Complications in Oral and Maxillofacial Surgery: Management of Hemostasis and Bleeding Disorders in Surgical Procedures

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KEYWORDS

• Von Willebrand disease • Hemophilia
• Coagulation factors • Platelet disorders

Oral and maxillofacial surgeons perform a wide variety of surgical procedures including the removal of teeth, various tissue biopsies, endosseous implants, and major maxillofacial surgery. One of the major complications of these various surgical techniques is uncontrolled bleeding. The best management of perioperative hemorrhage is prevention. This includes proper preoperative patient evaluation, knowledge of the various bleeding disorders, and characterization of the correct methods of management.

Hemostasis in the normal patient population involves the interaction between four different biologic systems: (1) the blood vessel wall, (2) the blood platelets, (3) the coagulation cascade, and (4) the fibrinolytic system. Under normal conditions hemostasis occurs through two independent processes: the coagulation cascade and the platelet activation pathway.[1] When the integrity of the endothelial layer of the blood vessel is compromised the initiation of the coagulation process is activated. Blood vessel constriction is the essential first stage followed by platelet adhesion and aggregation. At the site of injury the hemostatic mechanism is initiated by local activation of the surfaces and the subsequent release of tissue thromboplastin.[2] This results in the formation of fibrin. However, in oral surgery through a series of triggering steps fibrinolysis may occur causing a breakdown of the clot. Clearly, the process is complex and requires a good level of understanding to allow the clinician to properly manage the hemostasis.

The causes of hemorrhage can be reduced to either local issues at the site of surgical intervention or inherent systemic factors. The local factors result from tissue damage at the site of surgery.[2,3] Poor surgical technique with injury to soft tissue, hard tissue, or vessels may lead to excessive bleeding. Systemic causes include the various inherited coagulation disorders, acquired coagulation abnormalities, and platelet disorders. The following discussion evaluates various causes of bleeding and identifies both local and systemic and pathways. Considerations of treatment for patients with these various disorders are discussed as to the best management options for adequate hemostasis.

SYSTEMIC FACTOR PROBLEMS

Systemic factors involving inherited coagulation disorders include von Willebrand disease, hemophilia, rare coagulation factor deficiencies, and various platelet disorders. In addition, there are acquired coagulation abnormalities and drug-induced platelet defects, which interfere with normal clot formation (**Box 1**).

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Box 1
Common medications that affect platelet function

- American Society of Anesthesiologist (ASA)
- Nitroglycerin
- Nonsteroidal antiinflammatory drugs
- H_2 antagonists
- Antimicrobials
  - Penicillin
  - Ampicillin
- Propranolol
- Dipyridamole
- Sulphinpyrazone
- Clofibrate
- Tricyclic antidepressants

Von Willebrand Disease

Von Willebrand disease is the most common inherited bleeding disorder. It affects up to 1% of the population resulting in issues of surgical and nonsurgical bleeding. Increased easy bruising, epistaxis, and significant oral surgical bleeding are the most common manifestations of the disease. Von Willebrand disease results from quantitative and qualitative defects in the von Willebrand factor, an important protein in hemostasis.[4] Von Willebrand disease is divided into three different categories: type 1 is a partial deficiency of the protein factor, type 2 represents qualitative defects within the protein, and type 3 represents a severe deficiency of the total protein complex.[5]

Treatment depends on the particular type of von Willebrand disease. Most type I and some type II patients respond to desmopressin acetate, which stimulates the release of von Willebrand factor for endothelial cells. This raises the plasma level of the von Willebrand factor and factor VIII by three to five times. The half-life is approximately 8 to 12 hours, improving the primary hemostasis, and may require additional infusions. Patients who do not respond to desmopressin require pooled human plasma.[4]

Hemophilia

Hemophilia is an inherited sex-linked bleeding disorder resulting from either decreased factor VIII (hemophilia A) or factor IX (hemophilia B). The classification of hemophilia is divided into three groups: (1) severe, (2) moderate, and (3) mild. Patients with severe hemophilia have a factor level of less than 1%, moderate hemophilia represents a level of 1% to 5%, and mild hemophilia characterizes a group of patients with factor levels between 5% and 35%. The prevalence of hemophilia is about 1 in 5000 males with up to 90% having a deficiency of factor VIII. Type B hemophilia represents only about 10% of all the diagnosed hemophilia.[6]

The classic clinical signs of a patient with a factor deficiency are bruising, muscle and joint hemorrhage, and excessive bleeding after trauma or surgical procedures. The diagnosis must be determined by specific laboratory tests. The classification often predicts the risk factors for bleeding in the specific patient.

