

Hemostatic Agents Used in the Field of Dentistry: An Overview

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Abstract

Intraoperative or postoperative bleeding during any periodontal surgical procedure can to some serious complications. Difficulties related to bleeding can be seen in both healthy individuals as well as bleeding disorder patients, any systemic complications and patients under anticoagulant drug therapy. Having a clear perspective about the preventive measures to be taken to control the profuse bleeding is a must for a practitioner. The purpose of the literature review is to discuss the administration of different types of hemostatic agents available for controlling bleeding.

Keywords: Hemostasis, hemostatic agents, bleeding control.

Introduction

Bleeding is inevitable in case of any oral surgical procedures. The chief causative factor of bleeding is damage to the blood vessels during surgery. In this case, meticulous surgical procedures, availability of ideal hemostatic agents, proper postoperative care and follow up can reduce the complication to a greater degree. Profuse bleeding can to several complications like the formation of hematoma, delayed wound healing, persisting infection, wound dehiscence and necrosis. In this review, we discuss the preoperative, intraoperative and postoperative management of bleeding of patients undergoing periodontal or any kind of minor oral surgical procedures.

For evaluation and selection of ideal hemostatic agents for a particular case scenario, it is mandatory to understand the physiologic procedure of coagulation.

The hemostasis occurs, vasoconstriction, platelet plug formation, platelet adhesion, activation, and aggregation. Whenever there is an injury, vascular spasm occurs and this will initiate vasoconstriction which will gradually lead to a stoppage of blood flow. Following the vasoconstriction, collagen which was exposed from the damaged blood vessel will influence the platelets to adhere, activate and aggregate to form a platelet plug. Platelet adhesion is mostly mediated by Von Willebrand's Factor. Platelets are activated by enhancing their shapes into a more of a pseudopodia form that the adhesion of platelets into the damaged tissue surface. Once the platelets become activated, it will help in the attachment of VWF and fibrin. The activation is further intensified by producing thrombin via the hemostasis mechanism.

This review article focuses on various measures to control intraoperative and postoperative measures to control bleeding.

Mechanical method to control bleeding:

Application of pressure counteracts the hydrostatic pressure within the blood vessel. Applying pressure is usually able to control most of the hemorrhages. It should be applied directly over the bleeding site firmly over a gauze pack for at least five minutes. Hemostats are also called a hemostatic clamp, arterial forceps etc. Hemostat (mosquito, artery) forces are specially designed to catch

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bleeding points in the surgical area. Also, prefabricated stents can be used after surgery to trauma to the surgical site also gives it adequate protection.

Embolization of the vessel: With the help of angiography, the exact bleeding point can be localized. Agents that can be used for embolization include steel coils, polyvinyl alcohol foam, gel foam, silicon spheres, and methyl methacrylate. These particles are placed precisely into the bleeding vessel via a catheter.

It has shown significant results in implant surgery to control bleeding immediately after the tear in the lingual artery¹. Thus, it can be considered as a reliable method for hemostasis.

Thermal method to control bleeding:

Cautery: Hemostasis by using cautery is based on the principle of denaturation of proteins by heat. This proteins undergo precipitation and to coagulation of large areas of tissues. The heat produced by the cautery leads to protein denaturation which ultimately culminates into the coagulation of large areas in the tissue. In cauterization, heat is conducted directly into the target area (tissue) via the instrument.

Electrocautery: The fundamental of electrosurgery is based on the principle of using electrical energy which is directly transmitted to the tissue for inducing histological effects. Current range is 1.5 -7.5million per second or megahertz. Using two electrodes, an alternating current may be conducted through the body with almost no effects other than producing heat. The heat produced is solely the result of the resistance created by tissues to the current pathway. This results in a concentration of current at the smaller electrode and the effects are dehydration, warming of the area, coagulation or tissue destruction by heat depending on the type, the size and the frequency of the active electrode and the duration of application.

The argon beam coagulator (ABC): It provides radio frequency electrical energy (coagulator monopolar current) to tissue by using a heavy stream of argon gas. It delivers noncontact, monopolar, electrothermal hemostasis. In cases of bleeding from small diameter vessels(size \leq 3mm) where bleeding cannot be stopped using other hemostatic agents or ligatures, an argon coagulator is always a good option for these scenarios. This coagulator has also shown improved results in control of presacral bleeding².

