European Review for Medical and Pharmacological Sciences 2023; 27 (3 Suppl): 135-140

Topical hemostatic agents in oral surgery: a narrative review

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Abstract. – Sufficient hemostasis during oral surgical procedures is crucial for successful outcomes and to reduce healthcare resource utilization. The purpose of this narrative review is to give a rational insight into the management of bleeding in oral and dental practice through modern drugs. A narrative literature review has been performed on the present topic identifying all articles on Pubmed/Medline and Google Scholars. Acceptable hemostasis during oral surgery is also required to improve visibility and provide a dry operational area. Many oral surgeons, in their daily practice, encounter problems in controlling postoperative bleeding and use a topical hemostatic agent to promote platelet activation or aggregation to form a stable clot.

Key Words:
miRNA-106, Pediatric osteosarcoma, PI3K/AKT signaling pathway.

Introduction

Bleeding is one of the complications that can occur during dental surgery. It can present as oozing at the extraction site or severe intraoral hematomas that compromises the airway, causing anemia, hypovolemia and can be life-threatening. This is true especially in patients affected by bleeding diathesis, who may need hospitalization and transfusions (using replacement factors) with the impending risk of viral infection or various factor inhibitors. These bleeding diatheses may be acquired, autoimmune, or genetic and can be classified in disorders of platelets (thrombocytopenias or alterations in platelet function), disorders of coagulation including the use of therapeutic anticoagulants, vascular disorders, disorders of fibrinolysis and diffuse intravascular coagulopathy[1]. Furthermore, the number of patients with cardiovascular problems undergoing anticoagulation therapy is increasing, exposing them to risk of intra and postoperative bleeding.

During dental surgery, it is important to stop the bleeding to improve visibility and the success of surgery, reducing the stress for the operator and the patient, minimizing operating time and risk of postsurgical complications like swelling, hematoma and infections. Several hemostatic techniques can be used to stop the bleeding: mechanical methods (manual pressure, ligature, suture), thermal methods (electrocauterization or laser cauterization) and topical hemostatic agents. Mechanical methods can be insufficient, especially in patients with anticoagulant therapy or coagulopathies, while thermal methods can

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cause necrosis of bone and damage tissues or can be difficult to use in areas with poor accessibility[2]. In these cases, topical hemostatic agents can be used in association with sutures and gauze packing to prevent bleeding. The ideal hemostatic agent should be biocompatible, easy to apply, safe and have an immediate effect[3]. Our paper reviews old and new products for an updated use in common practice.

Topical hemostatic agents can be classified in[3,4]:

- Active agents that contain fibrinogen and thrombin and activate the coagulation cascade. These agents are useful in patients with a coagulation disorder.
- Mechanical or passive agents: promote coagulation from the individual's own fibrin production, activating the extrinsic clotting pathway. Mechanical hemostats are only useful for patients with a functioning coagulation system because, in the absence of coagulation factors, like factors VIII and XII, they cannot promote an adequate hemostasis.

The literature review has been performed re-collecting and summarizing all empirical evidence that fits pre-specified topic. The articles have been identified on Pubmed/Medline and Google Scholars. To conduct a high-quality analysis, the authors analyzed the articles according to the following sub-categories: active agents, mechanical agents.

Active Agents

Fibrin Sealants (Tissucol®/Tisseel®, Crosseal®/Quixil®, Evicel®, Vistaseal®)