Treatment for hemophilia is through replacement of factors VIII or IX. This is done through the use of purified plasma-derived concentrate or more recently recombinant factor concentrates. Dosage depends on the severity of the bleeding disorder.[7] Surgical procedures require preoperative doses of factor concentrations to allow for adequate control of postoperative bleeding. Occasionally, in mild cases the use of desmopressin can raise the levels of factor VIII that allow for adequate hemostasis after minor procedures.[6]

Other Congenital Factor Deficiencies

It is relatively rare to encounter other factor deficiencies. These include factors V, VII, X, and XIII. In addition, there can be deficiency of fibrinogen and prothrombin. Each of these has an occurrence rate of less than 1 in 1 million. However, when this does occur the genetic transfer is related to autosomal-recessive traits. The replacement is usually through the use of cryoprecipitate, fresh frozen plasma, recombinant factors, or various complex concentrations of the missing specific agent. One of the best ways to identify these deficiencies is to take a thorough complete medical history involving past surgical procedures.[8,9]

IATROGENIC COAGULATION ABNORMALITIES

Many patients are now being treated on a long-term basis with anticoagulation therapy using warfarin or in some cases heparin. These therapies have been researched and are now used in the prevention and management of various thrombolytic events. Thrombotic and throboembolic blockage of blood vessels are the main cause of ischemic events in the heart, lungs, and brain.[10]

Warfarin is a vitamin K antagonist, inhibiting the y-carboxylation of glutamic acid on the clotting factors. Therapeutic doses of warfarin reduce the production of functional vitamin K–dependent clotting factors by approximately 30% to 50%. Warfarin has two main functions: to cause

anticoagulant activity and to provide an antithromotic effect. Warfarin's affect is monitored by the international normalized ratio (INR; a standardization of the prothrombin time assay). The therapeutic INR range varies for most patients but is usually in the 2 to 3 range. This protects most patients from various venous or arterial thromboembolism events.[11,12] Recently, the use of hand laboratory devices allows the clinician to check the therapeutic levels of warfarin at the time of outpatient surgery. This increases the ability of the clinician to adequately evaluate the patient's risk factors for bleeding.

Heparin is a proteoglygan that functions as a cofactor of the naturally occurring anticoagulant antithrombin. Because the half-life of heparin is short (60 minutes), the therapeutic levels are maintained by intravenous bolus injections followed by monitored infusion. The therapeutic range is monitored by prolongation of the activated partial thromboplastin time. There are several different types of heparin. Low-molecular-weight heparin has a longer half-life and can be delivered subcutaneously once or twice a day. Patients on long-term therapy with heparin do not require laboratory monitoring; however, when monitoring is required a test evaluating the anit-Xa assay is used because the partial thromboplastin time is not predictably prolonged.[13]

PLATELET DISORDERS AND ABNORMALITIES

Platelet disorders can routinely be divided into two categories: defects of function or defects related to the total number of platelets. This can also include a combination of defects of the total numbers and of function. Broadly speaking, they can include the various thrombocytopenias, defects of adhesion, aggregation defects, and granular defects. In addition, there is an entire category of drug-induced defects (**Box 2**).

