophilia B (Christmas disease)

It is also an "X" linked recessive disorder occurring due to the absence or deficiency of the clotting factor IX. The inheritance pattern and the symptoms of hemophilia B are same as that of the classic hemophilia. The occurrence of hemophilia –B is 1: 20000-34000. [1,2,3]

Hemophilia C

It is an autosomal recessive disorder exhibits bleeding symptoms because of the absence /deficiency of the factor XI. For inheriting the disease both parents must carry the defective gene. Reports are there as exceptions, that people have bleeding problems when only one of their parents has the gene which causes Factor XI Deficiency. Factor XI Deficiency affects males and females in equal numbers. The occurrence of the Hemophilia C is1:100000 [1]

Acquired hemophilia

This is very rare. The patient develops the condition during his/her lifetime and it does not have a genetic or heritable cause. It occurs when the body forms antibodies that attack one or more blood clotting factors, (usually factor VIII), thus preventing the blood clotting mechanism from working properly. Patients may be male or female and the pattern of bleeding is rather different from that of classical hemophilia, the joints being rarely affected. The disorder is particularly associated with old age and occasionally complicates pregnancy. [1,2,3]

SEVERITY OF HEMOPHILIA:

The severity of haemophilia is related to the degree of deficiency of the relevant clotting factor in the blood. There are three levels: severe, moderate and mild. A person with less than 1% of normal clotting activity is described as having severe haemophilia. A person with between 1% and 5% of normal clotting activity is described as having moderate haemophilia and a person with over 5% but less than 50% of normal activity is described as having mild haemophilia [5,15,14,]

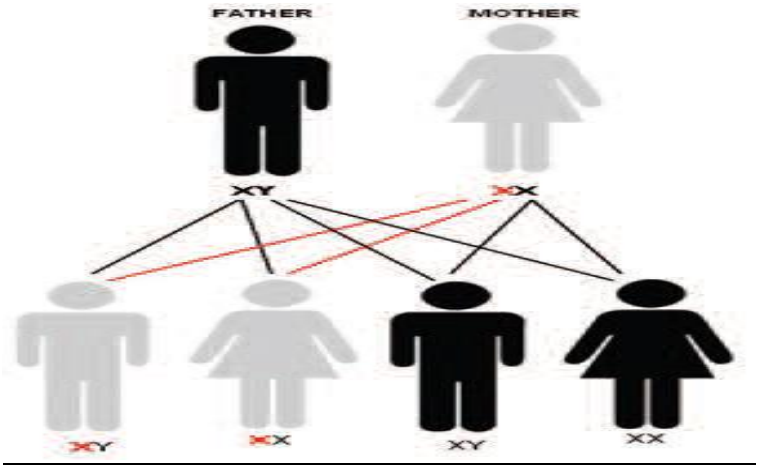

Figure 1: Inheritance pattern father has Haemophilia of Haemophilia.

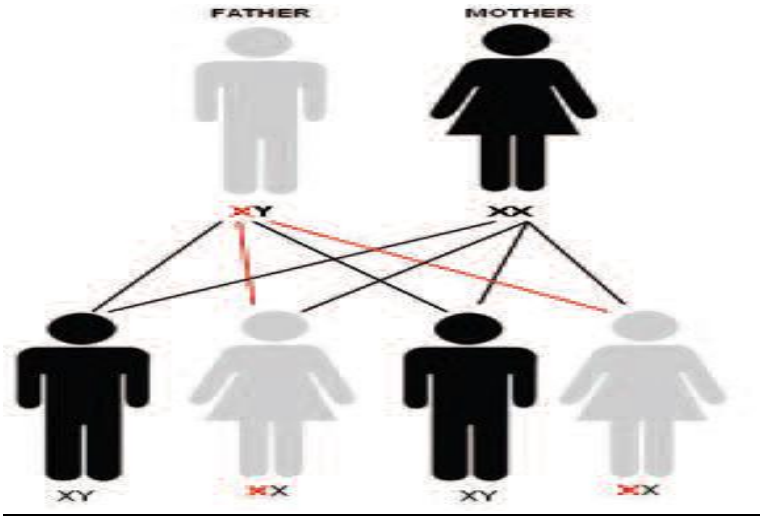

Figure 2: Inheritance pattern when the when the mother is a carrier of Haemophilia.

