Specialty dentistry for the hemophiliac: Is there a protocol in place?

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Abstract

Restorative dental care for the hemophiliac patient is of paramount importance for the fact that advanced dental conditions and subsequent treatments prove to be more complicated and risky. Quite often, dental health is neglected by hemophiliacs for fear of bleeding during procedures. Surprisingly, even dental specialists avoid these candidates and contribute to the conversion of a simple dental patient to an oral surgical patient. The complexities involved in diagnosing a bleeding disorder and the rarity of a standardized protocol to handle such patients contribute to this problem. This article prescribes a simple protocol to diagnose bleeding disorders and a modified scheme for endodontic and periodontal therapies in a hemophiliac patient.

Keywords: Endodontic surgery, hemophilia, periodontal surgery, restorative dentistry

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Bleeding disorders are certainly one of the most challenging medical conditions amongst health professionals, for reasons well known. Since common ailments are commoner, hemophilia requires a special mention. The highly vascular oral cavity is definitely a hot spot for hemorrhage in this group of patients. Unfortunately, known hemophiliacs neglect dental health for fear of bleeding during procedures and this has been the primary reason for lack of good dental care for them.[1] It is not infrequently that a dentist becomes the first person to diagnose a bleeding disorder while treating dental trauma in a child or performing extractions. Thorough knowledge and systematic approach is mandatory for any dental health professional raring to handle hemophiliacs, the absence of which can lead to disastrous outcomes. Fatal hemorrhage following regional anesthesia for operative dentistry in a known hemophiliac has been reported.[2] The most common emergency following dental procedure in a hemophiliac is airway obstruction by a developing hematoma in the oro-pharynx. Endo-tracheal intubation or creation of a surgical airway for a hemophiliac patient only adds to the misery by making situations worse.

References to excessive and unexplained bleeding have been made since antiquity. In the Babylonian Talmud, a collection of Jewish Rabbinical writings from the 2nd century AD, it was written that male babies did not have to be circumcised if two brothers had already died from the procedure. In the 12th century AD, an Arabian physician from Cordoba named Albusas wrote of males in a particular village, who had died of uncontrollable bleeding. Occasional references to bleeding can be found in the scientific literature of following centuries.

In the US, the transmission of hemophilia from mothers to sons was first described in the early 19th century. In 1803, the Philadelphia
The diagnostic laboratory findings in hemophilia can be summarized as follows: a prolonged activated partial thromboplastin time (APTT), thrombin clotting time (TCT), fibrin degradation products (FDPs), specific Factor assays and inhibitor screening tests. The PT is normally considered normal; however, bleeding may not be clinically significant until the bleeding time is greater than 15 min.

VIII or IX.

The APTT is considered normal if the control APTT and the test APTT are within 10 seconds of each other. Control APTT times are usually considered normal; however, bleeding may not be clinically significant until the bleeding time is greater than 15 min.

The severity of hemophilia is variable, but correlates well with the Factor VIII level of the plasma. Normal plasma contains 1 unit of Factor VIII per ml, a level defined as 100%. Factor VIII activity of less than 1% results in severe hemophilia with spontaneous bleeding, which typically becomes apparent in childhood with prolonged bleeding into muscles or joints (hemarthroses), easy bruising and prolonged bleeding from wounds following even minor injuries. Factor VIII activity of 1-5% causes moderate hemophilia while levels above 5% although grouped as mild hemophilia can cause minor trauma to bleed persistently. Bleeding after dental extractions is sometimes the first or only sign of a mild disease. Oral bleeding can be very persistent and troublesome due to fibrinolytic substances in the saliva.[7] A Factor VIII level above 25% causes very mild disease; the patient can generally lead a relatively normal life and may remain undiagnosed, but there can be prolonged bleeding following trauma or surgery. Absence of post-extraction hemorrhage cannot always rule out hemophilia but most will bleed excessively following a tonsillectomy.[8] An interesting observation is that the clotting time is within normal limits even at 1-2% of Factor VIII[9]