Throbocytopenias

The normal range for platelet levels falls within the range of 150 to 400 × 109/L however can vary for a given person into a narrower range. The platelet is routinely synthesized by the bone marrow and then destroyed by the spleen. Abnormalities generally are placed into two broad categories: those of inherited abnormalities and those of acquired abnormalities. Acquired abnormalities are relatively rare and usually represent a change in size and are associated with a specific syndrome.[14]

More common is acquired thrombocytopenia. This condition can be related to either an immune response or is of nonimmune origin. The most common immune response is thrombocytopenic purpura. Often this is related to an acute infection or as a portion of a greater autoimmune syndrome.[15]

Box 2
Common drugs causing thrombocytopenia

- Quinine/quinidine group
- Heparin
- Gold salts
- Antimicrobials
- Antiinflammatory drugs
- Cardiac medications and diuretics
- Benzodiazepines
- Antiepileptic drugs
- H_2 antagonists
- Sulfonylurea drugs
- Iodinated contrast agents
- Retinoids
- Antihistamines
- Illicit drugs
- Antidepressants
- Miscellaneous drugs
  - Tamoxifen
  - Actinomycin-D
  - Papverine

The nonimmune causes of thrombocytopenia are generally related to drug toxicity or some underlying disease state. Various chemotherapeutic agents can cause thrombocytopenia resulting in increased bleeding if the overall count drops below 50 × 109/L. The improvement of the platelet count can be accomplished by the use of platelet transfusions before surgical procedures. It is imperative that the platelets be evaluated before surgery for anyone who is being treated actively with chemotherapeutic agents.

In addition to the thrombocytopenias, there are adhesion defects, aggregation defects, and granular defects. Platelet adhesion defects result from abnormalities of the various protein complexes. There are four primary proteins involving the adhesive receptors. Genetically there can be abnormalities of any of these proteins resulting in poor platelet adhesion and associated mucosal bleeding, surgical bleeding, or easy bruisability. When this diagnosis is defined, it usually requires a platelet transfusion before a surgical procedure.[16,17]

Aggregation defects of the platelets are rare. Platelet–platelet interaction is critical to clot formation and depends on the integrity of the proteins in the integrin complex. The defect in this diagnosis

is an autosomal-recessive trait caused by qualitative or quantitative problems within the protein complex. As a result of this defect there are problems of platelet aggregation resulting in bleeding and in clot retraction. This not only causes acute bleeding issues but also impacts long-term wound healing. In most cases of this genetic disorder, the signs of abnormal bleeding are diagnosed early in life and are related to bruising, epistaxis, and prolonged bleeding related to surgical procedures.

Granular defects can also impact the coagulation cascade resulting in prolonged bleeding after minor surgical procedures. Essentially, platelets contain two important storage granules: alpha granules and dense granules. Each of these granules is released after activation and is critical to the overall hemostatic mechanism. Studies have shown that both types of granules can be decreased in number and lead to prolonged bleeding. In rare instances there can be qualitative deficiencies of both granules leading to episodes of bleeding. Some have suggested that this is caused by the absence of secreted ADP.[18]

Bleeding associated with milder defects of the granules can be treated with desmopressin; however, the outcome of this therapy is difficult to predict and a trial of the desmopressin is suggested before a major procedure.

Drug-Related Platelet Defects

The most common issues with regards to platelet function are the alteration of the platelet related to ingested drugs. There are a variety of drugs both prescribed and over-the-counter medications that alter the platelet through function or through decreased numbers.

The relationship of decreased numbers of platelets and medications is not uncommon. Gold therapy, quinidine, and certain antibiotic combinations can cause marked decreased numbers of platelets. In addition, some patients who have received heparin therapy developed thrombocytopenia. This can occur in 5% to 40% who receive this type of treatment.[19]

Platelet function can be altered by several medications; however, the most common is aspirin therapy. Aspirin attenuates platelet activity through the blockage of the TxA2 release from the platelet. This is a permanent blockage and renders the platelet dysfunctional for its life. This results in aspirin therapy causing bleeding and antithrombotic activity for the life of the platelet.[20]

Several other medications can cause altered platelet function. Unlike aspirin, the nonsteroidial antiinflammatory drugs only inhibit the function of the platelet during the time that the drug is in direct contact with the platelet. Once the blood concentration is diminished there is no longer an abnormal affect on the platelet. In addition to the nonsteroidial drugs several other medications that can be obtained over the counter can cause altered function. Various H_1 antagonists, antibiotics, antidepressants, early β-blockers, and nitroglycerine have all been implicated in causing function impairment.[21]