CAUSES OF HEMOPHILIA

People with hemophilia are born with it. It is caused by a fault in one of the genes that determine how the body makes blood clotting factor VIII or IX. These genes are located on the X chromosome. [6,7]

To understand how hemophilia is inherited, it is important to learn about chromosomes.

Chromosomes:

Chromosomes are blocks of DNA (deoxyribonucleic acid). They contain very detailed and specific instructions that determine:

- How the cells in a baby's body develop.
- What features the baby will have, including, for example, hair and eye color.
- Whether the baby is male or female.

In humans there are 23 pairs of chromosomes, including the sex chromosome pair. There are two types of sex chromosome:

- The X chromosome
- The Y chromosome

All humans have a pair of sex chromosomes:

- Males have an X + Y pair
- Females have an X + X pair

What chromosomes do we inherit from our parents?

- A Male inherits his
  - X chromosome from his mother
  - Y chromosome from his father
- A Female inherits
  - One X chromosome from her mother
  - One X chromosome from her father

  She does not inherit both X chromosomes from her mother. She has no Y chromosomes.

How can we calculate the risk of hemophilia in offspring?

(Before reading on, remember that the faulty gene is never on the Y chromosome. If it is present, it will be on the X chromosome.)

- Female ($X + X_{faulty}$) is a carrier, but does not have hemophilia. The "good" X chromosome allows the production of enough clotting factor to prevent serious bleeding problems.
- Male ($Y + X_{faulty}$) will develop hemophilia and can pass it on.

If the father has hemophilia and the mother has no faulty gene (is not a carrier):

Father ($Y + X_{faulty}$). Mother ($X + X$).

- There is no risk of inherited hemophilia in their sons because boys will inherit their X chromosome from the mother, not the father (they inherit the father's Y chromosome only, which does not have the faulty gene).
- All the daughters will be carriers but will not develop hemophilia although they will inherit the father's X chromosome, which has the faulty gene. However, their maternal X chromosome, which does not have the faulty gene, usually allows the production of enough clotting factor to prevent serious bleeding problems. [12,13]

If the father does not have hemophilia and the mother has a faulty gene:

Father ($Y + X$). Mother ($X + X_{faulty}$).

- There is a 50% chance that sons will develop hemophilia because:
  - There is a 50% risk that a son will inherit his mother's X_{faulty} chromosome, plus his father's Y chromosome - he will have hemophilia.
  - There is a 50% chance he will inherit his mother's "good" X chromosome, plus his father's Y chromosome - he will not have hemophilia.
- There is a 50% chance that daughters will be carriers, (but no chance of developing hemophilia), because:
  - There is a 50% chance she will inherit her mother's X_{faulty} chromosome, making her a carrier.
- There is a 50% chance she will inherit her mother's "good" X chromosome, which would mean she would not be a carrier.

Approximately one third of patients with hemophilia have no family history of the disease, either because of new genetic mutations, or because previous affected generations either had daughters (who were carriers) or sons who died in early childhood from hemophilia or any other cause or who were not affected.

Coagulation and blood clot:

Coagulation is a complex process by which the blood forms clots to block and then heal a lesion/wound/cut and stop the bleeding. It is a crucial part of hemostasis - stopping blood loss from damaged blood vessels. In hemostasis a damaged blood vessel wall is plugged by a platelet and a fibrin-containing clot to stop the bleeding, so that the damage can be repaired.

Coagulation involves a cellular (platelet) and protein (coagulation factor) component.

When the lining of a blood vessel (endothelium) is damaged, platelets immediately form a plug at the site of the injury, while at the same time proteins in the blood plasma respond in a complex chemical reaction, rather like a waterfall, to form fibrin strands which reinforce the platelet plug.
Primary hemostasis - when the platelets gather at the site of an injury to plug (block) it. Secondary hemostasis - proteins (coagulation factors) act in a series of chemical reactions to strengthen the plug and allow healing to begin. [8,9]

Platelet:
A platelet is a disc-shaped element in the blood that is involved in blood clotting. They aggregate (clump together) during normal blood clotting. They are classed as blood cells, but are in fact fragments of large bone marrow cells called megakaryocytes. [10]

Fibrin:
Fibrin is an insoluble protein involved in blood clotting. Fibrin is deposited around the wound in a form of mesh to strengthen the platelet plug. The whole thing dries and hardens (coagulates) so that the bleeding stops and the wound then heals. Fibrin is developed in the blood from a soluble protein, fibrinogen. When platelets come into contact with damaged tissue thrombin is formed as a result of a series of chemical processes (coagulation cascade) that culminate in the formation of fibrin from fibrinogen. [11]

