Galore International Journal of Health Sciences and Research
Vol.3; Issue: 4; Oct.-Dec. 2018
Website: www.gijhsr.com
Review Article ***P-ISSN: 2456-9321***

Hemostatic Agents in Dentistry

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ABSTRACT

Bleeding intraoperatively and postoperatively in oral surgery poses a great threat to the patient and can lead to serious consequences if uncontrolled. The dentist should be familiar with the range of hemostatic agents available in market and their application if any bleeding episode occurs. Bleeding complications can occur in healthy as well as in patients who are systemically compromised. Having a broad knowledge of the management approaches will allow the clinician to know when to apply a particular approach. The purpose of this article is to review the literature regarding the applications of various local hemostatic agents available in the management of bleeding in oral surgery, their mechanism of action, their indications and contraindications.

Keywords: Hemostasis, Local hemostatic agents, Oral surgery, Bleeding.

INTRODUCTION

Bleeding can occur during or after surgery which can be troublesome for both patient and the surgeon and if uncontrolled can lead to serious life threatening consequences. Bleeding may also compromise visibility and possibly the procedure itself. It normally occurs when a vessel is cut or injured during surgery or due to trauma which can be managed successfully in most cases by applying pressure. The source of bleeding can be either from hard tissue or soft tissue i.e. bone or mucosa. Bleeding can be classified as arterial, venous or capillary bleeding based on the source of the vessel involved in injury. The source of bleeding can be identified by proper illumination, adequate retraction, and thorough suctioning. In major oral and maxillofacial surgical procedures and periodontal surgical procedures electrocautery and suture ligatures are most commonly used to control bleeding from small and major vessels. But if generalized oozing is present, and when use of pressure is not effective and the use of electrosurgical instruments could endanger teeth or adjacent nerves, topical hemostatic agents may be needed. Local hemostatic agents provide control of external bleeding by enhancing the natural clotting process through various physical reactions between the agent and blood or by various mechanical means. [1]

TYPES OF HAEMORRHAGE [2]

The classification of a haemorrhage is important as it has direct clinical implications.

Haemorrhage following minor oral surgical procedure can be classified in relation to timing:

- PRIMARY HAEMORRHAGE: Bleeding occurs at the time of the surgery.
- REACTIONARY HAEMORRHAGE: Bleeding that occurs 2–3 hours after the procedure as a result of cessation of vasoconstriction.
- SECONDARY HAEMORRHAGE: Bleeding that occurs up to 14 days after the surgery. The most likely cause of this is supposed to be infection.

The haemorrhage may also be classified according to the site affected:
Soft tissue, Bone, Vascular.

HEMOSTASIS PROCESS

Various processes involved in hemostasis process are:

- ❖ Vasoconstriction,
- ❖ Formation of a platelet plug, and
- ❖ Coagulation (secondary hemostasis).

Step 1. Vasoconstriction:

Immediate constriction of damaged blood vessels is caused by vasoconstrictive paracrine released by the endothelium cells which results in a temporary decrease in blood flow within the injured vessel.

Step 2. Formation of a platelet plug:

Following which mechanical blockage of the defect occurs by a plug that forms as platelets stick to the exposed collagen at site of injured endothelial (platelet adhesion) and become activated, releasing cytokines (serotonin, thromboxane A2, and endothelin 1) into the area around the injury. Released platelet factors (adenosine diphosphate, fibronectin, thrombospondin, fibrinogen, and platelet-derived growth factor) reinforce the vasoconstriction process and activates more platelets that stick to one another (platelet aggregation)to form the platelet plug at the site of injury.

Step 3. Coagulation (Secondary hemostasis):

At the same time, exposed collagen and tissue factor initiates a series of reactions known as the coagulation cascade that ends in the formation of fibrin polymer. The fibrin protein fiber mesh helps in stabilization of the platelet plug to become a blood clot.

The clotting cascade (secondary hemostasis) is traditionally broken up into two basic pathways:

- Intrinsic pathway: Also known as contact activation pathway, is primarily activated by collagen, which is exposed at the site of injury and binds Factor XII to initiate this coagulation cascade.
- Extrinsic pathway: Also known as tissue factor pathway, is stimulated by tissue factor, which is exposed by the tissue injury and through Factor VII activation initiates this pathway.