SURGICAL TREATMENT CONSIDERATIONS IN PATIENTS WITH VARIOUS BLEEDING DISORDERS

Clearly, the most important aspect of bleeding complications is the ability to prevent a significant event from occurring. This should take into account the proposed surgical procedure and the nature of the bleeding disorder. The type of surgery, the location of the intervention, and the extent of the procedure impact how the potential problem can be avoided. Therefore, the ability to blend the issues of systemic intervention with the local interaction of the tissues impacts the overall safety and efficacy of the procedure.

Several considerations need to be addressed with regards to the surgical event. The first is the site of the surgery and ability locally to control the issues of bleeding. For instance, the removal of tooth in the anterior maxilla makes local control of that area quite easy and does not cause the clinician to manipulate the systemic issues with regards to bleeding abnormalities. However, dissection deep into the neck requires adequate safe guards to prevent hemorrhage into the neck and subsequent airway compromise. Therefore, the surgical location becomes very important in the planning stages of a procedure to prevent uncontrolled hemorrhage or hematoma formation. Such considerations as the type of local anesthesia block or infiltration may be paramount to the safe management of the patient and their systemic disorder. It may be possible to infiltrate the area with local anesthesia, obtain good local pain control, and not require the patient to undergo systemic alteration of their drug regime or various types of transfusions. Clearly, the surgical technique for the removal of a single tooth may need to be altered so that there is a minimum of trauma, reducing need for postsurgical control of the bleeding.

One of the more common questions is the influence of oral anticoagulants on oral surgical procedures and whether the particular anticoagulant needs to be altered. There are several studies that have been completed in the last 10 years stating that the discontinuance of oral anticoagulation therapy does not lead to a higher risk of postoperative bleeding.[22] It is now generally accepted

Box 3
Recommended therapeutic range for warfarin therapy

- Low-intensity (INR goal 2.5 with a range of 2–3)
  - Prophylaxis of venous thrombosis (high-risk surgery)
  - Treatment of venous thrombosis
  - Treatment of pulmonary embolism
  - Prevention of systemic embolism
  - Tissue heart valves
  - Acute myocardial infarction
  - Atrial fibrillation
- High-intensity (INR goal 3 with range of 2.5–3.5)
  - Most mechanical prosthetic heart valves
  - Prevention of recurrent myocardial infarction

Data from Refs.[21,23–26]

that patients with an INR of between 2 and 4 may be treated safely without discontinuation (Box 3).[22]

In those patients who still have some postoperative bleeding, topical hemostatic agents are effective. More recently, dental implant therapy has been questioned as to whether it is appropriate to perform these procedures in the presence of active anticoagulation therapy. Again, the evidence does not support stopping therapy.[27] Larger, more invasive procedures, such as bone grafts, may require some alteration of the INR to ensure that there are no postsurgical bleeding complications. In addition to the use of warfarin therapy, it is also adequate to maintain low-dose aspirin therapy (100 mg/day) in the face of minor oral surgical procedures.[23]

In the past, minor oral surgical procedures in patients with hemophilia or von Willebrand disease required hospitalization and associated transfusions (Fig. 1). These transfusions using replacement factors carried a substantial risk of viral infection or the formation of various factor inhibitors.[28] Today, the use of recombinant non–plasma-derived products reduces this risk. One of the key agents is desmopressin treatment, which induces the release of factor VIII and von Willebrand factor. Often, these agents must be combined with local hemostatic agents or antifibrinolytic agents.[29]

Key preventive measures in patients with bleeding disorders include the following:

1. Avoid flap procedures when possible.
2. Consider techniques to minimize trauma to the area, such as limiting the number of teeth removed or the sectioning of difficult teeth.
3. Totally eliminate the associated granulation tissue in tooth sockets or the surrounding areas.
4. Consider primary closure where flaps have been elevated.
5. Use nonresorbable sutures to control the tension on the flap and eliminate the possibility of premature breakdown of the suture material.
6. Use hemostatic materials, such as the chitosan dental dressing, in the surgical site topically to reduce bleeding.
7. Use lasers or electrocautery to reduce bleeding at the time of surgical intervention.
8. Use fibrin sealants, such as Tinsel, to stabilize the fibrin clot.
9. Topical rinses, such as tranexamic acid, to inhibit fibrinolysis.
10. Use various pressure dressings to the appropriate locations of the oral cavity can be very beneficial to the control of bleeding even in the compromised patient.