Fibrin sealants are part of active agents and are made of human fibrinogen and thrombin that are mixed using a dual-syringe delivery system and form the fibrin clot. Thanks to adhesive properties, they can be used for wound healing, suture support, and tissue sealing. Adhesives are metabolized by fibrinolysis and phagocytosis. To stabilize clotting and accelerate coagulation, factor XIII, fibronectin and antifibrinolytic agents (aprotinin or tranexamic acid) can be present. If these components have an animal origin (bovine aprotinin in Tisseel, bovine products in Vitagel, or equine products in Tachosil), they could cause hypersensitivity and coagulopathy, so fibrin sealant without animal components should be preferred (Evicel)[5]. A complete autologous fibrin glue has been proposed to avoid the risk of transmission of viral or immunological reactions because the fibrinogen derives from the patient's own blood, in contrast to the fibrin adhesive available commercially, where it is prepared from pooled donor plasma. Two components of autologous fibrine glue (fibrinogen solution with platelet growth factors and thrombin solution) are obtained by centrifugation of the patient's own blood[5]. Tisseel® was the first fibrin sealant approved by the FDA, available in a pre-filled syringe. It is composed of human thrombin and fibrinogen, with $CaCl_2$ and aprotinin, a bovine protein, potential allergen. Evicel® and Quixil® (in the EU)/Crosseal™ (in US) do not contain synthetic or bovine aprotinin so they have a reduced potential for hypersensitive reactions. Evicel® differs from Quixil®/Crosseal™ in that its fibrinogen component does not contain the antifibrinolytic agent tranexamic acid, which is potentially neurotoxic, resulting in Quixil®/Crosseal™ being contraindicated for the use in neurosurgery[6]. Limits of their use are the necessity to respect the cold chain in order to preserve components, and to respect defrosting temperature and storage time once opened.

Fibrin sealants have been used after dental extraction in patients with bleeding disorders for more than 20 years, but also in maxillary sinus lift procedure, cleft lip and palate patients to repair residual fistulas or clefts, in flap closure following periodontal surgery[7,8].

Flowables (Surgiflo®, Floseal®)

Another category is flowable, containing an animal gelatin matrix with thrombin, that can easily adapt to irregular wounds thanks to their flowability. FloSeal (Baxter, Deerfield, IL, USA) combines a bovine-derived microgranular gelatin flowable matrix with thrombin, but no fibrinogen, so clotting requires contact with the patient's native fibrinogen (i.e., exposure to the patient's blood). Surgiflo is composed of a porcine gelatin matrix, combined with a bovine-derived thrombin.

Ali et al[9] demonstrated that Floseal protocol was useful to prevent post dental extraction hemorrhage in patients with inherited bleeding disorders, also for patients with pre-existing clotting factor inhibitors or anaphylaxis to clotting concentrates. Floseal protocol is equipotent and more economical than the traditional perioperative factor replacement protocol.

Topical Thrombin (Thrombin-JMI®, Evithrom®, Recothrom®)

Thrombin promotes the transformation of fibrinogen into fibrin. Topical thrombin hemo-

stats can derive from bovine or human plasma or recombinant DNA techniques. Thrombin-JMI (Pfizer), from bovine plasma, can cause fatal severe thrombosis from the development of antibodies against bovine thrombin, or fatal bleeding from the development of antibodies against bovine factor V, with cross-reactivity to human factor V[10]. For these reasons bovine thrombin was replaced by thrombin derived from human plasma (Evithrom®) and recombinant human thrombin (Recothrom®), approved by the Food and Drug Administration in 2008. Thrombin can be applied as a dry powder, a paste, a spray, or a combination with collagen or gelatin such as Gelfoam®[11].

A comparative study between recombinant human thrombin and bovine thrombin by Browman et al[12] demonstrated that rhThrombin is effective for achieving hemostasis within 10 minutes of administration, and is equally effective as bovine thrombin, with a significantly lower risk of immunogenicity and viral transmission.

Antifibrinolytics (Tranex®, Ugurol®, Lysteda®, Cyklokapron®, Amicar®, Caprolisin®)

Antifibrinolytics, such as Epsilon-Aminocaproic Acid (EACA) and Tranexamic Acid (TXA), are synthetic analogs of the amino acid lysine and prevent plasminogen conversion into plasmin binding to the lysine-binding sites on plasmin[11]. TXA is more effective than EACA. Applying a gauze soaked with TXA (4.8%) topically is more frequent, but it can also be used as a mouthwash or systemically.

De Vasconcellos et al[13] in their review analyzed randomized clinical trials comparing TXA (mouthwash) and other hemostatic agents in anticoagulating patients and demonstrated a protective effect on bleeding after minor oral surgery, more than a placebo and aminocaproic acid.