These two pathways later converge in a common pathway where thrombin converts fibrinogen to fibrin and then the final clot formation takes place. [2]

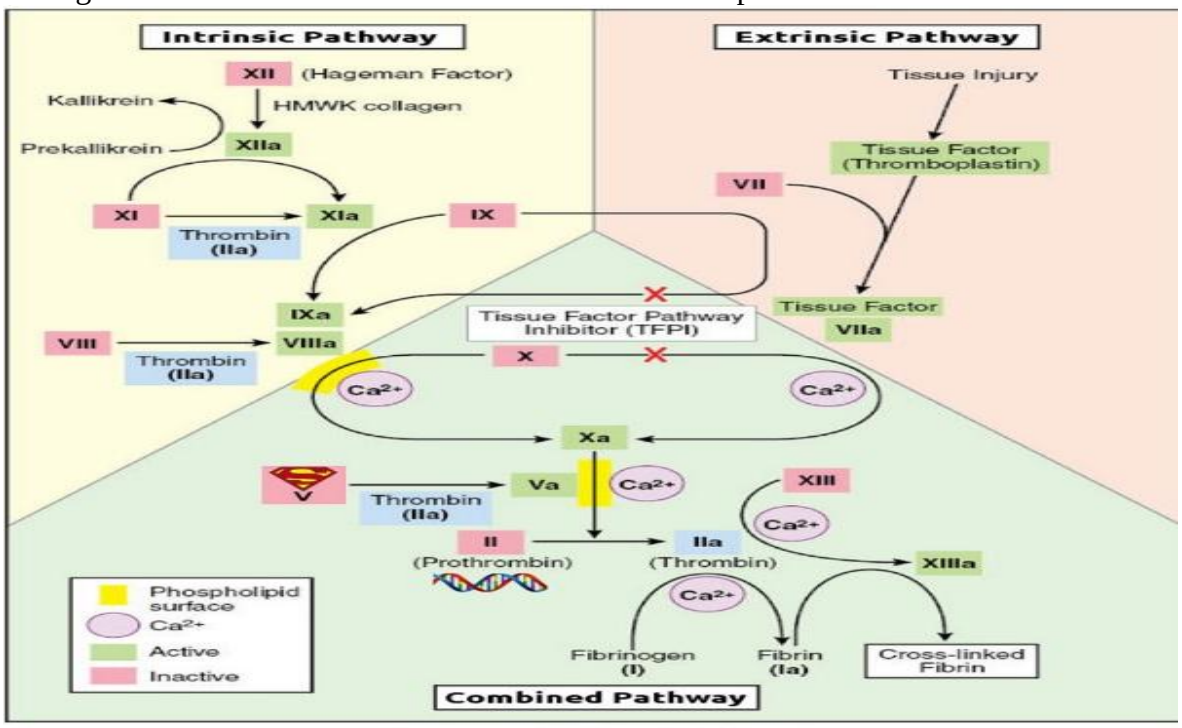

Figure: Coagulation cascade

HEMOSTATIC AGENT

A hemostatic agent (antihemorrhagic) is a substance that promotes hemostasis (stops bleeding).

PROPERTIES: The ideal hemostatic agent should be effective, and the agent itself, along with its metabolic breakdown products, should be biocompatible to be used in the body and should be affordable.

Local hemostatic agents can be classified as: [3]

1. Passive hemostatic agents 2. Active hemostatic agents

Sr.no	Passive hemostatic agents	Active hemostatic agents
1	Collagen-based products Microfibillar collagen (Avitene) Absorbable collagen hemostat sponge (Helistat) Colla-Cote, Colla-Tape, Colla-Plug.	Thrombin
2	Cellulose-based products Oxidized regenerated cellulose (Surgicel) ActCel and Gelitacel	FloSeal (flowablehemostatic agent)
3	Gelatin-based products Gelfoam	Sealants Fibrin sealant (tisseel)
4	Polysaccharide hemospheres	Albuminderived hemostat(bioglue)