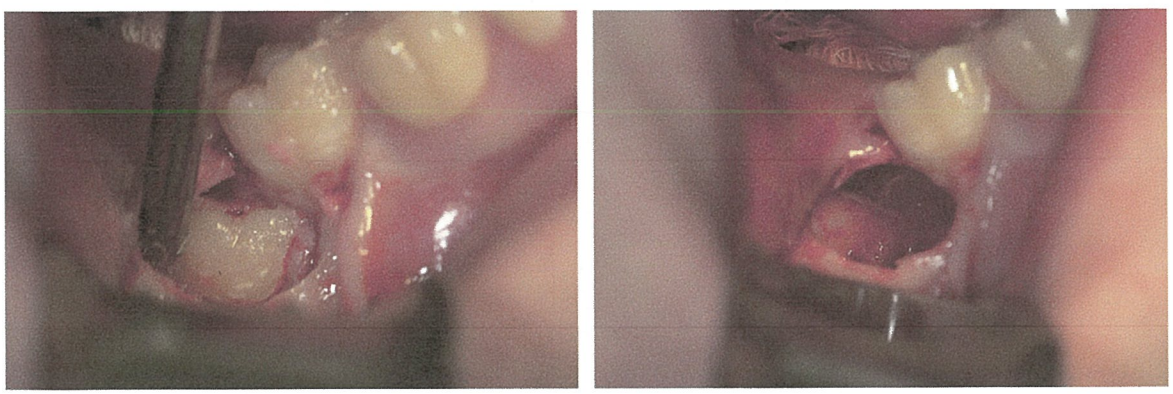

Fig. 1. Example of a minor oral surgical procedure.

