Hemophilia comprises a group of hereditary bleeding disorders caused due to the deficiency of one or more clotting factors. It is broadly divided into hemophilia A, B, and C, which occur due to deficiency of factors VIII, IX, or XI (F VIII, F IX, F XI) respectively. Hemophilia A is an X-linked recessive hereditary disorder and most common of the three. It accounts for 80 to 85% of bleeding disorder. Understanding this complex entity is very important for a dentist to provide appropriate dental treatment and to avoid undesirable consequences. The aim of this article is to report a case of hemophilia A, who was diagnosed postextraction with review of dental management of hemophilic patients.

**Keywords:** Dental extractions, Hemophilia, Management.


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**Conflict of interest:** None

## ABSTRACT

Hemophilia is a hereditary disease of blood clotting, clinically manifested as a tendency to bleed which presents a serious challenge in dental practice.\(^1\) The normal mechanism for blood clotting is a complex series of events. When a blood vessel is injured, platelets collect over the injured area and form a temporary plug to prevent further bleeding. This temporary plug, however, is too disorganized to serve as a long-term solution, so a series of chemical events occur, resulting in the formation of a more reliable plug. The final plug involves tightly woven fibers of a material called fibrin.\(^2\) The production of fibrin requires the interaction of several chemicals, in particular a series of 13 proteins called clotting factors. In hemophilia, certain clotting factors are decreased in quantity, absent, or improperly formed. Since the clotting cascade uses amplification to rapidly plug up a bleeding area, absence or inactivity of just one clotting factor can greatly increase bleeding time.\(^2,3\)

Hemophilia A is the deficiency of factor VIII\(^1,4\) (antihemophilic factor), and hemophilia B also called Christmas disease is the deficiency of factor IX\(^1,4,5\) (Christmas factor). Hemophilia C involving factor XI\(^1,5,6\) (plasma thromboplastin antecedent) is very rare but much milder than hemophilia A or B. The normal plasma concentration of factors is 50 to 100 IU/dL. When the plasma concentration falls below 1 IU/dL, disease manifestations are severe; ranges between 2 and 4 IU/dL are moderate and a range between 6 and 40 IU/dL is mild.\(^3,7\) In hemophilia, laboratory investigations reveal isolated prolongation of activated partial thromboplastin time (APTT), although the bleeding time, prothrombin time (PT), and thrombin time are usually normal.\(^8\)

Hemophilia is further classified on the concentration of factors as mild when the concentration is 0.05 to 0.35 IU/mL or 5 to 35% and it presents as no spontaneous bleeding, delayed onset of bleeding after trauma or surgery or dental extractions.\(^5\) It is considered moderate when factor concentration is 0.01 to 0.05 IU/mL or 1 to 5%, and it presents as bleeding into joints or muscles with minor trauma and excessive bleeding with surgery. It is considered to be severe when concentration is <0.01 IU/mL or <1%. It presents as spontaneous joint, muscle, and internal bleeding and excessive bleeding with trauma or surgery.\(^9\)

## CASE REPORT

A 20-year-old male patient presented to the Department of Oral and Maxillofacial Surgery, RajaRajeswari Dental College & Hospital, Bengaluru, Karnataka, India, with a chief complaint of uncontrolled bleeding since 9 days from the site of tooth removal. The tooth was extracted in a private clinic as a part of his orthodontic treatment 10 days earlier.

A detailed case history was taken in which patient gave history of several episodes of delayed wound healing in his childhood and also history of jaundice 1 year back. Patient did not report any other medical condition and was not on any kind of medication. His past dental history revealed that patient had started his orthodontic treatment 1 month ago. As a part of treatment plan, all four 1st premolars were planned to be extracted. Accordingly, the upper right 1st premolar was extracted 10 days back in a private clinic. On the 3rd postoperative day, he noticed bleeding from the extraction site. He reported back to the private clinic for the
same where the clinician controlled the bleeding with pressure pack followed by suturing. However, the patient again noticed slow and continuous bleeding after 2 days which continued till 9 days after which he was referred to RajaRajeswari Dental College and Hospital, Bengaluru, Karnataka, India, for further evaluation.

On general physical examination, it was observed that patient was moderately built and nourished with a normal gait. He had spoon-shaped nails. He showed signs of pallor and had pitting edema in his right feet. On oral examination, we observed a huge clot, bluish-black in color measuring 3 × 3 cm, loosely hanging from the extraction socket in relation to 14. The clot was friable, which bled instantly on slight touch (Fig. 1).