NEWER HEMOSTATIC AGENTS

Chitosan-based products
Polysaccharide-based hemostats
Poly-N-acetyl glucosamine-based materials
QuikClot (inorganic hemostat)

HEMOSTATIC SOLUTIONS

Styptics
Tannic acid
Lysine analogs
Tranexamic acid

VARIOUS ABSORBABLE AGENTS USED:

Generic (Brand)	Directions	Adverse Effects	Precautions
Absorbable gelatin sponge (Gelfoam)	May be cut into various sizes and applied to bleeding surfaces	May form nidus for infection or abscess	Should not be overpacked into extraction site or wound—may interfere with healing
Oxidized cellulose (Oxycel)	Most effective when applied to wound dry as opposed to moistened	May cause foreign-body reaction	Extremely friable and difficult to place; should not be used adjacent to bone—impairs bone regeneration; should not be used as a surface dressing—inhibits epithelialization
Oxidized regenerated cellulose (Surgicel Absorbable Hemostat)	May be cut to various shapes and positioned over bleeding sites; thick or excessive amounts should not be used	Encapsulation, cyst formation, and foreign-body reaction possible	Should not be placed in deep wounds—may physically interfere with wound healing and bone formation
Microfibrillar collagen hemostat (CollaCote, CollaTape, CollaPlug)	May be cut to shape and applied to bleeding surface	May potentiate abscess formation, hematoma, and wound dehiscence; possible allergic reaction or foreign-body reaction	May interfere with wound healing; placement in extraction sockets has been associated with increased pain
Thrombin (Thrombostat)	May be applied topically to bleeding surface	Allergic reaction can occur in patients with known sensitivity to bovine materials	Must not be injected into tissues or vasculature—can cause severe (and possibly fatal) clotting

PASSIVE HEMOSTATIC AGENT:

They form a physical, lattice-like matrix which can adhere to the bleeding site; this matrix then activates the extrinsic clotting pathway and provides a basic platform around which platelets can aggregate to form blood clot. They are appropriate for use in patients who have an intact coagulation cascade. Passive hemostats are mostly used as first-line agents because they are easily available, no special storage is required, and are relatively inexpensive. They are effective in the presence of heavier bleeding because of their absorption capacity and they provide greater mass by their more fibrous/dense structures. [4]

Passive hemostatic agents have the potential to expand many times than their original mass when they come in contact with fluids, it is recommended to use the less amount of the agent required to achieve hemostasis and remove as much of the agent as possible once hemostasis has been achieved or else it

can compress the surrounding structures like nerves, vessels. Passive topical hemostatic products include collagens, cellulose, gelatins, and polysaccharide spheres. [5]

ACTIVE HEMOSTATIC AGENTS:

They have biologic activity and directly participate in the coagulation cascade to induce a clot formation. Active agents include thrombin and those product formulations in which thrombin is combined along with a passive agent to provide an active product. Thrombin is a useful choice for patients who are on antiplatelet or anticoagulation medications. It is normally used with gelatin foam. Many of the hemostatic agents are contraindicated in contaminated wounds. [6,7]

PASSIVE HEMOSTATIC AGENTS: COLLAGEN-BASED PRODUCTS:

These products are derived from either bovine tendon or bovine dermal collagen. They are non-toxic and non-pyrogenic.

They are further divided into *microfibrillar & absorbable collagen* products.

MICROFIBILLAR COLLAGEN (AVITENE):

It is derived from purified bovine dermal collagen which is a fibrous in nature, water-insoluble partial hydrochloric salt. They get absorbed in 10-14 days.

Advantages:

1. Products can be stored at room temperature.
2. They are immediately available for use, and should not be resterilized.
3. It attracts platelets and stimulates aggregation of platelets to form the fibrous mass resulting in the formation of a physiologic platelet plug, degranulation, and release of clotting factors, leading to initiation of the coagulation cascade.

Adverse effects:

Allergic reaction, adhesion formation, inflammation, foreign body reaction, and potentiation of wound infections which may lead to abscess formation.

