Dental management of patients with inherited bleeding disorders: a multidisciplinary approach

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Bleeding disorders can be inherited or acquired and demonstrate different levels of severity. Dentists may be called on to treat patients who have bleeding disorders such as hemophilia A and von Willebrand disease (vWD). Dental extraction in any patient with clotting factor defects can result in a delayed bleeding episode. Local hemostatic measures provide effective results in a majority of cases but are insufficient in patients with severe hemophilia A and vWD. Therefore, consultation with the patient's hematologist is required to ensure preoperative prophylactic coverage. Dental care providers have to be aware of any signs of bleeding disorders and refer patients for further medical investigations. This article aims to provide dental care providers with the knowledge to manage patients with inherited bleeding disorders, especially hemophilia A and vWD.

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Bleeding disorders can result from inherited genetic defects or be acquired due to use of anticoagulant medications or medical conditions such as liver dysfunction, chronic kidney disease, and autoimmune disease.[1-3] During blood vessel injury, hemostasis relies on interactions between the vascular vessel wall and activated platelets as well as clotting factors.[4] Any marked defect at one of these stages results in bleeding disorders. Vascular wall defects, platelet defects, or deficiency of clotting factors can affect the severity level of bleeding episodes.[5] Thus, patients may have mild, moderate, or severe episodes of bleeding.

Sources of inherited bleeding disorders

Vascular wall defects

A patient's bleeding disorder may be unrecognized, and bleeding episodes can appear spontaneously or after dental extraction. Patients with inherited bleeding disorders that are marked by a vascular defect, such as Marfan syndrome, hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome), and Ehlers-Danlos syndrome, rarely have a severe bleeding episode after dental extraction. Usually, these patients can receive dental treatment in the primary care setting.[6] Management includes coordination with the hematologist, minimally invasive dentistry, local hemostatic measures, and avoiding analgesics such as aspirin and other nonsteroidal anti-inflammatory drugs.[7]

Platelet defects

Inherited platelet defects result in qualitative dysfunction, and patients are best treated after consultation with a hematologist, who might advocate for platelet transfusion prior to any invasive dental procedures.[8,9] Specific laboratory investigations are required to assess platelet function, which is measured by the platelet aggregation capacity. Different types of blood tests can be considered to evaluate patients with inherited platelet defects during referral to the hematologist. These include the bleeding time, platelet aggregation test, and peripheral blood smear (film).

Clotting factor defects

Management of patients with inherited clotting disorders, such as hemophilia A and von Willebrand disease (vWD), is not straightforward and requires consultation with a hematologist.[10-14] This article will review the literature on recommended dental management of patients with inherited bleeding disorders, specifically patients with hemophilia A and von Willebrand factor (vWF) deficiency.

Hemophilia A

Hemophilia A is an inherited coagulation disorder involving a deficiency of factor VIII.[1] The prevalence of hemophilia A is

Table 1. Severity levels of hemophilia A and general recommendations for dental management.

Severity	Plasma level of factor VIII (%)	Dental management
Mild	6%-50%	• Preventive dentistry in the primary care setting should be emphasized. • All dental treatment can be delivered in the primary care setting. However, shared care with prior consultation with a hematologist is recommended.
Moderate	2%-5%	• Dental care providers should consider managing patients with a moderate level of hemophilia A as if they were patients with a severe level who require management in a secondary care setting. • Patients at these levels may require preoperative prophylactic factor replacement therapy. Therefore, consultation with the treating hemophilia center or hematologist is necessary. • Following consultation with the patient's hematologist, preventive dentistry measures, including oral hygiene instructions, diet analysis, pit and fissure sealing, and fluoride applications, are important.
Severe	<1%	

different from country to country and depends on the national economies. For example, countries with a high income have the highest prevalence, which increases over time.[15] Hemophilia A is inherited as an autosomal X-linked recessive trait; therefore, the disease mainly affects males.[16,17] However, females with a factor VIII activity level of less than 50% are considered to be carriers and are treated as patients with mild hemophilia.[18]

Depending on the level of factor VIII in the plasma, hemophilia A is categorized into 3 types: mild, moderate, and severe (Table 1).[19] It is necessary to determine the level of factor VIII, which helps to individualize management preoperatively and postoperatively. Laboratory investigations are necessary before any dental procedures that are likely to cause postoperative bleeding. These include the activated partial thromboplastin time (aPTT), bleeding time, and factor VIII coagulant level in plasma.