Coagulation factors (Clotting factors)
Coagulation factors are proteins, mostly manufactured by the liver. They were originally numbered in the order of their discovery, traditionally using Roman numerals from I-XIII. Some of the numbers such as III and VI are not used any more and in recent years, many proteins that affect blood clotting have been discovered but have been given a name rather than a number. When a blood vessel wall is damaged, or any kind of wound occurs, a complex set of chemical reactions involving these coagulation factors (and acting rather like a waterfall) takes place. The final step of the cascade of chemical reactions is to convert fibrinogen - Factor I - into fibrin, forming a mesh which clumps platelets and blood cells into a solid clot, plugging the hole and stopping the bleeding. Patients with Hemophilia A have deficient levels of Factor VIII, while patients with Hemophilia B have deficient levels of Factor IX. [12]

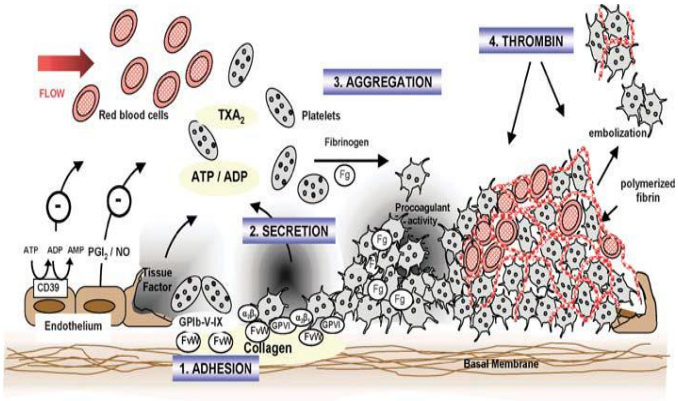

Figure 3. Hemophilia: A deficient hemostatic System

SYMPTOMS AND DIAGNOSIS
Hemophilia symptoms vary, depending on the degree of blood clotting factor (coagulation factor) deficiency and they also depend on the nature of any injury. [1,7]
Three levels of hemophilia are recognized, according to the level of clotting factor amounts in the blood. These are often expressed as percentages of normal:

- Above 5% - mild hemophilia
- 1% to 5% - moderate hemophilia
- Less than 1% - severe hemophilia

Mild hemophilia
People with inherited mild hemophilia may not have any symptoms until an event occurs which wounds the skin or tissue, such as a dental procedure or surgery, and results in prolonged bleeding. In societies where male circumcision is carried out soon after birth, mild hemophilia will be detected earlier. Joint bleeding is uncommon.

Moderate hemophilia
Those with inherited moderate hemophilia will be noticeable early on. The child will bruise easily and may also experience internal bleeding symptoms, especially around the joints, and after a blow or a fall. Bleeding that occurs inside a joint is usually referred to as a joint bleed. A blood sample from the newborn baby can be used to make a diagnosis. This applies to mild, moderate and severe cases. In at least 30% of cases of hemophilia there is no known family history, the occurrence of hemophilia is presumed to be the result of a spontaneous genetic mutation

The first symptom of hemophilia is usually in the form of extensive bruising as the child learns to crawl or walk, Moderate and mild hemophilia may not be diagnosed until later in childhood or in some cases even in adulthood. The process of diagnosis involves many and other members of the family. The Irish Haemophilia Society is available to offer support to all family members and provides a range of education and support programmers for all age groups. complex laboratory tests on blood samples and takes several days to complete. The time around diagnosis can be a difficult period for parents particularly where there is no family history of the condition. It is important that parents become informed about hemophilia and the impact it is likely to have on their child. A blood sample from the newborn baby can be used to make a diagnosis. This applies to mild, moderate and severe cases. In at least 30% of cases of hemophilia there is no known family history, the occurrence of hemophilia is presumed to be the result of a spontaneous genetic mutation[14,15].