In the same way, Ockerman et al[14] demonstrated the efficacy of TXA mouthwash in patients on non-vitamin K oral anticoagulants (NOACs) undergoing dental extraction, reducing the rate of periprocedural or early postoperative oral bleeding compared to a placebo.

Epinephrine

Epinephrine causes vasoconstriction by activating alpha-adrenergic receptors but may increase pulse rate and blood pressure. Cotton or gauze impregnated with solutions of 1:100 to 1:10.000 epinephrine has been used for years as a local hemostatic. Cotton or gauze can leave fibers in the surgical site causing foreign body reaction and hindering wound healing, so some authors[15] recommend the use of absorbable collagen impregnated with epinephrine. Racellets® are hemostatic cotton pellets with 1.5% racemic epinephrine hydrochloride. Vy et al[15] used Colla-Cote® sponges saturated with as much as 7.5 mg (range, 2.1-7.5 mg) of 2.25% racemic epinephrine directly into the cancellous bony crypt, with no evidence of cardiovascular changes because the immediate local vasoconstriction of the capillaries reduced absorption into the systemic circulation, and thus little systemic effect.

Mechanical Agents

Gelatin (Gelfoam®, Surgifoam®, Gelfilm®, Gelita-Spon®, Geli Putty®)

Gelatin is a hydrocolloid obtained from porcine dermal collagen. It is available in sponge and powder and can be placed dry or after wetting it with saline. It provides a porous matrix that promotes platelet aggregation and the formation of a fibrin clot. It is extremely hygroscopic and can absorb 40 times its weight in fluid which can cause surrounding wound pressure. Gelatin matrix is completely resorbed by hydrolysis in 4-6 weeks[4].

Kim et al[16] demonstrated that the use of an absorbable gelatin sponge after third molar extraction significantly decreased postoperative swelling, mucosal petechiae, and skin ecchymosis.

Collagen (Helistat®, Instat®, Helitene®, Avitene®, Collaplug®, Colla Tape®)

Collagen offers a large surface area for platelet activation and aggregation and the release of clotting factors such as thromboxane A2, so it is less effective in patients with severe thrombocytopenia, but useful in the case of heparinization. Microfibrillar collagen is derived from bovine skin or tendon and available in powder, nonwoven sheets, sponge and pad forms[11]. It usually does not swell significantly and is absorbed in less than 8 weeks. Kim et al[17] in their split-mouth RCT in 31 patients with bilateral mandibular impacted third molars, demonstrated that collagen reduced early-stage post-operative complications and enhanced initial healing of soft tissues and periodontal defects, reducing pain (VAS score) and probing depth. Ranganathan et al[18] in their

split-mouth study demonstrated that Collaplug is beneficial to the patient in postoperative wound healing and also for better bone formation after third molar extraction. Different studies[19] demonstrated the efficacy of Avitene in periodontal surgery, especially in palatal donor site of tissue autografts. The authors demonstrated a reduction of bleeding time (1 minute compared with nearly 20 minutes in the control group) and a significant 51% reduction ($p < 0.01$) in the blood flow rate after 10 minutes of application, but no differences in the rate or quality of healing nor the degree of pain were perceived by the patients.

Oxidized Regenerated Cellulose (Surgicel®, Oxycel®, Gelita-Cel®)

Oxidized cellulose consists of absorbable fibers prepared from cellulose, available in sheets. It can be either regenerated (ORC, organized fibers are formed before oxidation) or non-regenerated (ONRC, with unorganized fibers prior to oxidation). The ONRC seems to be more effective, but unhandy[20]. It has an acidic pH, so it is antimicrobial, causes hemolysis and cannot be used with topical thrombin. It is absorbed in approximately 8 weeks, but the acidic pH may delay resorption and cause complications such as granulation formation and clinical diagnosis of abscess, for this reason it should be removed[4,20]. Its use should be avoided in proximity to nerve structures.

