Topical Hemostatic Agents
What the Oral and Maxillofacial Surgeon Needs to Know

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KEYWORDS

• Topical hemostatic agents • Hemostasis • Oral and maxillofacial surgery

KEY POINTS

- Hemostatic agents can be useful adjuncts for oral and maxillofacial surgery procedures.
- Knowledge of normal and abnormal hemostatic mechanisms is necessary to safely practice surgery.
- Different hemostatic agents can be used, depending on the type of surgery and estimated or actual blood loss encountered.
- Cost factors must be weighed against efficacy and side-effect profiles when selecting a topical hemostatic agent.

INTRODUCTION

Hemostasis is a key concept in the safe practice of any surgical procedure. This concept is especially true for any procedures of the head and neck, where the local robust vascular supply exists with the necessity of maintenance of a patent airway. Loss of hemostasis after dentoalveolar procedures has been documented to compromise the airway and cause hypovolemia, even in otherwise healthy individuals without known bleeding diatheses.[1] Orthognathic surgery usually carries a greater risk of significant blood loss, generally increasing with the number of surgical sites/procedures.[2,3] Major head and neck procedures to address neoplasia may further increase both blood loss and the probable need for transfusion of bank blood products.[4] Therefore, concentration on prevention of blood loss in surgery is a laudable goal. Herein is presented a review of various methods of topical hemostasis with which oral and maxillofacial surgeons may wish to take advantage.

REVIEW OF NORMAL HEMOSTASIS

Although a complex process, hemostasis can be divided into 4 distinct phases[5]:

1. Vascular contraction—acutely injured arteries and arterioles, having a muscular tunica media, are able to undergo vasospasm to decrease the amount of intravascular fluid loss.
2. Endothelial injury and platelet plug formation—endothelial cell injury and subendothelial collagen exposure causes adhesion of platelets under the influence of von Willebrand factor. Aggregation of other platelets is followed by conformational changes in platelets and liberation of several substances that increase both platelet aggregation and direct activation of thrombin.
3. Initiation of the clotting cascade—this has classically been described as having 2 arms, the extrinsic (tissue factor activated) and the intrinsic (intravascular) pathways, which join at the common pathway. At that stage, activated

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factor X complex cleaves prothombin to thrombin, forming a complex that then cleaves fibrinogen to fibrin, which then forms a network of cross-linked fibrin mesh that ensnares the platelets and erythrocytes to form a retracted clot. The details of this cascade have recently been found to be much more interactive and complex than originally thought, with multiple positive and negative feedback mechanisms.[6]

4. Modulation of clotting—plasma antithrombin and tissue factor pathway inhibitor, which freely circulate, are negative amplifiers of the coagulation cascade. Proteins C and S are activated by several proteins in the coagulation pathway, inhibiting activated factors V and VII. As a part of healing, several proteolytic enzymes, notably plasmin (activated by tissue plasminogen activator or urokinase), disrupt the fibrin clot into fibrin degradation products, restoring blood vessel patency.

BLEEDING DIATHESIS

Blood loss associated with surgery can be magnified by the presence of a bleeding diathesis. Such a state may be acquired, autoimmune, or genetic and may involve either the formation of the platelet plug, coagulation pathway, or both[7] (**Box 1**). Such situations may make the use of appropriate topical hemostatic agents desirable.

Box 1
Summary of hemorrhagic diatheses

Disorders of platelets

Thrombocytopenias
- Immune thrombocytopenias
- Drug-induced thrombocytopenias (chemotherapy and heparin-induced)
- Myelodysplasia/aplastic anemia
- Hypersplenism

Alterations in platelet function
- Adhesion disorders (genetic)
- von Willebrand disease
- Therapeutic platelet inhibitors
  - $P2Y_{12}$ inhibitors (clopidrogel and prasugrel)
  - Cyclo-oxygenase inhibitors (aspirin)
  - Phosphidiesterase inhibitors (cilostazol)
  - GP IIB/IIIA inhibitors
  - Adenosine reuptake inhibitors (persantine)

Disorders of coagulation

Hemophilias
- Factor VII (classic/A), IX (B), and XI (C), others
- Liver dysfunction
- Factor antibody syndromes

Therapeutic anticoagulants
- Warfarin
- Heparins
- Factor X inhibitors (rivaroxaban and apixaban)
- Factor II inhibitor (dabigatran)

Diffuse intravascular coagulopathy

Massive transfusion states

OVERVIEW OF TOPICAL HEMOSTATIC AGENTS

Certain surgical procedures (vascular procedures, nerves grafts, and large open surgical defects of soft tissue) do not lend themselves to physical methods of hemostasis, such as electrocautery or chemical cautery. Other patients have bleeding disorders that may not be totally correctable prior to surgery and can benefit from the use of topical hemostatic agents. Topical agents are not to be used intravascularly or unintended thrombosis can occur.

Topical hemostatic agents can be classified as scaffold/matrix, biologically active, styptic, tissue adhesive, sealant, occlusive, and vasoconstrictive. Each has indications for application, drawbacks, and contraindications, which are reviewed.

Scaffold/Matrix Agents

Scaffold/matrix agents have been available for decades and are widely used in all areas of surgery. They are generally applied as a dry agent and allowed to help propagate the fibrin/platelet matrix. Four types of agents are generally available: gelatin matrix, microfibrillar collagen, porous polysaccharides, and oxidized methylcellulose.

Gelatin matrix

Processed from porcine dermal collagen product that is fomented and dried, gelatin matrix has a neutral pH. Marketed as Gelfoam (Pfizer, New York, NY) and Surgifoam (Ethicon US LLC, Somerville, NJ), gelatin matrix is available as a sponge or as a powder.[8] It is believed to provide a porous matrix in which platelet enmeshing and fibrin clot formation are supported. Extremely hygroscopic, gelatin matrix can absorb 40 times its weight in fluid.[9] Doing so, it increases in size and may cause surrounding wound pressure,