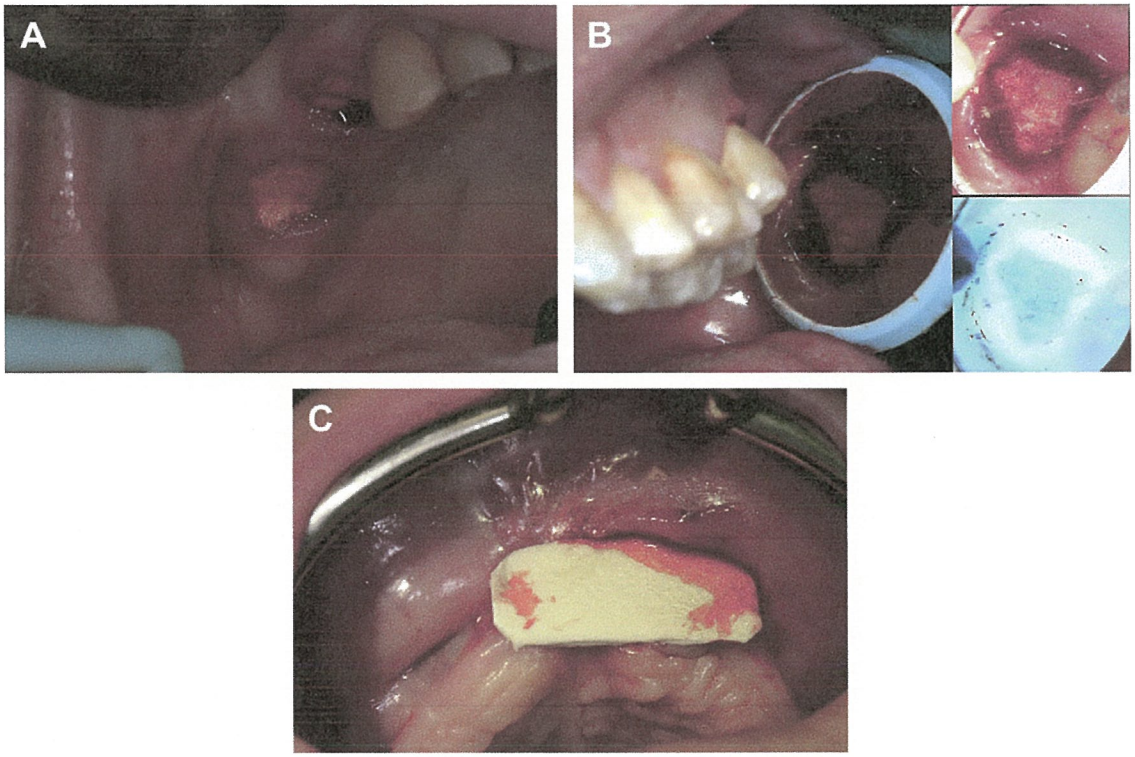

Fig. 2. (*A–C*) The use of the chitosan bandage for socket hemostasis.

11. Treat the patient early in the day, allowing for observation throughout the day for any bleeding problems.
12. The risk of significant bleeding in patients on oral anticoagulants and with a stable INR in the normal therapeutic range of 2 to 4 is extremely small and the risk of increased thrombosis in patients who are withdrawn from anticoagulants outweighs the risk of bleeding from the intraoral procedure. Oral anticoagulants should not be withdrawn from most patients who are undergoing outpatient oral surgical procedures.
13. Patients who are undergoing oral surgical procedures and who must be covered with a single dosage of antibiotics for prophylaxis against endocarditis do not need to have their anticoagulant regime altered.

THE MANAGEMENT OF POSTOPERATIVE HEMORRHAGING

Occasionally, and regardless of the techniques used, there is the postsurgical episode of bleeding requiring early intervention. This often occurs within the first 24-hour period and requires additional treatment. The most effective way to control the bleeding is to use an application of pressure to the wound area. Very often this is not well understood by the patient and even sometimes by the clinician. An adequate application of pressure to the wound area for 30 minutes or longer very often is the only procedure needed to control the bleeding. However, in more remote cases the application of additional materials may be needed to control the oozing or frank bleeding.

Various materials have been advocated for placement into the tooth socket or wound, such as gelatin materials (Gel foam); hemostatic collagen products, such as Collatape or Helistat; and various cellulose products or even bone wax. More recently, the use of chitosan-derived hemostatic bandages for intraoral use has changed the approach to topical hemostasis (Fig. 2). Termed the "HemCon bandage," this chitosan bandage when topically applied intraorally can stop the excessive bleeding through a process independent of the intrinsic or extrinsic pathways of hemostasis. The negatively charged cells interact with the positively charged HemCon bandage forming an adhesive viscous clot, which seals the wound and then activates the other various coagulation pathways. This material adds an additional pathway to stopping an acute bleed and allows the clinician the ability to treat those patients who have compromised INR readings in the face of anticoagulant therapy.[30]

SUMMARY

The possibility of postoperative bleeding exists whenever a surgical procedure is undertaken.

This is further complicated when the patient is being treated with continuous oral anticoagulant therapy to decrease the risk of thromboembolism or has an inherited problem with a particular bleeding disorder. Particular treatment regimes are followed to minimize the risk of postoperative bleeding. It is now quite clear that the alteration of anticoagulant therapy is no longer necessary to decrease the incidence of postoperative bleeding after oral and maxillofacial surgery. The use of common conservative techniques in conjunction with hemostatic materials allows for the continued treatment of patients who previously were thought to be at risk for bleeding problems. It has been shown that patients who undergo oral surgery procedures have no greater risk toward bleeding than patients with normal coagulation numbers. Close collaboration with the patient and their primary physician can eliminate the need to interfere with ongoing medications for anticoagulation therapy. Safe, effective surgery and proper management of the patient can provide a predictable atmosphere for healing.

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