A differential diagnosis like thrombocytopenia, Von Willebrand disease, platelet dysfunction, liver disease, dysfibrinogenemia was given. To evaluate whether the bleeding abnormality resided in vessel walls or platelets or was a process of coagulation, various investigations were advised, which included a complete hemogram, PT, APTT, and international normalized ratio (INR).

Intraoral periapical radiographs showed complete removal of the tooth 14. The site (socket) was then debrided and explored to find out the source of bleeding: Whether it was from soft tissue or bone. Bleeding was found to be from bone. The site was then packed with a local hemostatic agent (Abgel) followed by figure of eight suturing, which was done using silk sutures. The patient was also prescribed Tab styptovit 500 mg TID. The patient was then admitted to the hospital for further evaluation where he was prescribed Tab Limcee 500 mg and Injection VCEF forte (Ceftriaxone 1000 mg, Sulbactam 500 mg).

The routine blood results suggested that hemoglobin, bleeding time, clotting time, red blood cells, white blood cells, and platelet count were within the normal range. The PT screens the extrinsic limb and common coagulation pathway. Prothrombin time was slightly prolonged, i.e., 17.4 seconds, which suggested that patient was on warfarin anticoagulant therapy, was vitamin K deficient, or deficiency of factors V, VII, X, prothrombin/fibrinogen. The INR measures the extrinsic pathway of coagulation. Raised INR of 1.45 suggested use of warfarin, underlying liver damage, vitamin K deficiency. Partial thromboplastin time (PTT) screens the intrinsic pathway and common coagulation pathway. Raised APTT was 83.1, suggestive of hemophilia. If both tests, i.e., PT, PTT are prolonged, it implies deficiency of factors II, V, X, and vitamin K deficiency; liver disease can be suspected.

After 48 hours following admission of the patient to the hospital, he reported of mild bleeding from the site. On exploring the site, bleeding was found to be from the palatal mucosa. Bleeding was arrested with pressure pack and 1 dose of tranexamic acid injection into the site, following which he was advised to undergo factor VIII and IX assay. The results showed that the factor VIII value was decreased to 38% and factor IX was decreased to 46%, suggestive of mild hemophilia.

The patient was discharged on 4th day and socket showed signs of healing. Two weeks follow-up was uneventful. The patient was instructed about the condition like avoiding injury and usage and role of tranexamic acid in controlling bleeding.

**DISCUSSION**

Patients with hemophilia are at high risk of secondary bleeding following oral surgery. Close cooperation between hematologists and oral surgeons is necessary to prevent excessive hemorrhage. International guidelines strongly recommend the use of clotting factor replacement therapy for all invasive surgical interventions.6 The World Federation of Hemophilia advises the use of factor

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**Fig. 1:** Preoperative, patient presented with a huge clot in the extraction site of 14

**Fig. 2:** Postoperative intraoral view showing the sutured 14 socket site
Management of Hemophilia Patient

concentrates to cryoprecipitate or fresh frozen plasma for replacement therapy in patients with hemophilia.

One unit of infused recombinant factor VIII per kilogram of body weight should lead to a rise of plasma factor VIII level of approximately 2% in patients with hemophilia A and in the absence of an inhibitor. The half-life of factor VIII is approximately 8 to 12 hours. The following formulas can be applied for calculating the factor dose:

\[
\text{Dosage (units)} = \text{body weight (kg)} \times \text{desired factor VIII rise (IU/dL or % of normal)} \times 0.5
\]

and

\[
\text{Dosage (units)} = \text{body weight (kg)} \times \text{desired factor IX rise (IU/dL or % of normal)}
\]

One unit of infused plasma-derived concentrates of factor IX per kilogram of body weight will raise the plasma factor IX activity by approximately 1% in patients with hemophilia B in the absence of an inhibitor. In contrast to the native plasma-derived factor, the recombinant factor IX has a lower recovery. One unit of infused factor IX per kilogram body weight should raise the plasma factor IX level by approximately 0.8% in adults and 0.7% in children. The half-life of factor IX is approximately 18 to 24 hours.

The conventional replacement therapy is not effective in patients with antibodies to factor VIII and IX. Approximately 8 to 20% of the patients with severe hemophilia A and 2.5 to 16% of those with severe hemophilia B are affected. A variety of genetic and immunologic factors are responsible in inhibitor development. However, an activated prothrombin complex concentrate or a recombinant activated factor VIII concentrate can be used in these patients.