Symptoms of a joint bleed:

- Tingling sensation in the joint
- Pain in the joint
- Irritation in the joint

If left untreated, the patient may eventually experience:

- More severe pain in the joint
- Joint stiffness
- The affected area becomes swollen, tender and hot

Joint bleeds most commonly affect the:

- Ankles
- Knees
- Elbows

Severe hemophilia

Symptoms are similar to those found in moderate hemophilia. A child with severe hemophilia will often bleed for no apparent reason, often referred to as spontaneous bleeding. Most commonly, in early childhood from about 18 months of age, the nose or mouth start to bleed or apparently spontaneous bruises appear, particularly on the legs. Parents are sometimes suspected of causing non-accidental injury (deliberate harm) to their children. [1]

Symptoms of hemophilia type bleeding may include:

- Several large or deep bruises
- Joint pain or swelling
- Unexplained bleeding or bruising
- Blood in feces (stools) and urine
- Unexplained nosebleeds
- Unexplained gum bleeding
- Tightness in the joints

Intracranial hemorrhage (bleeding inside the skull)

About 1 in every 30 patients with hemophilia will have intracranial hemorrhage at least once during their lives. This should be treated as a medical emergency. Spontaneous intracranial hemorrhage is rare and in many cases bleeding inside the skull will be the result of a blow to the head.

Symptoms of intracranial hemorrhage include:

- A bad headache
- Vomiting
- Confusion
- Fitting (Convulsion)
- Loss of balance
- Slurred speech, or other speaking difficulties
- Stiff neck
- Vision problems
- Loss of coordination
- Some of the facial muscles do not work (sometimes all of them)

Cuts and scratches:

In most cases minor cuts and scratches do not pose any problems for people with haemophilia. A little pressure is usually enough to stop the bleeding. A person with a bleeding disorder does not cut more easily, bleed more profusely or bleed faster than normal. They simply bleed for longer[16,17].

Joints and Muscles:

For those severely affected, a major problem can be internal bleeding into joints, muscles and soft tissues. All of us damage our muscles in small ways in the activities of everyday life. Most people repair that damage automatically. For the person with a severe bleeding disorder however, the tiny breaks in the blood vessels in joints and muscles may continue to bleed as a result of normal everyday activity. These bleeds are sometimes described as "spontaneous" because it is impossible to identify a cause. An ache or irritation in an affected area is usually an indication that a person with haemophilia is getting a bleed. If left untreated pain may become excruciating. In the case of joint bleeding, the blood which has escaped into the joint has a very damaging effect on the surface of that joint. Once a joint becomes damaged then bleeding will occur more

frequently resulting in a "target joint". The majority of bleeds into joints and muscles occur in the lower limbs, with ankles and knees being the worst affected in most people. [1,13]

Soft tissue Bruises:
Soft tissue bruises will always occur in people with bleeding disorders. Although these may look serious they usually do not require any treatment. Sometimes if the bruise is increasing in size and causing pain, then treatment with factor may be recommended.

Head Face and neck injuries:
After a blow to the head, face or neck, sufficient factor must be given immediately to bring the factor level to 100%. These injuries must be assessed at a treatment centre. If the injury is significant enough, a person with a bleeding disorder may need to be admitted to hospital and may require a CT scan to ascertain the extent of bleeding, if any.

Minor Head injuries:
These are injuries that can lead to bruising or even small cuts on the head. These injuries should always be treated either at home or at the treatment centre.

Serious Head injuries:
These result from a severe bump on the head. A head injury is always serious if the person is knocked unconscious. These injuries should be treated as quickly as possible and the patient must be taken to the nearest haemophilia centre.

How is hemophilia diagnosed?
Prenatal testing - if a pregnant woman has a history of hemophilia, a hemophilia gene test can be done during pregnancy. A sample of placenta is removed from the uterus and tested. This test is known as a CVS (chorionic villus sampling) test.

Blood test - If a doctor suspects a child may have hemophilia a blood test can determine whether the patient has hemophilia A or B, and how severe it is. Blood tests can be performed from the time of birth onwards.

TREATMENT FOR HEMOPHILIA
Haemophilia is treated by replacing the missing clotting factor in the blood through an intravenous infusion of clotting factor concentrate. Each bleeding episode must be promptly treated. Once the bleeding stops, pain rapidly diminishes and use of the limb returns. The clotting factor concentrate is manufactured as a white powder and is reconstituted with the sterile water provided with the factor concentrate. The Factor VIII and Factor IX used for the treatment of haemophilia is called "recombinant factor". What cannot be emphasised enough is that a person with haemophilia must have treatment as soon as a bleed starts. It prevents further bleeding, pain and most importantly, reduces the likelihood of permanent damage to joints (target joints). All surgical procedures, including dental extractions and fillings, will require treatment beforehand and should be organised through your Haemophilia Treatment Centre.[1,12] The main breakthrough in treatment occurred when coagulation factor deficiencies linked to hemophilia could be identified and then replaced, using products derived from human blood[21,18].

