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Chapter

Thrombostatic Agents and Tissue Adhesives in the Emergency Department: Stopping the Bleeding, Closing the Wound, and Novel Applications

Donald Jeanmonod, Guhan Rammohan and Rebecca Jeanmonod

Abstract

Complaints of bleeding are frequent presentations to the emergency department, and although most bleeding can be controlled with direct pressure, increased use of antiplatelet agents and anticoagulants complicates what might be otherwise simple bleeding. Industry has met the demand for hemostatic adjuncts, and a number of products are available for the emergency physician to assist in hemostatic control and wound closure. This chapter will cover the various available technologies, covering their preferred use and discussing particular bleeding scenarios and which technology may be best for each scenario.

Keywords: topical hemostatic agent, tissue adhesive, bleeding scenarios

1. Introduction

Control of bleeding wounds has always been a priority in managing injured patients, and providers have used numerous adjuncts to staunch bleeding for decades, with variable success. The earliest use of topical hemostatic agents dates from the end of the nineteenth century when thrombin was used by boxers and barbers to control bleeding from lacerations [1]. Almost a century before the clotting cascade was completely elucidated, in 1909 Bergel had described using topical fibrin to stop surgical bleeding [2–4]. Subsequently, surgeons utilized fibrinogen in plasma as well as bovine thrombin to assist in a variety of surgical scenarios, including nerve repair and skin grafting [5, 6]. Commercial products first became available in Europe in 1972, but the Food and Drug Administration did not approve fibrin sealants in the United States until 1998 [3]. Over the course of time, numerous other types of hemostatic agents have been developed, each unique in their load bearing capacity, biomechanical properties, handling, derivation, and application [7].

Cutaneous and mucous membrane bleeding are common presentations to emergency departments. Data from the National Hospital Ambulatory Medical

Care Survey in 2002 estimated that there were 7.27 million emergency department visits for lacerations, representing approximately 6.6% of all emergency department visits [8], and data from HCUP National Emergency Department Survey in 2013 estimated about 7 million emergency department visits or 5.2% of all visits for lacerations [9]. There are no data to quantify how many of these visits are associated with uncontrolled or major bleeding. The mainstays of treating bleeding remain the simple application of direct pressure with a pressure bandage and application of tourniquet if hemostasis is unable to be obtained. However, there are times that application of hemostatic agents can assist in bleeding control. In the modern era, with widespread use of anticoagulant and antiplatelet agents, as well as physiologically induced coagulopathies from liver disease and uremia, development of topical hemostatic agents to assist in terminating complex bleeding scenarios has become important.

We will briefly review classes of tissue adhesives, topical hemostatic agents, and the best practice data regarding each in the setting of the emergency department. We will provide common clinical bleeding scenarios and the application of these materials in those situations.

2. Topical hemostatic agents

Topical hemostatic agents generally fall into one of two categories: the physical agents that work by providing a physical substrate which promotes hemostasis and the biologically active agents that enhance coagulation at the site of action (**Table 1**). In the emergency department, topical hemostatic agents are primarily used as adjuvant therapy to direct pressure to stop persistent bleeding from lacerations and abrasions that are not amenable to suture control, such as distal fingertip avulsions, flap lacerations with avulsion of the flap, and skin tears in the elderly. As well, topical hemostatic agents can be used to assist with persistent bleeding from nasal mucosa, gingival tissue after tooth extraction, and from vascular bleeding sites such as persistently bleeding dialysis access sites or bleeding lower extremity varices.

Little data exists to suggest superiority of a single agent over others, and often selection of an agent is based on availability, familiarity with its use, patient and wound characteristics, and cost.

2.1 Physical matrix topical hemostatic agents

2.1.1 Gelatin matrix (Gelfoam® [Pfizer Inc., New York, NY, USA], Surgifoam® [Ethicon Inc., Somerville, NJ, USA], Floseal® [Baxter International, Deerfield, IL, USA])

Gelfoam® and Surgifoam® are porcine derived, non-soluble, gelatin matrices that are in a compressed sponge form [10, 11]. They can be cut to appropriate size for application and when applied to bleeding sites are able to absorb 45 times their weight in whole blood. Floseal® is a combination of bovine-derived, liquid gelatin matrix and human-derived thrombin that is supplied in a syringe with an applicator tip that assists with mixing the components and application at the site of bleeding [12]. The mechanism of action of gelatin matrix is poorly understood but is thought to be due to its physical properties, providing a structural support for clot formation rather than a direct effect on the clotting cascade. In clinical use, these agents are appropriate for topical application to persistently bleeding sites, such as dental extraction sites, in the management of epistaxis, and in fingertip avulsion injuries. These agents typically have minimal tissue reaction and are absorbed within