Although local hemostatic measures often provide successful results in patients with bleeding disorders, these measures are insufficient to control postoperative bleeding in some patients with severe hemophilia A.[6] To help prevent and manage postoperative bleeding episodes, the dentist should consult with the hematologist preoperatively by sending a referral letter that explains the intended dental procedures, underlines the medical conditions, and describes the types of postoperative local hemostatic measures that will be applied.[13,20] Various types of medical interventions can be selected by the hematologist to increase the level of factor VIII based on the current deficiency of factor VIII and severity of the dental procedures. Agents that can be administered include desmopressin acetate, factor concentrate, recombinant factor VIII, and antifibrinolytic agent (tranexamic acid).[21]

Patients with hemophilia A face many barriers to oral health care. Hemophilic patients usually visit dental clinics with extensive dental treatment and complex management needs.[14] Long waiting lists at the hospital as well as the high cost of traveling and treatment could be obstacles to seeking treatment earlier.

Mobility problems also may complicate access to dental care. Recurrent bleeding into the joints in the severe type of hemophilia A leads to joint deformity and clinical hip abnormalities that require joint replacement therapy.[22] These deformities limit the patient's activity and complicate accessibility to the dental clinic. The patient may rely on a wheelchair; as a result, the dental team has to assess the patient's ability to transfer to a dental chair or consider the availability of a wheelchair recliner.

It is not uncommon for a patient with hemophilia A to have many medical appointments, including consultations with a hematologist, a physical therapist to help manage recovery following hemarthrosis, and a psychologist to help cope with social stigma and poor quality of life.[23,24] Therefore, dental care providers should attempt to accommodate the schedule of the patient and caregiver for appointments.

All of the factors that may impact access to care should be evaluated during the first dental visit. Appropriate education for patients, caregivers, and families will help to improve the oral health of the patient.[25] As a result, these patients require a shared care approach.[23]

Von Willebrand disease

Von Willebrand disease is an inherited disease marked by vWF deficiency.[7,26] It is considered the most common congenital bleeding disorder, affecting 1% of the population of both sexes equally; symptomatic prevalences are reported to range from 1 in 1000 to 1 in 10,000 of the population.[11,27-29] In rare cases, acquired von Willebrand disease may develop in elderly patients and is associated with various underlying diseases.[30,31]

Von Willebrand factor acts as a carrier for factor VIII and increases its half-life.[32] In addition, vWF attaches to collagen and membranes of blood vessels. All these functions aid in clot formation.[32] Three types of vWD with different subtypes and different patterns of inheritance have been recognized: type 1

(mild), type 2 (moderate), and type 3 (severe).[20,33,34] This classification is important to help understand the dental management and reduce the risk of bleeding following dental procedures. The clinical features of this disease range from an unrecognized, mild form that requires local hemostatic measures to a severely debilitating form that requires preoperative and postoperative hematologic prophylaxis.[35]

Patients with vWD are diagnosed via a prolonged bleeding time, prolonged aPTT, and low levels of vWF antigen (VIII:Ag) and ristocetin cofactor (RcoF) in a factor VIII assay.

Dental management of patients with vWD is generally similar to treatment of patients with an equivalent level of hemophilia A.[18] For instance, management of patients with type 3 vWD, marked by a complete absence of vWF, is similar to the management of patients with a severe form of hemophilia A.

Desmopressin acetate is usually the treatment of choice for patients with the mild to moderate form of vWD.[7] However, selection of the treatment is not clear-cut, because it depends on the type of vWD, the patient's response to desmopressin acetate, and the decision of the hematologist.[36] Laboratory investigations are necessary prior to any dental procedures that are likely to cause bleeding. These tests include the aPTT, bleeding time, and factor VIII level in the plasma (vWF:Ag, RCoF, and factor VIII coagulant). The severe form of vWD requires replacement therapy with factor concentrate that is rich in vWF because there is no recombinant therapy for vWF.[11,37]

Guidelines for dental management of patients with hemophilia A and vWD

Dental management of patients with hemophilia A and vWD is similar. Coordination with the patient's hematologist in association with a dental risk assessment is the first step that should always be taken prior to any dental procedures.[20] A thorough medical and dental history, including details of medical condition, medications, and response to any previous dental treatment, must be obtained and updated at the beginning of every visit.[7] Additionally, it is important to assess the hematologic needs of the patient prior to any invasive dental procedures, such as periodontal surgery, deep scaling, and dental extraction.