In the past patients used to receive whole blood or plasma infusions to control episodes of bleeding. Even though this helped, levels of clotting factors, especially factors VIII and IX, never reached the levels required for really effective blood coagulation, nor could these levels be sustained-in other words, serious bleeding was only partly treated. Cryoprecipitate, made through the cold precipitation of frozen plasma from1965 onwards, was the first really effective treatment for hemophilia A. Freeze-dried concentrates made from human plasma containing the right levels of Factors VIII and IX became available in the late 1960s and early 1970s. Being able to keep the treatment at home and use it as required meant that patients could travel, leave the home, go to work, and enjoy a level of independence. However, a large number of patients subsequently became infected with blood-borne pathogens, such as hepatitis –B , hepatitis-C and HIV. From the mid 1980s rigorous donor selection and viral inactivation procedures reduced the risk of blood-borne viral transmission to nearly zero. During the 1990s it became possible to prepare synthetic (recombinant) factors, using specially prepared mammalian cells and these recombinant concentrates are now widely used.

Hemophilia treatment will mainly depend on its severity and for patients with Hemophilia A or B involves clotting factor replacement therapy. There are two approaches:

- **On demand** - giving treatment to stop prolonged bleeding when it occurs. This is more common in the management of patients with mild hemophilia.
- **Preventative treatment (prophylaxis)** - medication to prevent bleeding episodes, and subsequent complications, such as joint and/or muscle damage. More commonly used for patients with moderate or severe hemophilia[19].

Clotting factor concentrates

Clotting factor concentrates can be made in two different ways:

- **Plasma-derived clotting factors** - prepared from the plasma of donated human blood.
- **Recombinant clotting factors** - the first generation of recombinant products use animal products in the culture

  medium and had human albumin (a human blood product) added as a stabiliser. Second generation products use animal-derived materials in the culture medium but do not have added albumin and instead use sucrose or other non-human derived material as a stabiliser. Third generation clotting factors have no albumin present at any stage of their preparation. Mouse monoclonal antibodies have been routinely used in the purification of coagulation factors for many years but a recently licensed recombinant factor VIII employs a synthetic ligand for this step. This has resulted in the production of the first factor VIII concentrate to be free of all exogenous human and animal protein, a goal which was reached for hemophilia B when the first recombinant factor IX was licensed in 1997.

Desmopressin (DDAVP)(for mild hemophilia A)

It is a synthetic analog of the anti diuretic hormone vasopressin (1-deaminocys-8D arginini-vasopressin). It is useful in mild hemophilies This medication is a synthetic hormone which encourages the body to produce more of its own Factor VIII. It is unsuitable for patients with hemophilia B and those with severe hemophilia A. In patients with milder forms of hemophilia A, factor VIII replacement therapy may be necessary, especially for severe bleeds, or after serious injury or major surgery. [1]

RICE (Rest, Ice, Compression, Elevation)

RICE is a treatment many health care professionals recommend for joint bleeds. It also reduces swelling and tissue damage when used together with clotting factor concentrates.

Administering clotting factor concentrates

The medication is injected into a vein - generally in the back of the hand or at the crook of the elbow. Initial treatments are usually administered by a doctor or nurse at a hospital or clinic. Most adults can learn how to do these themselves, which means they can stop bleeding rapidly and effectively wherever they are. If the patient is a child the parents or caregivers (UK/Ireland/Australia: carers) can learn how to administer treatment. The majority of very young patients can receive most of their treatment at home.

If a patient is finding it hard to access a suitable vein, or if intensive treatment is required, a port-a-cath, or an external catheter called a Broviac or Hickman line can be placed surgically into a vein, allowing factor replacement therapies to be given, and blood to be drawn easily for routine emergency tests. The use of such catheters can be complicated by infection and blockage and they have to be used with great care[20].

Treating bleeds

Bleeding episodes (bleeds) are an inevitable complication for patients with hemophilia A and B, even for patients with mild forms. As the underlying problem is one of prolonged bleeding, rather than rapid bleeding, they often appear not to be medical emergencies.