Polysaccharide Hemospheres (Arista™AH)

Polysaccharide hemospheres are produced from potato starch and processed into microporous spheres, presented in powder form. They act by dehydrating the blood and concentrating erythrocytes and platelets, aiding in hemostasis and are resorbed in 24 to 48 hours by tissue amylases, thus reducing the risk of infection or granuloma formation[4]. Attention should also be paid to diabetic patients, using no more than 50 g and around foramina of bone, removing the excess[20]. Arista®AH is the only FDA-approved one in this category.

Cyanoacrylates (Tissu-Glu®, Histoacryl®, Dermabond®, Surgiseal®, Tisuacryl®)

This material is composed of acrylate monomers that polymerize in contact with body fluids. Cyanoacrylates are classified by the length of their side chains: intermediates Tissu-Glu® and Histoacryl® and long-chain as Dermabond® and Surgiseal®[11]. Perez et al[21] treated 130 patients with the adhesive and 30 with suture, after different surgeries (apicectomy, extraction of molars, and mucogingival grafting). The authors obtained immediate hemostasis, a normal healing of incisions and pain relief, when Tisuacryl was used upon donor sites and mucosal ulcerations. Oladega et al[22] compared cyanoacrylates and silk suture in 120 subjects with impacted mandibular third molar. Cyanoacrylate tissue adhesive showed no significant difference in postoperative pain, swelling, wound dehiscence and infection but a statistically significant difference in postoperative bleeding (day 1), with more bleeding in the control group.

Bone Wax (Waxocare, Oriwax)

Introduced by Sir Victor Horsley in 1886, bone wax is a soft and malleable wax composed of beeswax, salicylic acid, and almond oil, used to stop bleeding and visualize the origin of the hemorrhage. It does not promote coagulation but just obliterates the vascular spaces in cancellous bone[23]. Thanks to its insolubility, it is not absorbed and promotes the risk of inflammation, foreign body reaction and infection of the site, also inhibiting bone healing. For these reasons it should be used in very limited quantities and the excess removed[11]. Krasny et al[24] used bone wax to stop bleeding in 176 patients on chronic anticoagulant therapy after tooth extraction or surgical extraction of a retained tooth and demonstrated that bone wax is an efficient and safe material to block bleeding after tooth extractions, also in patients on chronic anticoagulant therapy without stopping or adjusting the therapy. Katre et al[25] described a case of inferior alveolar nerve damage caused by bone wax in third molar surgery. The patient, who had had the lower third molar removed 11 years prior, complained 2 months of paresthesia of cutaneous distribution of the right mental nerve. CT scan demonstrated a focal rounded expansion of the right inferior alveolar canal, measuring 9 mm in diameter. The lesion was excised, the nerve grafted (sural nerve donor site) and on dissecting the specimen a large piece of bone wax was removed. After 1 year follow-up the patient was pain free and recovered sensibility. In this case, foreign body reactions to bone wax compressed and infiltrated neural tissue.

Aluminum Chloride ($AlCl_3$)

Other chemical agents can be used during endodontic surgery, when it is necessary to stop bleeding to improve visibility and to use materi-

als for root canal obturation. Aluminum chloride ($AlCl_3$) creates a barrier formed by coagulated blood proteins that prevents blood flow from the arteries. It is widely used because it is easy to apply, cheap, and commercially available. When used as a paste, it can adhere to bony crypt walls and the residual particles can cause localized foreign body reactions and delay healing, so the bone defect should be cleaned with a bone curette or a small round bur[26].

Ferric Sulfate

Ferric sulfate (FS) interacts with blood proteins and leads to coagulation, but it has a very low pH (0.8-1.6), and it is cytotoxic, so can cause bone damage, extreme foreign body reactions and abscess formation[26].

Calcium Sulfate

Calcium sulfate (CaS) is a characteristic agent that is cheap, quick setting, and can be easily removed. Experimental studies[27,28] reported the high biocompatibility of CaS with excellent results without any negative influence on the outcome and a lack of inflammatory reaction. It acts as a physical barrier, so it can be removed or left *in situ*[28]. This material is totally resorbable and biocompatible, and, no problems should arise if some CaS particles are left around the tooth at the end of the surgery. It has been used in clinical practice with efficacy for bleeding control during endodontic surgeries[26,29]. Also, it has been used as a hemostatic agent after tooth extraction in patients with undergoing anticoagulant therapy[30] and to control bleeding in the surgical-orthodontic treatment of impacted teeth[31].