Postoperatively, it is recommended that the patient avoid any analgesic medications that increase the possibility of bleeding, such as aspirin and other nonsteroidal anti-inflammatory drugs (eg, ibuprofen and naproxen sodium).[3] Paracetamol (acetaminophen) can be used safely.[38] Some dental procedures may necessitate antibiotic use; therefore, the hematologist should be consulted.

Local anesthesia

Dental care providers can provide some dental treatments without local anesthesia, such as preliminary examination, pit and fissure sealing, dental impressions, minimally invasive dentistry, and supragingival scaling. However, if local anesthesia is necessary, there is an 80% chance that a patient with hemophilia will develop a hematoma following the administration of an inferior alveolar nerve block injection without prior factor VIII infusion.[39] The hematoma could be fatal if it accumulates in the mediastinum and compromises the airway.[40,41] Preoperative prophylactic coverage should be discussed with the patient's hematologist prior to any local anesthesia in the floor of the mouth or lingual infiltration.[42]

Buccal infiltration to the mandibular first molars with 4% articaine hydrochloride (1:100,000 epinephrine) shows a more effective result than 2% lidocaine hydrochloride, and patients find the procedure more acceptable than inferior alveolar nerve block injection.[43,44] Mental nerve block injection in the mandibular arch is considered safe and requires no hematologic coverage prior to administration; therefore, it facilitates administration of local anesthesia in the primary care setting.[6] However, other local anesthetic techniques, such as intrapulpal, intraligamentary, and buccal infiltration, are safer.[39]

Dental extraction

Mild form of disease

After consultation with the hematologist prior to dental extraction, patients with the mild forms of hemophilia A and vWD are normally treated preoperatively by desmopressin acetate, which stimulates the release of vWF from the Weibel-Palade bodies of endothelial cells.[45] This in turn increases the levels of vWF (as well as coagulant factor VIII) threefold to fivefold.[6] One hour prior to the dental procedures, desmopressin acetate can be administered intravenously (0.3 µg/kg in 50 mL of normal saline), subcutaneously (0.3 µg/kg using the 15-µg/mL concentration), or intranasally (150 µg).[18] However, intravenous administration of desmopressin acetate may have cardiovascular side effects, such as a slightly elevated heart rate, hypotension, and headache.[18,45] Desmopressin acetate is not recommended for young children and patients with ischemic heart disease.[18]

Moderate to severe forms of disease

Before dental extractions, patients with moderate to severe disease require replacement therapy with either factor concentrate (patients with either disease) or recombinant factor VIII (patients with hemophilia A); there is no recombinant therapy available for vWF.[6,18] However, factor concentrate is expensive and may result in the development of autoantibodies or inhibitors that impair clotting, which is why unnecessary dental procedures should be avoided. This will help to decrease the repetition of replacement therapy and reduce the chance of inhibitor formation.[18]

Replacement therapy can be administered by the healthcare provider, the patient's caregiver, or the patient as a prophylactic option and/or as emergency treatment in case of prolonged bleeding.[18] It is recommended to deliver the intended dental treatment within 30-60 minutes following the administration of factor concentrate.[18] Recombinant factor VIII can be given in patients with the moderate to severe forms of hemophilia A, which helps reduce the possibility of blood-borne infection that could result from transfusion of infected blood.[46]

It is necessary to measure the level of factor VIII in patients with hemophilia A prior to any invasive dental procedures.[6] Hematologists recommend that the patient's level of factor VIII should be between 50% and 75% prior to minor oral and periodontal surgery.[7,47] However, the factor VIII level should be between 75% and 100% before maxillofacial surgery.[7] Tranexamic acid (in the form of mouthwash with a concentration of 15-25 mg/kg 4 times a day for 7-10 days; or oral administration of tablets, 1 g, 3 times a day for 7-10 days) may add stability to the clot.[48] It has been reported that postoperative bleeding tendency was reduced from 5.4% in a group of patients

Table 2. Local hemostatic measures and precautions required after dental extraction for patients with any bleeding disorder.