	Product	Manufacturer
Physical matrix topical hemostatic agents		
Gelatin matrix	Gelfoam®	Pfizer Inc., New York, NY, USA
	Surgifoam®	Ethicon Inc., Somerville, NJ, USA
	Floseal®	Baxter International, Deerfield, IL, USA
Oxidized regenerated cellulose	Surgicel®	Ethicon Inc., Somerville, NJ, USA
	SafeGauze®	Medicom, Montreal, QC, Canada
Microporous polysaccharide spheres	Arista® AH	CR Bard Inc., Murray Hill, NJ, USA
Microfibrillar collagen	Avitene®	CR Bard Inc., Murray Hill, NJ, USA
Chitosan	HemCon®	Tricol Biomedical Inc., Portland, OR, USA
	Chitoflex®	Tricol Biomedical Inc., Portland, OR, USA
	TraumaStat®	Ore-Medix, LLC Company, Lebanon, OR, USA
	Celox®	Medtrade Products LLC., Crewe, UK
	ChitoSAM®	Sam Medical, Tualatin, OR, USA
	Axiostat®	Axio Biosolutions PVT LTD. Gujarat, India
Biologically active topical hemostatic agents		
Topical thrombin	Thrombin JMI®	Pfizer Inc., New York, NY, USA
Tranexamic acid (TXA)	Multiple generics	
	Cyklokapron® 100 mg/ml	Pfizer Inc., New York, NY, USA
	Erfa Tranexamic® 100 mg/ml	Erfa Canada 2012, Inc., Montreal, QC, Canada
Kaolin	QuickClot®	Z-Medica LLC., Wallingford, CT, USA

Table 1.
Topical hemostatic agents.

6 weeks when placed within soft tissues or liquified and absorbed within 2–5 days when applied to bleeding mucosal sites.

Little data exists studying the efficacy of gelatin matrices for bleeding complications in the emergency department setting. In a small prospective, randomized study of patients who failed anterior packing for epistaxis, Floseal® application demonstrated equal rates of hemostatic control as repeat anterior packing by a specialist, and lower, but not statistically significant, rates of hospitalization [13]. A larger, prospective randomized sample of patients with epistaxis managed initially with Floseal® versus anterior packing demonstrated that Floseal® was associated with improved patient satisfaction and less rebleeding [14]. In a small convenience sample of patients presenting with posterior epistaxis, Floseal® was successfully used to control bleeding in 80% of patients at a significantly reduced cost when compared to surgery, posterior packing with hospital admission, and embolization [15].

Complications from gelatin matrix applications are reported to be minimal but include the potential to form a nidus for infection or abscess formation, foreign

body reactions with encapsulation of reactive fluid, and toxic shock when used in nasal application.

2.1.2 Oxidized regenerated cellulose (Surgicel® [Ethicon Inc., Somerville, NJ, USA], SafeGauze® [Medicom, Montreal, QC, Canada])

Surgicel® is a sterile, knitted, absorbable fabric produced from plant cellulose. The mechanism of action of Surgicel® is poorly understood, but is thought to produce a mechanical scaffolding for clot formation rather than have a direct effect on the clotting cascade [16]. In clinical use, these agents are appropriate for topical application to persistently bleeding sites, such as dental extraction sites and in the management of epistaxis. As opposed to the gelatin matrices, which can be used wet or dried, the efficacy of Surgicel® is superior if it is applied dry to the area of bleeding, so it may not be appropriate for use with topical thrombin. As Surgicel® undergoes reaction with the tissue, it produces an acidic environment, which has been demonstrated to have in vivo bactericidal properties. The acidic environment that it produces may impair wound healing, perhaps making it a less optimal choice for controlling bleeding in large areas of tissue avulsion. Complications of its use have primarily reported to be localized tissue reactions.

2.1.3 Microporous polysaccharide spheres (Arista® AH [CR Bard Inc., Murray Hill, NJ, USA])

Arista® AH is a powder hemostatic agent derived from plant polysaccharides. The mechanism of action of Arista® is poorly understood, but is thought to produce a mechanical scaffolding for clot formation rather than have a direct effect on the clotting cascade [17]. Its powdered form has limited use in an emergency department environment.

2.1.4 Microfibrillar collagen (Avitene® [CR Bard Inc., Murray Hill, NJ, USA])

Avitene® is a microfibrillar collagen hemostat available as a sponge, sheet, and powder. The collagen matrix of Avitene® is thought to promote platelet activation, inducing clot formation [18]. Avitene® has been on the market for more than 40 years and has widespread applications in surgical hemostasis and epistaxis treatment.