Basically, hemophiliacs can be grouped into those who have nonfunctioning Factor VIII analogues and the others who do not even have the abnormal Factor VIII. Fortunately, the former group forms the majority because those in the latter group may develop antibodies to Factor VIII during transfusion.[10]

General Considerations

Hemophilia is the most common hemorrhagic diathesis across the globe with an occurrence of 1 per every 10,000 people[6] It is caused by congenital deficiency in the blood, of Factor VIII (antihemophilic globulin, AHG). It is a sex-linked recessive characteristic, transmitted by asymptomatic female carriers and manifest in males although as female hemophilia has been reported by Gilchrist in 1961. Sons of carriers have a 50:50 chance of developing hemophilia while daughters of carriers have a 50:50 chance of being carriers. All daughters of an affected male are carriers but sons are normal. The defective gene on the X chromosome causes a deficiency of Factor VIII, which can be either complete or partial. Hemophilia A arises from a variety of mutations; some 150-point mutations have been characterized.

Clinical Laboratory Tests

Basically, laboratory tests for investigating bleeding disorders can be aimed at evaluating either primary or secondary hemostasis[11] The two clinical tests used to evaluate primary hemostasis are platelet count and bleeding time. Normal platelet counts are 250,000 ± 150,000 / mm³. Spontaneous clinical hemorrhage is not usually observed with platelet counts above 15,000 to 20,000 / mm³. Surgically related or traumatic hemorrhage is more likely with platelet counts below 50,000 to 80,000 / mm³. Bleeding times between 3 to 7 min are usually considered normal; however, bleeding may not be clinically significant until the bleeding time is greater than 15 min.

Numerous tests evaluate the status of secondary hemostasis, including prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin clotting time (TCT), fibrin degradation products (FDPs), specific Factor assays and inhibitor screening tests. The PT is normal if both the control and patient's test plasma are 12 ± 1 second. The APTT is considered normal if both the control APTT and the test APTT are 10 ± 2 seconds. This test evaluates the extrinsic system and measures the presence or absence of clotting Factors I, II, VII and X. Its most common use is to measure the effects of dicumarol and the reduction of vitamin K-dependent Factors II, VII, IX and X. Since the extrinsic system uses only Factors I, II, VIII and X, it does not measure the reduction of Factors VIII or IX.

The APTT is considered normal if the control APTT and the test APTT are within 10 seconds of each other. Control APTT times are usually 25 ± 10 seconds. The TCT is used specifically to measure levels of fibrinogen and its conversion to fibrin. Additionally, it is used to measure the presence of heparin, FDPs or other para proteins that inhibit the conversion of fibrinogen to fibrin; the normal level of circulating fibrinogen is 250 mg/dl.

Diagnosis

Although the disease is congenital it may not manifest clinically for several years[12] Identifying these patients via the health history, clinical examinations and laboratory tests is of prime importance. Health questioning should cover (a) History of bleeding after previous surgery or trauma, (b) Past and present drug history, (c) History of bleeding problems among relatives and (d) Illness associated with potential bleeding problems.

Hemophilia has often been called the “Royal Disease.” Queen Victoria of England (1837-1901) was a carrier of the hemophilia gene and subsequently passed the disease on to several royal families.[4] Victoria’s eighth child Leopold had hemophilia and suffered from frequent hemorrhages, which were reported in the British Medical Journal in 1888. Leopold died at the age of 31 of a brain hemorrhage. Leopold’s daughter Alice was a carrier and her son, Viscount Trematon was born with hemophilia. Viscount died in 1928, of a brain hemorrhage similar to the one that killed his grandfather.