Factor replacement therapy carries a risk of transmission of viruses or new pathogens and may lead to develop inhibitors. Therefore, reducing the number of patients and times requiring factor replacement therapy is helpful. A preoperative single dose of 0.3 μg/kg of factor VIII of body weight can increase the factor VIII level three- to sixfold in good responders. It is much less expensive than coagulation factor concentrates. There is no risk of transmission of infections and no risk of immunization. A prior testing of patient’s response a few weeks before surgery is necessary.

**Dental Extractions**

In patients with inherited bleeding disorders, careful treatment planning is essential. If several extractions are needed, it would be advisable to perform them one at a time. The following techniques are suggested:

- Avoid nerve blocks while doing an extraction.
- A dental impression should be taken prior to the extraction and cast in the laboratory. The tooth being extracted is removed from the model and a soft vacuum-formed splint is constructed to cover the socket completely.
- Rubber band extractions should be the preferred technique.
- The tooth should be extracted as atraumatically as possible and the socket filled with fibrin glue. If fibrin glue is not available, the socket may be packed with a resorbable gelatin sponge (Gelfoam) or a recombinant activated factor VIII concentrate can be used in these patients.
- The tooth should be extracted as atraumatically as possible and the socket filled with fibrin glue. If fibrin glue is not available, the socket may be packed with a resorbable gelatin sponge (Gelfoam). It may be possible to substitute oxidized cellulose (Surgicel) for the gelatin sponge, as they work in a similar manner.
- The splint should then be fitted and left in situ for at least 48 hours.
- The patient should be observed for 24 hours following the extraction.
- The patient should be instructed not to wash the mouth vigorously while wearing the splint, although they may eat and drink normally.
- Tranexamic acid tablets (1 gm, or 15 mg/kg, every 8 hours) should ideally be started the day before treatment for a total of 7 days. If this is not possible, it may be taken immediately before the extraction.
- After 48 hours, socket is checked by removing the splint. If a good clot has formed, the splint may be removed and standard mouth care protocol should be followed. The splint may be cleaned and replaced if necessary.
- The use of antibiotics following a dental extraction is controversial. In this group of patients, it may be useful to prescribe them prophylactically to reduce the risk of a secondary infection. If there are problems achieving hemostasis, the following strategies may be helpful:
  - Topical thrombin may be used either as a mouthwash or by direct application to the socket. It is important that the splint be replaced immediately after treatment and left undisturbed. This treatment may be repeated if bleeding persists.
  - Tranexamic acid 10% solution has been used as a mouthwash and shown to reduce bleeding. The splint should be removed and the patient asked to rinse the mouth for 1 minute. The splint should be replaced immediately. This may be repeated every 2 to 3 hours if there is a reduction in bleeding.
  - The patient’s blood pressure may increase due to worry and pain and should be monitored. If the patient has pain, a suitable analgesic should be prescribed. If there is no pain, a small dose of a benzodiazepine or similar medication will help to minimize anxiety and reduce blood pressure.
  - The antifibrinolytic treatment with tranexamic acid prevents postoperative bleeding by inhibiting the
activation of plasminogen to plasmin and promoting the clot stability. It is usually given as an oral tablet three to four times or by intravenous (IV) infusion two to three times daily. Tranexamic acid should be prescribed for 7 days following dental extractions in patients with intrinsic bleeding disorders. Tranexamic acid has also been successfully used locally for the reduction of oral bleeding.

Oral surgeons have to use all techniques to minimize the probability of intra- and postoperative bleeding. Local hemostatic measures like pressure pack, sutures, collagen, oxycellulose, gelatin, fibrin glue, and cyanoacrylate are necessary following dental extractions in these patients. Different agents can be combined with each other to potentiate the hemostatic effect. Wagner et al presented an overall activity ranking of the materials used: Collagen > gelatin > oxidized regenerated cellulose. To prevent late bleeding, absorbable sutures can be used in order to avoid suture removal. For pain control, nonsteroidal anti-inflammatory drugs and aspirin which affect platelet function must be avoided. Paracetamol is a safe alternative to prevent postoperative pain.