Contraindications:

1. In known cases of allergies or sensitivities to materials of bovine origin.
2. Should be avoided in any area where it may exert pressure on adjacent vital structures because of fluid absorption and expansion. [7-9]

ABSORBABLE COLLAGEN HEMOSTAT SPONGE (HELISTAT):

Helistat is collagen derived from purified and freeze-driedbovine flexor tendon which is available as soft, white, pliable, non-friable, coherent, sponge like structure.

Advantage:

1. This product is highly absorbent and able to hold many times their own weight of fluid.
2. When helistat comes in contact with blood, collagen causes aggregation of platelets, which bind in large numbers to the collagen fibrils. These aggregated platelets degranulate, releasing factors such as thromboxane A2.
3. This sponge also provides a three-dimensional (3D) matrix for strengthening the blood clot.
4. These collagen materials are completely resorbed within 14-56 days.

Indications:

Wound protection and for control of oozing or bleeding from clean oral wounds.

Contraindication:

1.Not to be used in infected or contaminated wounds.

2.Contraindicated in patients with known allergies or sensitivities to materials of bovine origin. [10,11]

Disadvantages

It may serve as a nidus for abscess formation and may favor bacterial growth. [12]

CELLULOSE-BASED PRODUCTS (SURGICEL):

Oxidized regenerated cellulose is derived from plant based alpha cellulose and is available in an absorbable white, knitted, fabric which may be single or multiple

sheets that is either available in high or low-density.

It achieves hemostasis by mechanical pressure. It is relatively bacteriostatic when compared with other hemostatic agents. Absorption of Surgicel will occur in approximately 4-8 weeks.

Disadvantages:

1. It has low pH and this acidic nature may cause inflammation and necrosis of the adjacent tissue. Thrombin is ineffective with this agent due to its acidic nature.
2. Encapsulation of fluid and foreign body reaction can occur if the product is left in the wound.

Contraindication:

1. In bony defects (fractures) as it may interfere with bone regeneration.

ACTCEL AND GELITACEL:

It is a new topical hemostatic agent made from treated and sterilized cellulose, available as meshwork like Surgicel hemostatic agent. It is used to control bleeding in periodontal and orthognathic surgeries. One study has demonstrated that Actcel adheres to calcium ions, thus making calcium more available for the coagulation cascade. It has a role in the modifying intrinsic pathway.

Gelitacel is relatively fast-working, oxidized resorbable cellulose hemostatic gauze of natural origin made from highest alpha-grade selected cotton. It resorbs as quick as in 96 hours, therefore giving it decreased risk for encapsulation. [13]

GELATIN-BASED PRODUCTS:

Gelfoam is commonly employed agents for the control of minor bleeding which is a porous. Absorbable gelatin sponge is prepared from purified pork skingelatin. It is manufactured in the form of films, gelatin sponges i.eGelfoamor powder that is mixed to form a paste. Gelfoam has very little tissue reaction and liquefies in the oral cavity within a week, fully absorbing within 4-6 weeks. It is very useful in managing post-operative bleeding after dental extractions and periodontal surgeries and addition of thrombin improves its efficacy. Gelatine based hemostat have been reported to induce a better quality clot than collagen based hemostats. [14,15]

POLYSACCHARIDE HEMOSPHERES:

These are new type of topical hemostatic agent derived from vegetable starch. These hemostatic agents are used to control capillary, venous and small arterial bleeding by producing a hydrophilic effect, thereby dehydrating the bloodand concentrating its solid components and increasing barrier formation. They have no intrinsic coagulation activity but are designed to stimulate clot formation by providing a three dimensional scaffold which can be used for clot organization. [16,17]

The efficacy of passive hemostatic agents varies among various products available. According to research microfibrillar collagen was the most effective of the passive topical hemostatic agents, followed by collagen sponge, gelatin sponge and then oxidized regenerated cellulose. [18,19]

ACTIVE HEMOSTATIC AGENTS

THROMBIN:

Thrombin hemostatic agents are derived from either bovine or humanplasma or they are manufactured using recombinant DNA techniques. Thrombin can be used topically as a dry powder or as a solution along with gelatin sponges mixed with agelatin matrix or in the form of spray. Thrombin converts soluble fibrinogen into fibrin. Mostly thrombin is used with gelfoam to treat moderate to severe bleeding. Thrombin should never be injected into the bloodstream or allowed to enter the bloodstream through large, open blood vessels because it can cause extensive intravascular clotting which can prove to be fatal.