Measure or precaution	Explanation
Local anesthesia	An aspirating syringe with epinephrine (vasoconstrictor) should always be used. A study suggested the use of 4% articaine hydrochloride with 1:100,000 epinephrine in the mandibular molar area, specifically the first molars, instead of inferior alveolar nerve block injection.[43]
Atraumatic dental extraction	Atraumatic tooth extraction with a flapless technique is preferable.
Resorbable hemostatic dressing	Hemostatic agents (eg, Surgicel, Ethicon; and Gelfoam, Pfizer) can be used to facilitate hemostasis and stabilize blood clots.
Suturing	A simple suturing technique, followed by pressure with a gauze pack, could be valuable after tooth extraction to reduce bleeding and stabilize surgical flaps.
Postextraction instructions	Verbal and written instructions should be provided to the patient.
Hospital contact number	The contact number of the acute emergency dental department must be given to patients in case of persistent bleeding.

using other local hemostatic measures, without tranexamic acid, to 3.6% in a group of people using tranexamic acid alone.[48-52] It is recommended that the patient start use of the mouthwash 2 hours before the dental procedure and continue 4 times daily for 7 to 10 days.[18] Additional local hemostatic measures, including suturing and resorbable hemostatic dressing, will help stabilize the bleeding clot. Close postextraction monitoring of the patient is necessary, because patients with hemophilia A or vWD may have delayed bleeding episodes.[6] Table 2 shows recommendations to help reduce bleeding after dental extraction in patients with any bleeding disorder.

Scaling and periodontal treatment

Scaling in patients with hemophilia A and vWD depends on the severity of the probing depths and the patient's level of oral hygiene. Supragingival scaling with local hemostatic measures (eg, tranexamic acid) is considered safe in patients with the mild form.[38,53] Consultation with the hematologist to obtain replacement therapy is recommended for patients with the moderate to severe forms.[47] Any periodontal surgery or deep root surface debridement requires that the patient have a factor VIII level of at least 50%-75% preoperatively.[7]

Restorative, prosthodontic, and endodontic treatment

Dental care providers must attempt to minimize trauma to the soft tissues during placement of rubber dams, clamps, interdental wedges, and matrix bands.[47] Although it is preferable to use a supragingival margin over a subgingival one, crowns and fixed partial dentures are associated with a low risk of bleeding and can be performed in a primary care setting.[18] Moreover, full and partial removable prostheses are considered safe treatments.[38]

Rafique et al suggested the use of nonmetallic trays during impression procedures to avoid soft tissue trauma.[6] Covering the suction tip with gauze also might help reduce trauma to the oral mucosa.[44] Dentists also should consider managing these patients with noninvasive dental procedures, such as atraumatic restorative treatment, air abrasion, and chemomechanical caries removal agents.[54,55]

Root canal treatment is considered safe. Bleeding from the vital pulp might prolong pain, which can be eliminated by irrigation with 4% sodium hypochlorite and the administration of calcium hydroxide.[20,38]

Orthodontic treatment

It is safe to deliver orthodontic treatment to patients with bleeding disorders, but any need for tooth extraction should be discussed with the oral surgeon or special care dentist and hematologist.[20] Sharp edges or extruded wire that might cause bleeding should be trimmed from appliances. Maintenance of good oral hygiene during orthodontic treatment is essential.[53]

Conclusion

Patients with mild bleeding disorders can be treated in a primary care setting after consultation with the hematologist, while patients with a moderate to severe level of bleeding disorder who require invasive dental procedures are best treated in a hospital setting. Consultation with the hematologist prior to any dental procedure is recommended to assess the patient's needs for prophylactic replacement therapy. Factor replacement therapy is required before inferior alveolar nerve block, lingual infiltration, or floor of the mouth injection. Restorative, prosthodontic, endodontic, and orthodontic treatments are considered safe in the majority of patients with bleeding disorders unless more complex dentistry is required. The use of aspirin and other nonsteroidal anti-inflammatory drugs (such as ibuprofen and naproxen sodium) should be avoided in patients with bleeding disorders. Dental care providers must immediately report cases of prolonged bleeding, dysphagia, or difficulty speaking and breathing following dental procedures to the patient's hematologist.

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