Conclusions

Despite several studies having compared the efficacy of some topical hemostatic agents, there is currently not enough literature to attest the superiority of one topical agent over other ones, so further randomized controlled trials with similar methodology should be conducted, especially on patients with coagulopathies or undergoing coagulation therapy, or anti-vitamin K treatment.

To choose a topical agent, the clinician should know its characteristics, indications and possible side effects. To prevent bleeding during surgery, knowledge of the patient's medical and drug history and the prescription of blood chemistry tests (such as bleeding indices) remains essential.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Authors' Contribution

All authors were involved with the literature review and performance of the surgery. All authors read and approved the final manuscript.

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References

1) Triplett DA. Coagulation and Bleeding Disorders: Review and Update. Clin Chem 2000 1; 46: 1260-1269.
2) Akolkar. Bleeding control measures during oral and maxillofacial surgical procedures: A systematic review [Internet]. (accessed: 2022 Jul 8). Available at: https://www.jdrr.org/article.asp?issn=2348-2915;year=2017;volume=4;issue=4;spage=79;epage=89;aulast=Akolkar.
3) Mani A, Anarthe R, Kale P, Maniyar S, Anuraga S. Hemostatic agents in dentistry. Galore Int J Health Sci Res 2018; 3: 40-46.
4) Campos N de, Furlaneto F, Buischi YDP. Bleeding in Dental Surgery [Internet]. IntechOpen 2019 (accessed: 2022 Jul 8). Available at: https://www.intechopen.com/online-first/69934.
5) Thorn JJ, Sørensen H, Weis-Fogh U, Andersen M. Autologous fibrin glue with growth factors in reconstructive maxillofacial surgery. Int J Oral Maxillofac Surg 2004; 33: 95-100.
6) Dhillon S. Fibrin sealant (evicel® [quixil®/crosealTM]): a review of its use as supportive treatment for haemostasis in surgery. Drugs 2011; 71: 1893-1915.
7) Davis BR, Sándor GK. Use of fibrin glue in maxillofacial surgery. J Otolaryngol 1998; 27: 107-112.
8) Use of fibrin glue in periodontal flap surgery Jathal B, Trivedi A, Bhavsar N. J Indian Soc

Periodontol [Internet] (accessed: 2022 Jul 8). Available at: https://www.jisponline.com/article.asp?issn=0972-124X;year=2008;volume=12;issue=1;spage=21;epage=25;aulast=Jathal