Hemophilia played an important role in the Russian royal family as well. Two of Queen Victoria’s daughters, Alice and Beatrice, were carriers of hemophilia. They passed the disease on to the Spanish, German and Russian royal families, ensuring that the disease would be present in future generations. Alexandra, Queen Victoria’s granddaughter, married Nicholas, the Tsar of Russia in the early 20th century. Alexandra was a carrier of the disease and her first son Alexei was born with hemophilia. Nicholas and Alexandra were preoccupied by the health problems of their son at a time when Russia was in turmoil. The monk Rasputin gained great influence in the Russian court, partly because he was the only one able to help the young Tsarevich Alexei. He used hypnosis to relieve Alexei’s skin pain. The use of hypnosis not only relieved pain, but may have also helped slow or stop the boy’s hemorrhages. The illness of the heir to the Tsar’s throne, the strain it placed on the Royal family and the power wielded by the mad monk Rasputin were all factors leading to the Russian Revolution of 1917. In 1916, the 45-year-old faith-healer Rasputin was assassinated in Petrograd by a group of noblemen bent on ridding Russia of the monk’s corrupting influence on Nicholas II and Alexandra.[5]
The diagnostic laboratory findings in hemophilia can be summarized as follows: a prolonged activated partial thromboplastin time (APTT), normal prothrombin time (PT), normal bleeding time (BT), low Factor VIII. Factor VIII assay is generally required because even the APTT may be normal in mild cases.

### General Management

Factor VIII must be replaced to a level adequate to ensure hemostasis if bleeding starts or is expected. Replacement of missing factor is achieved with porcine Factor VIII or recombinant Factor VIII. Heat and chemical treatment of blood products began in 1986 but plasma (fresh or frozen), cryoprecipitate or fractionated human factor concentrates obtained from pooled blood sources still carry the risk of transmitting blood-borne pathogens like hepatitis virus or HIV. The world federation of Hemophilia conducted a global surgery in 2004 and reported that while 31% of hemophiliacs died of bleeding episodes, a further 20% died from AIDS-related illness and 13% from liver diseases. Gene therapy of hemophilia is still in its infancy.

One unit of Factor VIII concentrate per kilogram of body weight raises the Factor VIII level by 2% and hence an average 70 kg individual would require infusion of 3500 units to raise the factor level from less than 1% to 100%. Thus a simple formula may be derived as

\[
\text{Dose to be infused (Units)} = \frac{\text{Weight (kg)} \times \text{Increment needed (U/dl)}}{2}
\]

Three methods of replacement therapy have been employed to maintain circulating factor levels above the 20% minimum necessary for hemostasis during the surgical and healing phases. These include:

1. Intermittent replacement therapy
2. Continuous intravenous factor replacement therapy
3. A single concentrate with an antifibrinolytic

Cover for surgery, other than very minor procedures or for mild hemophiliacs, requires maintenance of normal Factor VIII levels for approximately one week, followed by a period of reduced dosage during convalescence. This can be achieved either by repeated bolus injections every 12 hours (paying particular attention to trough levels) or by continuous infusion. It must be noted that the doses required during the immediate postoperative period may be considered more than expected.

In mild hemophilia, desmopressin and antifibrinolics such as tranexamic acid may be adequate. Desmopressin, a synthetic analogue of vasopressin is available for intranasal spray and intravenous infusions. It provides adequate transient increases in coagulation factors in some patients with mild to moderate hemophilia avoiding the need for plasma concentrates. Tranexamic acid is a synthetic derivative of amino acid lysine. It is available for topical and systemic usage. However, nausea is a common adverse effect. The anti-fibrinolytic agent Epsilon amino caprioic acid (EACA) given orally or IV is a potent inhibitor of initial clot dissolution (Ramstrom). Post-surgical use of EACA has been shown to reduce the quantity of factor required to control bleeding when used in conjunction with pre-surgical concentrate infusion sufficient to raise the plasma Factor VIII and IX levels to 50% (Walsh). A regimen of 50 mg/kg body weight EACA given orally as a 25% oral rinse every six hours for seven to ten days appears adequate as an adjunct. Still tranexamic acid is 10 times more potent than EACA with fewer side-effects (Walsh).

### Dental Aspects

There are no basic differences in the oral health problems of the hemophilic and those of the average individual; however, optimal dental health is more of a necessity for the hemophilic in view of the problems posed by dental surgery. Therefore, it is reasonable to expect that today's dental health professionals can and should provide the care so desperately needed by the hemophiliacs.