Lasers: Lasers to perform surgeries with less or almost no blood, as these effectively coagulate the small blood vessels while tissue cutting or sectioning. It provides a clean, dry surgical field with improved visualization³. It was seen that it has enhanced the bactericidal effect when used in implant sites without extreme heat production⁴. An in vitro thromboelastographic study showed that after three and six seconds there is a decrease in coagulation time while using 10 W of continuous-wave laser irradiation of 10 ml of blood and resulted in increased clot formation rate⁵. In the present scenario, LASER is widely used because it aids in pain relief, improved healing and speeds up the tissue repair.

Chemical method to control bleeding:

Adrenaline: Adrenaline or epinephrine, applied topically induces vasoconstriction and thus helps in achieving hemostasis. However, adrenaline has a dual-action called a vasomotor reversal, at low doses it causes vasoconstriction but later it leads to vasodilation. Thus, extensive application or undiluted preparation can cause systemic effects therefore, care should be exercised while using adrenaline. It can also be injected with L.A in a concentration of 1: 80,000 to 1:2,00,000.

Astringent and stryptics: When astringent comes in touch with the injured tissue surface, a thin film is formed upon the surface and the superficial membranes and blood vessels are contracted to cause shrinkage of the tissue and thus resulting in protein precipitation⁶. Monsel's solution which is quite effective in controlling capillary bleeding contains Ferric sulfate and it acts by precipitating proteins. Tannic acid also has the same mechanism of action. A study showed that messaging astringent gels in the edentulous areas showed improved keratinization in the denture wearers.

Bone wax: The material is a combination of beeswax, salicylic acid, and almond oil. The mechanism of action of bone wax is mostly mechanical. It can be applied directly to a particular bleeding point in bone. It is normally non-absorbable in blood or saliva. It results in the formation of a soft and malleable mass when heated and manipulated. Commonly supplied in sterile sticks.

Another product BoneSeal® which is a composite of biodegradable polylactic acid with hydroxyapatite and having wax-like handling properties⁷. BoneSeal is designed to promote hemostasis and deliver improved

bone regeneration when compared to bone wax.

Thrombin: Thrombin agents are produced from either human or bovine plasma. It can also be derived from recombinant DNA techniques. The topical use of thrombin acts by converting fibrinogen into a fibrin clot⁸. It shouldn't be injected in the bloodstream or open, large blood vessels which can cause intravascular clotting. It was found in a study that a thrombin Arg-Gly-Asp complex helps in cell adhesion⁹.

Gelfoam: It is an absorbable gelatin sponge containing fine, dry, heat-sterilized powder prepared by milling absorbable gelatin. It is insoluble in water, porous and pliable in nature. The mechanism it uses for hemostasis is more physical and it does not affect the blood clotting pathways. Gelfoam is absorbed completely, with little tissue reaction when used in less amount. Normally it is absorbed inside the wound area within 4-6 weeks. It doesn't in abundant scar tissue formation. It was reported that it can produce better results in clot formation than collagen¹⁰. It is contra indicated for skin closure because it might interfere with the healing of the incision lines.

Oxycel or surgicel (ORC): It is also known as Surgicel or Oxycel for commercial use. It is derived from plant-based alpha-cellulose. It is an absorbable hemostatic agent that has been used to control bleeding safely, simply and effectively. It soaks up the blood and transforms into a gel at the target area. It results in lowering the pH and also caused localized vasoconstriction. ORC also acts as a scaffold or matrix for platelet adhesion and also supports the newly formed platelet plug. It was used in the treatment of intrabony defects and it has shown a significant reduction of CAL and PPD¹¹.

Fibrin glue: Fibrin glue or Fibrin sealant is comprised of fibrinogen and thrombin that is used in the damaged tissue sites with the purpose of tissue adhesion. Some fibrin sealants also contain aprotinin, fibronectin and plasminogen. The thrombin(enzyme) leads to the conversion of fibrinogen into fibrin monomers incorporated 3-D gel-like structure within the period of 10-60 seconds.

Each fibrin sealant system is made up of two parts. The first part consists of: It is available as a two-component system: the first component contains fibrinogen, factor XIII, fibronectin, and traces of other plasma proteins. The second part contains thrombin, calcium chloride, and antifibrinolytic agents such as aprotinin. Combining

the two parts initiates blood clotting mechanism along with the formation of fibrin.