FLOSEAL (FLOWABLE

HEMOSTATIC AGENT):

Floseal agent is a proprietary combination of two independent hemostatic agents and consists of bovine derived

gelatin granules which are coated in human-derived thrombin that works in combination to form a stable clot at the bleeding site. This agent is resorbed by the body within 6-8 weeks, that is with the time frame required for normal wound healing. [20-22]

SEALANTS:

Sealants mechanism of action is by forming a barrier that is impervious to the flow of most liquids. Various types of sealants to achieve surgical hemostasis are:
Fibrin sealants, PEG polymers, albumin with glutaraldehyde and the new cyanoacrylate sealant. [22,23]

FIBRIN SEALANT:

Fibrin sealant is a naturally derived or synthetic combination hemostatic agent which is also tissue adhesive. It has an impact on angiogenesis and wound healing. Fibrin sealants consists of fibrinogen, fibrin stabilizing factor, thrombin. When applied to the surgical site it forms a fibrin clot. These products are applied using a syringe-like applicator or sprayed over a larger area using a gas-driven device.
Uses:
In bone grafting procedures particularly sinus lift surgery.

They can be used in patients with coagulopathies who have insufficient fibrinogen to form a blood clot and can also be used on patients who are receiving heparin.

Fibrin sealants control local as well as diffuse bleeding from the site; however, they are not useful in control of vigorous bleeding.

It is contraindicated in patients who are sensitive to bovine proteins. An excessively thick sealant layer may prevent revascularization at the surgical site, causing tissue necrosis. [23,24]

VARIOUS NEWER HEMOSTATIC AGENTS:

QuikClot (inorganic hemostat)
Chitosan-based products
Polysaccharide-based hemostats
Poly-N-acetyl glucosamine-based materials

Hemostatic solutions:

Styptics: Examples are aluminum solutions when applied locally cause hemostasis by contracting tissue to seal injured blood vessels.

Tannic acid: Tannic acid is a commercial compound which is similar to the plant polyphenol tannin, that stops bleeding from mucous membrane via vasoconstriction.

Tranexamic acid, Epsilon-aminocaproic acid, Hemocoagulase (botroclot).

Various Bone haemostats includes *Bone wax*, Ostene which is bone wax like substance of water-soluble alkylene oxide copolymers.

LITERATURE REVIEW FOR USE OF LOCAL HEMOSTATIC AGENTS FOR ACHIEVING HEMOSTASIS:

Bornert *et al*. and Peisker *et al*. have concluded that local hemostatic agents are useful in the management of post-operative bleeding in oral surgery patients with congenital hematologic disorders. [25,26]

CONCLUSION

Local hemostatic agents are beneficial in controlling bleeding during oral surgical procedures in patients with congenital and acquired bleeding disorders and also in patients who are on antithrombotic medications for their systemic conditions.

REFERENCES

1. Ogle OE, Swantek J, Kamoh A. Hemostatic agents. Dent Clin North Am 2011; 55:433-9.
2. Robinson PD. Tooth Extraction: A Practical Guide (Chapter 5). Oxford: Elsevier, 2000.
3. Kamoh A, Swantek J. Hemostasis in oral surgery. Dent Clin North Am. 2012; 56(1):17-23.
4. Brodbelt AR, Miles JB, Foy PM, Broome JC. Intraspinal oxidised cellulose (surgical) causing delayed paraplegia after thoracotomy: A report of three cases. Ann R CollSurg Engl.2002;84(2):97-9.
5. McCarthy JR. Methods for assuring surgical hemostasis. Denver. 2009;137-94.