The current literature reports successful treatment protocols to prevent bleeding complications following oral surgery procedures. Management of patients with coagulation factor deficiency who require dental extraction or any other complex procedure is summarized as follows: In patients with mild hemophilia A before extraction/nerve block, Desmopressin 0.3 μg/kg (maximum dose 20 μg) intravenously over 20 to 30 minutes or subcutaneously should be given. Postextraction antifibrinolytic agents (e.g., tranexamic acid, 25 mg/kg t.i.d.) for 3 to 5 days should be given. Patient is advised to take soft diet for 7 days. In patients with moderate to severe hemophilia A before extraction, recombinant factor VIII concentrate 20 to 25 IU/kg can be given. Reevaluate patient postprocedure. In patients with hemophilia B (mild, moderate, severe) before extraction, recombinant factor IX concentrate 40 to 60 IU/kg should be given. Reevaluate patient postprocedure.

Various other preventive measures should be taken to prevent dental problems. Patients must be taught about the importance of regular cleaning (tooth brushing) with proper technique. The use of plaque disclosing tablets in the clinic is of value, as they will show the areas that are not being cleaned properly. The patient and their caretakers are advised to restrict the intake of sugary foods and drinks at mealtime. Regular dental checkup should be done, which will allow early diagnosis and prompt treatment of dental problems. It is very unlikely that a routine scaling and polishing, including the use of ultrasonic scalers, will cause significant bleeding. If the gingival condition is poor and there is a worry about bleeding, a 5-day course of metronidazole (200 mg 3 times a day), along with a chlorhexidine mouthwash can be used twice a day. This will often reduce the inflammation to a level where a routine scale and polish can be carried out. The procedure may need to be carried out over several visits, as each treatment will further reduce inflammation and the possibility of bleeding.

Removable prosthodontics are unlikely to cause any problems in patients with inhibitors. Similarly, fixed and removable orthodontic appliances may be used along with regular prevention and hygiene therapy. Restorative dentistry, including the provision of crowns and bridges, can be carried out safely provided the local anesthetic guidelines are followed.

Complications

Uncontrolled Bleeding following a Dental Extraction

Early bleeds: Within 24 hours of extraction, the splint should be removed and the area inspected to ensure that there are no mucosal tears. If there is mucosal damage, it should be sutured to prevent further problems. If the bleeding appears to be from the socket, it may be necessary to remove the blood clot and fibrin plug, irrigate the socket, and examine the area to ensure that there are no foreign bodies causing the problem. The socket should be packed and the splint should be fitted. Oral antibiotics should be prescribed if any foreign body has been located, as there may be some remaining infection.

Late bleeds: These usually occur between 2 and 5 days after the extraction and are commonly thought to be due to infection, although there is no evidence available in the recent literature to support this theory. If the bleeding is from the socket, the clot should be removed and the socket irrigated and repacked as earlier. The splint should be replaced and left in situ for at least 2 days. Oral antibiotics should be prescribed.

Infection

Minimal facial swelling: Dental problems that cause minimal swelling can often be treated first with high-dose antibiotics, usually given intravenously. The patient should be monitored and if the swelling worsens, surgical intervention may be required. The cause of the infection, usually a decayed tooth, needs to be removed as soon as possible using the local measures previously described.

Marked facial swelling: Dental sepsis, which causes significant facial swelling, can become life-threatening. The patient should be treated with IV antibiotics and, if there is any risk of airway compromise, urgent surgical drainage should be performed. If the airway is not at risk, the patient should be closely monitored and, if the swelling
worsens, surgical drainage should be performed. If the swelling reduces with antibiotics, the patient should be treated as for minor swelling. Patients requiring surgical drainage will require factor concentrates. The regimens already available for the management of surgery in this group of patients should be followed.

CONCLUSION

Based on the results, the following conclusions may be drawn: Prior to any dental procedure the patient should be referred to a hematologist to obtain a complete blood picture and to rule out deficient clotting factors, vitamin K deficiencies, and their plasma concentrations.

Surgical treatment, including a simple dental extraction, must be planned to minimize the risk of bleeding, excessive bruising, or hematoma formation. Emergency surgical intervention in dentistry is rarely required as pain can often be controlled without resorting to an unplanned treatment. All treatment plans must be discussed with the hemophilia unit if they involve the use of prophylactic cover. After dental procedures, blood loss of all kinds can be controlled locally with direct pressure or periodontal dressings with or without topical antifibrinolytic agents. If the patient exhibits heavy bleeding especially after extraction, then tranexamic injection should be given immediately after the procedure.

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