Fibrin glue can be used in various surgical procedures like implant placement in the anterior tooth region. In a comparative study done in 2008 stated that the use of fibrin sealants is superior to using regular suture material because it is easy to handle, helps in induce hemostasis, proper adhesion of tissues and aids in wound healing¹².

Sealants must be used carefully because an excessive amount of sealant can to tissue necrosis¹³.

Co-seal: It is made up of polyethylene glycols (PEGs) mixed with hydrogen chloride and sodium phosphate. It is a non-toxic, FDA approved material that is biocompatible and can be easily delivered¹⁴. When the solution is mixed, it transformed into a hydrogel which attaches itself to the damaged tissues. It is synthetic in nature and doesn't contain Glutaraldehyde. The mechanism of action is mostly physical as the gel swells up in volume (almost 4 times) and can undergo further swelling as it undergoes resorption.

Platelet-rich plasma gel: Platelets contain several growth factors such as platelet-derived growth factor, transforming growth factor, insulin-like growth factors I and II, and epithelial growth factor. Because of this property, autologous platelet concentrate(APC) is widely used to boost postoperative healing. The platelet concentrate can be prepared via centrifugation by using patients own blood. The thrombocyte count of PRP was 1,035,000/L (mean). It also bears mucosa-adhesive properties thus widely used in the field of dentistry.

Ethamsylate: The hemostatic mechanism of ethamsylate is due to the activation of thromboplastin formation on damaged vessel walls. It also decreases prostacyclin 2 synthesis and facilitates platelet aggregation. It acts by correcting abnormal platelet adhesion. It exerts antihyaluronidase action, improves capillary wall stability not (not an antifibrinolytic).

Tranexamic acid: Tranexamic acid 4.8% is commonly used as a mouthwash because it helps in clot stabilization. It also helps in down regulating plasminogen. Because of its antifibrinolytic activities, it can be used as a prophylactic in patients who are taking anticoagulant drugs. A study showed that the efficacy of tranexamic acid when combined with cetylpyridinium chloride, is significantly increased for treating periodontal diseases¹⁵.

Botroclot: It is a form of concentrated enzyme sources extracted from the venom of South American viper, *Bothrops atrox*. Botroclot (Jaggat pharmaceuticals) is a topical preparation that contains extracted hemocoagulase. It aids in healing and also having procoagulant property. Botroxobin, a WHO-approved product, has been introduced to treat the site of injury. It has shown improved healing property when used in extraction sockets¹⁶.

Protamine: A proteolytic enzyme from the venom of South American viper, *Bothrops atrox*. It also functions as a plasma clotting agent for fibrinogen. It is a protein molecule having a positive charge and it attaches with heparin which is negatively charged. The ultimate complex formed inside the body is removed by the reticuloendothelial system.

It was found that a combination of heparin and protamine has shown decreased postoperative bleeding¹⁷.

Desmopressin: It is a synthetically manufactured vasopressin analogue which was actually originated for treating diabetes insipidus¹⁸. Nevertheless, it was used as a hemostatic agent when its ability to release of VWF and factor VIII from the endothelial cells was discovered¹⁹. It also aids in primary hemostasis.

Vitamin K: Vitamin K plays a massive role in the coagulation process. It also helps in the production of fibrinogen and prothrombin in the liver, thus it can be considered as a vital factor for bleeding control. It can even prevent the chances of bleeding in patients taking high doses of anticoagulant drugs.

Newer hemostatic agents:

Chitosan-based dressings: Chitosan is a biocompatible, complex carbohydrate acquired from chitin (a natural compound derived from zeolites): when the deacetylation of chitin is above 70% it is called chitosan. It is a type of acid salt which has mucoadhesive property. It has a positive charge and it attracts RBCs and Platelets which have a negative charge. It also offers sealing action and antibacterial property. QuikClot (inorganic hemostat) is a chitosan-based product currently available

Polysaccharide-based hemostats: Polysaccharide hemostats, like STARSIL® and HEMOSTAT, seems to be useful in bleeding control. It is widely used in cardiac surgery procedures²⁰. Reduction of wound healing

complications (mostly seen after using bone wax) can be considered as additional.

Conclusion

Hemostasis can always be considered as the main pillar for the success of any surgical treatment. Even with the judicious application of local hemostatic agents, minor to moderate invasive surgeries can be safely performed. Several other factors like the application of local pressure during surgery, post-operative mouth rinses also aids in bleeding control. However, detailed medical history of the patient, case selection and proper knowledge of surgical anatomy- these factors also have a major part in implementing a safe and successful surgical procedure without any postoperative complication.