6. Samudrala S. Topical hemostatic agents in surgery: A surgeon's perspective. AORN J 2008;88(3): 02-11.
7. Schreiber MA, Neveleff DJ. Achieving hemostasis with topical hemostats: Making clinically and economically appropriate decisions in the surgical and trauma settings. AORN J 2011;94(5): 11-20.
8. McCarthy JR. Methods for assuring surgical hemostasis. In: Rothrock JC, Seifert PC, editors. Assisting in Surgery: Patient-Centered Care. 2009;137-94.
9. Schreiber MA, Neveleff DJ. Achieving hemostasis with topical hemostats: Making clinically and economically appropriate decisions in the surgical and trauma settings. AORN J 2011;94(5): S1-20.
10. Ogle OE. Perioperative hemorrhage. In: Dym H, Ogle OE, editors. Atlas of Minor Oral Surgery. Philadelphia, PA: W.B. Saunders; 2000. p. 62-3.
11. Andreoli TE, Bennett JC, Carpenter CC, Plum F. Platelets and primary hemostasis. Cecil Essentials of Medicine. 4th ed. Philadelphia, PA: WB Saunders;1997. p. 403.
12. CollaPlug [package insert]. Plainsboro, NJ: Integra Life Sciences Corp.; 2001.
13. Qin-Shang Z, Qing-Zhong. Application of S-99 soluble styptic gauze to wounds. Beijing Xuan Wu Hospital, Departments of Pathology and Stomatology. Beijing, China Personal Communication; December 31, 1982.
14. Spotnitz WD, Burks S. Hemostats, sealants, and adhesives: Components of the surgical toolbox. Transfusion 2008;48(7):1502-16.
15. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. Eur Spine J 2004;13 Suppl 1: S18-27.
16. Ward BB, Smith MH. Dentoalveolar procedures for the anticoagulated patient: Literature recommendations versus current practice. J Oral MaxillofacSurg 2007;65(8): 1454-60.
17. Spangler D, Rothenburger S, Nguyen K, Jampani H, Weiss S, Bhende S. *In vitro* antimicrobial activity of oxidized regenerated cellulose against antibiotic-resistant microorganisms. Surg Infect (Larchmt) 2003;4(3):255-62.
18. Tomizawa Y. Clinical benefits and risk analysis of topical hemostats: A review. J Artif Organs 2005;8(3):137-42.
19. Wagner WR, Pachence JM, Ristich J, Johnson PC. Comparative *in vitro* analysis of topical hemostatic agents. J Surg Res 1996;66(2):100-8.
20. Schreiber MA, Neveleff DJ. Achieving hemostasis with topical hemostats: Making clinically and economically appropriate decisions in the surgical and trauma settings. AORN J 2011;94(5): S1-20.
21. Spotnitz WD, Burks S. Hemostats, sealants, and adhesives: Components of the surgical toolbox. Transfusion 2008;48(7):1502-16.
22. Spotnitz WD, Burks S. State-of-the-art review: Hemostats, sealants, and adhesives II: Update as well as how and when to use the components of the surgical toolbox. ClinApplThrombHemost 2010;16(5):497-514.
23. Spotnitz WD, Burks S. Hemostats, sealants, and adhesives III: A new update as well as cost and regulatory considerations for components of the surgical toolbox. Transfusion 2012;52(10):2243-55.
24. Achneck HE, Sileshi B, Jamiolkowski RM, Albala DM, Shapiro ML, Lawson JH. A comprehensive review of topical hemostatic agents: Efficacy and recommendations for use. Ann Surg 2010;251(2):217-28.
25. Bornert F, Gros CI, Schmittbuhl M, Manière MC. Hemostatic management in pediatric patients with type I von Willebrand disease undergoing oral surgery: Case report and literature review. J Oral MaxillofacSurg 2011;69(8):2086-91.
26. Peisker A, Raschke GF, Schultze-Mosgau S. Management of dental extraction in patients with haemophilia A and B: A report of 58 extractions. Med Oral Patol Oral Cir Bucal 2014;19(1):55-60.

How to cite this article: Mani A, Anarthe R, Kale P et.al. Hemostatic agents in dentistry. Galore International Journal of Health Sciences & Research. 2018; 3(4): 40-46.

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