If a person with hemophilia experiences any of the following he should seek immediate skilled medical help:

- There is an injury to the neck, mouth, tongue, face or eye.
- There is a severe blow to the head.
- Bleeding is heavy or persistent.
- There is severe pain or swelling in any part of the body.
- An open wound requires stitching.

Most other bleeds, such as joint/muscle bleeds, small injuries and cuts that do not require stitches and nosebleeds are generally treated at home, but patients should always seek the advice of a healthcare professional when in doubt. Any treatment will be more effective if it is started early.

Storing treatment

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. Read instructions on product storage. If you are unsure, check with a health care professional or qualified pharmacist.

Inhibitors

Approximately 30% of people with severe hemophilia 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 hemophilia A will suffer from long term inhibitors. In recent years it has become possible to prevent inhibitors becoming persistent through immune tolerance induction therapy. Where inhibitors do not respond to this approach alternative treatments are available. Inhibitors rarely develop in mild hemophilia A or in hemophilia B of any severity[21].

Home Treatment

Both preventive and on demand treatment can be administered at home. Home treatment is the ideal method of treatment from a medical viewpoint as a minimum amount of time is lost between the recognition of a bleed and treatment. This has many advantages, it reduces the disruption caused by a bleeding episode to the person with haemophilia and his family and the patient feels more able to control his condition. The benefits of self in fusion at home not only include increased independence and the bonus of not having to travel to the hospital for treatment, but school and work attendance is more regular. If bleeds are treated promptly, the period of incapacity caused by each episode can be reduced. In adults and teenagers home treatment is usually carried out by the affected person. From a young age children will be taught how to self infuse. Alternatively, a device called a Port-a-Cath (Freddie) can be used to facilitate venous access until self infusion using the veins is practical.

Prophylaxis

It is recommended that all children with severe factor deficiencies should be commenced on a programme of factor concentrate prophylaxis. Prophylaxis involves small regular (2-3 per week) infusions of factor concentrate to prevent spontaneous bleeding and to minimise traumatic bleeding. This treatment regime, although it can be time consuming and at times difficult to learn, will prevent joint damage and lead to an improved quality of life. [1,7]

Genetic Counselling

For carriers or possible carriers it is advisable to undergo genetic counselling preferably before becoming pregnant. Genetic Counselling will provide information to enable a woman to make an informed decision in relation to family planning. [4]

PREVENTION

The transmittance of the hemophilia to the next generation can be prevented by the following methods.

1) Prenatal intrauterine diagnosis with termination of pregnancy as an option

2) Pre implantation genetic diagnostic testing (PGD)

3) IVF with egg/sperm donation.

FUTURE

Gene therapy, oral delivery of factor concentrates, long acting infusions, controlled release implants, prolonged release of other adjuvant therapy drugs are the areas to be concentrated for making the life of haemophilic patients easier

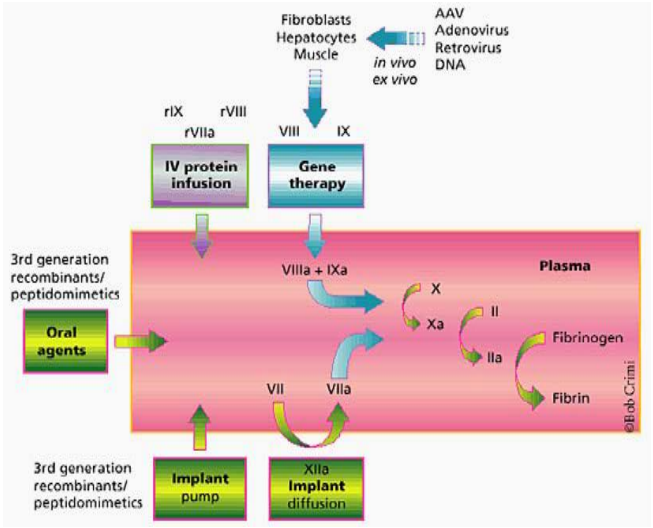

Figure 4. The possible future developments for the treatment of hemophilia

CONCLUSION:

Hemophilia is a bleeding disorder, very hard to live with. As the number of patients reported with hemophilia is comparatively less than other major diseases like cancer, cardiac diseases, and diabetics it seems to be less concentrated area by researchers. As technologies develop, the days are not far away when hemophilia is treated with ease and even complete cure possible.

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