9) Ali T, Keenan J, Mason J, Hseih JT, Batstone M. Prospective study examining the use of thrombin–gelatin matrix (Floseal) to prevent post dental extraction haemorrhage in patients with inherited bleeding disorders. Int J Oral Maxillofac Surg 2022; 51: 426-430.
10) Zehnder JL, Leung LLK. Immunological Consequences of Topical Bovine Thrombin. Am J Pathol 2001; 159: 2371.
11) Ruangchainicom N, Mahardawi B, Sakdejayont W. Topical hemostatic agents from an oral-surgery perspective. J Oral Maxillofac Surg Med Pathol 2021; 33: 249-255.
12) Bowman LJ, Anderson CD, Chapman WC. Topical recombinant human thrombin in surgical hemostasis. Semin Thromb Hemost 2010; 36: 477-484.
13) de Vasconcellos SJ de A, de Santana Santos T, Reinheimer DM, Faria-E-Silva AL, de Melo M de FB, Martins-Filho PRS. Topical application of tranexamic acid in anticoagulated patients undergoing minor oral surgery: A systematic review and meta-analysis of randomized clinical trials. J Craniomaxillofac Surg 2017; 4: 20-26.
14) Ockerman A, Vanassche T, Garip M, Vandenbriele C, Engelen MM, Martens J, Politis C, Jacobs R, Verhamme P. Tranexamic acid for the prevention and treatment of bleeding in surgery, trauma and bleeding disorders: a narrative review. Thromb J 2021; 19: 54.
15) Vy CH, Baumgartner JC, Marshall JG. Cardiovascular Effects and Efficacy of a Hemostatic Agent in Periradicular Surgery. J Endod 2004; 30: 5.
16) Kim JC, Choi SS, Wang SJ, Kim SG. Minor complications after mandibular third molar surgery: type, incidence, and possible prevention. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 102: 4-11.
17) Kim JW, Seong TW, Cho S, Kim SJ. Randomized controlled trial on the effectiveness of absorbable collagen sponge after extraction of impacted mandibular third molar: split-mouth design. BMC Oral Health 2020; 20: 77.
18) Ranganathan M, Balaji M, Krishnaraj R, Narayanan V, Thangavelu A. Assessment of Regeneration of Bone in the Extracted Third Molar Sockets Augmented Using Xenograft (CollaPlugTN Zimmer) in Comparison with the Normal Healing on the Contralateral Side. J Pharm Bioallied Sci 2017; 9: 180-186.
19) Cziperle DJ. AviteneTM Microfibrillar Collagen Hemostat for Adjunctive Hemostasis in Surgical Procedures: A Systematic Literature Review. Med Devices Auckl NZ 2021; 14: 155-163.
20) Huang L, Liu GL, Kaye AD, Liu H. Advances in Topical Hemostatic Agent Therapies: A Comprehensive Update. Adv Ther 2020; 37: 4132-4148.
21) Pérez M, Fernández I, Márquez D, Bretaña RM. Use of N-butyl-2-cyanoacrylate in oral surgery: biological and clinical evaluation. Artif Organs 2000; 24: 241-243.
22) Oladega AA, James O, Adeyemo WL. Cyanoacrylate tissue adhesive or silk suture for closure of surgical wound following removal of an impacted mandibular third molar: A randomized controlled study. J Craniomaxillofac Surg 2019; 47: 93-98.
23) Misch CE, Resnik R. Misch's Avoiding Complications in Oral Implantology. Elsevier 2017; 3: 907.
24) Krasny M, Krasny K, Fiedor P. Safety and efficacy of bone wax in patients on oral anticoagulant therapy. Acta Pol Pharm 2014; 71: 683-686.
25) Katre C, Triantafyllou A, Shaw RJ, Brown JS. Inferior alveolar nerve damage caused by bone wax in third molar surgery. Int J Oral Maxillofac Surg 2010; 39: 511-513.
26) Khater AGA, Al-Hamed FS, Safwat EM, Hamouda MMA, Shehata MSA, Scarano A. Efficacy Of Hemostatic Agents In Endodontic Surgery: A Systematic Review And Network Meta-Analysis. J Evid-Based Dent Pract 2021; 21: 101540.
27) Orsini G, Ricci J, Scarano A, Pecora G, Petrone G, Iezzi G, Piattelli A. Bone-defect healing with calcium-sulfate particles and cement: an experimental study in rabbit. J Biomed Mater Res B Appl Biomater 2004; 68: 199-208.
28) Scarano A, Orsini G, Pecora G, Iezzi G, Perrotti V, Piattelli A. Peri-implant bone regeneration with calcium sulfate: a light and transmission electron microscopy case report. Implant Dent 2007; 16: 195-203.
29) Scarano A, Artese L, Piattelli A, Carinci F, Mancino C, Iezzi G. Hemostasis control in endodontic surgery: a comparative study of calcium sulfate versus gauzes and versus ferric sulfate. J Endod 2012; 38: 20-23.
30) Scarano A, Sinjari B, Murmura G, Mijiritsky E, Iaculli F, Mortellaro C, Tetè S. Hemostasis control in dental extractions in patients receiving oral anticoagulant therapy: an approach with calcium sulfate. J Craniofac Surg 2014; 25: 843-846.
31) Scarano A, Carinci F, Cimorelli E, Quaranta M, Piattelli A. Application of calcium sulfate in surgical-orthodontic treatment of impacted teeth: a new procedure to control hemostasis. J Oral Maxillofac Surg 2010; 68: 964-968.