Many of the coagulation defects present a hazard to surgery and to local anesthetic injections but in general teeth erupt and exfoliate without problems and noninvasive dental treatment is safe. Close coordination is needed between the dentist and the physician to plan safe, comprehensive dental care. Education of parents and preventive dentistry should be initiated as early as possible. Local anesthetic injections can be followed by persistent bleeding for days or weeks; the hemorrhage cannot be controlled by mere pressure and may be life-threatening. Difficulties in the management of a hemophiliac dental patient include the following:

1. Dental neglect necessitating frequent extractions
2. Trauma and surgery
3. Factor VIII inhibitors (recombinant F VIII is an alternative solution)
4. Hazards of anesthesia and injections
5. Risk of hepatitis B and liver disease and HIV infection
6. Aggravation of bleeding by drugs
7. Anxiety and drug dependence

The bleeding tendency can be aggravated by NSAIDs. Safer alternatives for pain control are acetaminophen, codeine and Cox-2 inhibitors. Local anesthetic regional blocks, lingual infiltrations or injections into the floor of the mouth must not be used in the absence of Factor VIII replacement because of the risk of hemorrhage hazardous the airway and being life-threatening. Rarely, even submucosal LA infiltrations have caused widespread hemotoma formation. If Factor VIII replacement therapy has been given, regional LA can be used provided the Factor VIII level is maintained above 30%. Webster reported 80% chance of hematomas for hemophiliacs not treated with prophylactic factor replacement prior to Mandibular block injection. Infiltrations, intraligamentary, intraosseous or intrapulpal injections are still safer. Alternative anesthetic techniques like electronic anesthesia are definitely worth a mention in these cases. Lucas advocates the use of hypnosis as an alternative pain control technique. Intramuscular injections are best avoided and oral drugs are preferable.
There is no contraindication to movement of teeth in a hemophiliac. However, care must be taken to avoid sharp edges in appliances, wires and tranexamic acid are primary alternatives. Desmopressin can be as a slow intravenous infusion over 20 min of 0.3-0.5 µg/kg, 30 to 60 min prior to the surgical procedure. This results in a two- to threefold rise in Factor VIII activity with a mean half-life of 9.4h. Intranasal administration as a spray of 1.5 mg per ml with each 0.1 ml pump spray is an alternative, but it requires a tenfold higher dose of desmopressin to achieve a maximal twofold increase in Factor VIII activity after 90 min, limiting treatment to those hemophiliac patients whose basal factor levels are sufficiently high. Tranexamic acid significantly reduces blood loss and can be given topically or systemically. Systemically, it is given in a dose of 1g (30 mg/kg) orally, four times a day starting at least 1h preoperatively for surgical procedures. Tranexamic acid infusions can be given as 10 mg/kg in 20 ml normal saline over 20 min, then 1g tds orally for five days (child dose is 20 mg/kg). [3]

Local measures are important to minimize the risk of postoperative bleeding. Surgery should be carried out with minimal trauma to soft tissues and bone and careful postoperative mouth toilet is essential. Suturing is desirable to stabilize gum flaps and to prevent postoperative disturbance of wounds by eating. A non-traumatic needle must be used and the number of sutures minimized. Vicryl sutures are preferred and catgut is best avoided. Non-resorbable sutures such as black silk should be removed at four to seven days. One must not forget that suturing tissues and bone and careful postoperative mouth toilet is essential. Suturing is desirable to stabilize gum flaps and to prevent postoperative disturbance of wounds by eating. A non-traumatic needle must be used and the number of sutures minimized. Vicryl sutures are preferred and catgut is best avoided. Non-resorbable sutures such as black silk should be removed at four to seven days. 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Bleeding disorders have been of much concern to health professionals including dentists for quite sometime. Hemophilia is the commonest bleeding disorder affecting 1 per every 10,000 people worldwide. Dental health is quite often neglected by hemophiliacs for fear of bleeding complications. This article aims at simplifying the complexities involved in the diagnosis and management of a hemophiliac by suggesting a protocol and some essential tips to continue with specialty dental procedures without major risks.

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