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References

1. Hwang HD, Kim JW, Kim YS, Kang DH, Kwon TG. Angiographic embolization for hemorrhage control after dental implantation. *J Korean Assoc Oral Maxillofac Surg*. 2013 Feb;39(1):27-30
2. Saurabh S, Strobos EH, Patankar S, Zinkin L, Kassir A, Snyder M. The argon beam coagulator: a more effective and expeditious way to address presacral bleeding. *Tech Coloproctol*. 2014 Jan;18(1):73-6
3. Elavarasu S, Naveen D, Thangavelu A. Lasers in periodontics. *J Pharm BioallSci* 2012;4, Suppl S2:260-3
4. Savolainen HO. Effects of continuous-wave and pulsed laser on blood coagulation. An in vitro thromboelastographic study. *Ann ChirGynaecol*. 1993;82(1):37-41.
5. Schwarz F, Aoki A, Sculean A, Becker J. The impact of laser application on periodontal and peri-implant wound healing. *Periodontol* 2000. 2009;51:79-108.
6. Radke U, Kahar A, Zade P, Lambade D, Deshpande S, Radke P. Evaluation of Effect of Astringent on Oral Mucosa as a Non-surgical Preprosthetic Treatment Modality in Edentulous Patients: An In Vivo Study. *J Indian Prosthodont Soc*. 2014 Dec;14(Suppl 1):93-7.
7. Tham T, Roberts K, Shanahan J, Burban J,

- Costantino P. Analysis of bone healing with a novel bone wax substitute compared with bone wax in a porcine bone defect model. *Future Sci OA*. 2018 Jul 26;4(8):FSO326.
8. Bar-Shavit R, Sabbah V, Lampugnani MG, Marchisio PC, Fenton JW 2nd, Vlodaysky I, Dejana E. An Arg-Gly-Asp sequence within thrombin promotes endothelial cell adhesion. *J Cell Biol*. 1991 Jan;112(2):335-44.
 9. Tatakis DN. Blood coagulation factors in periodontal pathophysiology: a review with emphasis on the role of thrombin. *Semin Thromb Hemost*. 1992 Jan; 18(1):28-33.
 10. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. *Eur Spine J*. 2004 Oct;13 Suppl 1(Suppl 1):S18-27.
 11. Shiggaon LB, Prabhuji MV, Viswanath D, Kerudi VV. Usage of Surgicel® an absorbable hemostat as a graft for management of periodontal defects: An in vivo study. *SRM J Res Dent Sci* 2014;5:69-72
 12. Jathal B, Trivedi A, Bhavsar N. Use of fibrin glue in periodontal flap surgery. *J Indian Soc Periodontol* 2008;12:21-5
 13. 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 Oct;52(10):2243-55.
 14. Mehdizadeh M, Yang J. Design strategies and applications of tissue bioadhesives. *Macromol Biosci*. 2013 Mar;13(3):271-88.
 15. Lee JE, Lee JM, Lee Y, Park JW, Suh JY, Um HS, Kim YG. The antiplaque and bleeding control effects of a cetylpyridinium chloride and tranexamic acid mouth rinse in patients with gingivitis. *J Periodontal Implant Sci*. 2017 Jun;47(3):134-142
 16. Shenoy K V, Baliga M, Mahajan S, K V R. The Effects of Topical Hemocoagulase Solution on the Healing Process of Post-extraction Wounds: A Split Mouth Design. *J Maxillofac Oral Surg*. 2015 Sep;14(3):586-93.
 17. Runge M, Møller CH, Steinbrüchel DA. Increased accuracy in heparin and protamine administration decreases bleeding: a pilot study. *J Extra Corpor Technol*. 2009 Mar;41(1):10-4.
 18. Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first twenty years. *Haemophilia*. 2000 Jul;6 Suppl 1:60-7.
 19. Rodeghiero F, Castaman G, Mannucci PM. Clinical indications for desmopressin (DDAVP) in congenital and acquired von Willebrand disease. *Blood Rev*. 1991 Sep;5(3):155-61.
 20. Schmitz, C., Sodian, R. Use of a plant-based polysaccharide hemostat for the treatment of sternal bleeding after median sternotomy. *J Cardiothorac Surg* 2015;10:59.