2.1.5 Chitosan (HemCon® [Tricol Biomedical Inc., Portland, OR, USA], Chitoflex® [Tricol Biomedical Inc., Portland, OR, USA], TraumaStat® [Ore-Medix, LLC Company, Lebanon, OR, USA], Celox® [Medtrade Products LLC., Crewe, UK], ChitoSAM® [Sam Medical, Tualatin, OR, USA], Axiostat [Axio Biosolutions PVT LTD. Gujarat, India])

Chitosan is a naturally occurring polycationic polysaccharide derived from multiple sources including shrimp, crabs, and certain fungi. The hemostatic mechanism of chitosan is incompletely understood, but is thought to include gelatinous aggregation of red blood cells, platelet activation, and contact system activation [19].

In a case series of 35 patients on antiplatelet agents or anticoagulants who failed initial management with cautery and nasal packing, 32 patients were successfully treated with application of a foam anterior pack wrapped in a chitosan sheet [20]. A small study of 40 patients on oral anticoagulation undergoing multiple tooth

extractions compared a site treated with a chitosan pledget with a site treated with gauze and pressure and found decreased bleeding times and decreased postoperative pain in the chitosan treated site [21]. Another small study of 20 patients on oral anticoagulants undergoing dental extraction of multiple teeth found that the extraction sites treated with chitosan had shorter bleeding times than control extraction sites treated with a collagen matrix plug [22].

2.2 Biologically active topical hemostatic agents

2.2.1 Topical thrombin (Thrombin JMI® [Pfizer Inc., New York, NY, USA])

Thrombin is a protein which is part of the clotting cascade and has the effect of activating fibrinogen to fibrin, which is essential for clot formation, as well as activating platelets. Several formulations exist on the market, and thrombin can be of bovine or human origin. Topical thrombin can be applied to mucosal bleeding sites such as dental sites and epistaxis or can be applied topically. Additionally, topical thrombin can be used in conjunction with gelatin matrix sponges. No clinical trials comparing efficacy to other techniques have been published. Because these products are derived from other species or individuals, the primary complications include sensitivity reactions or rarely antibody formation against factor V, resulting in life-threatening bleeding complications [23].

2.2.2 Tranexamic acid (TXA) (multiple generics, Cyklokapron® 100 mg/ml [Pfizer Inc., New York, NY, USA], Erfa Tranexamic® 100 mg/ml [Erfa Canada 2012, Inc., Montreal, QC, Canada])

Tranexamic acid is a synthetic derivative of the amino acid lysine that inhibits fibrinolysis by reversibly blocking the interaction of plasminogen with the lysine fragments on fibrin. The intravenous formulation of TXA is typically 100 mg/ml, which is equivalent to a 10% solution. Intravenous TXA formulations can be used topically as adjuvant treatment for patients with epistaxis, oral bleeding, or bleeding from topical sites.

A randomized controlled trial of 216 patients who were randomized to receive an anterior nasal packing soaked in 5 ml of 10% solution versus lidocaine plus epinephrine found that those treated with TXA had more rapid resolution of bleeding and earlier emergency department discharge [24]. A study of 124 patients taking antiplatelet agents who were randomized to TXA versus anterior packing also found more rapid resolution of bleeding as well as decreased visits for rebleeding [25]. A retrospective analysis of oral bleeding in 542 patients demonstrated improvement in bleeding in patients treated with TXA-soaked gauze and compression over use of gauze alone [26]. A systematic review of 5 studies including 252 patients taking oral anticoagulants undergoing dental procedures found that TXA was significantly protective against bleeding with a RR of 0.13 (95% CI 0.05–0.36; $p < 0.0001$) [27]. In addition to using the intravenous formulation of TXA topically, a paste of TXA can be made by crushing several 650 mg TXA tablets and adding small aliquots of saline to form the paste.

2.2.3 Kaolin (QuickClot® [Z-Medica LLC., Wallingford, CT, USA])

Kaolin is an inorganic mineral that has been demonstrated to promote activation of Factor XII, which is the first step in the activation of the intrinsic pathway of the clotting cascade. Kaolin-impregnated gauze is primary developed for controlling

hemorrhage from external wounds in non-compressible sites in the setting of military and civilian trauma.

Little data exists evaluating the effectiveness of kaolin gauze in humans. In swine models of uncontrolled hemorrhage, QuickClot® outperformed comparative hemostatic agents in terms of survival [28].

Although the manufacturer states that there are no complications with the use of QuickClot® because it is not biologically derived, there is a case report of thermal burn with its use [29].

3. Tissue adhesives for wound closure

When it comes to primary wound closure, skin adhesives have several advantages over traditional suture repair. They bond quickly, resulting in saved time on the part of the physician performing the repair, and they are less painful than standard suture repair [30, 31]. They do not require a second visit for suture removal, saving the patient time and reducing the burden to the health-care system [30]. The closure is strong, similar in strength to healed tissue at 7 days post-repair [30]. In addition, the closure with tissue adhesives is cosmetically similar to that achieved with standard suture closure [31]. Tissue adhesives are more expensive than suture materials, but that cost is offset by the inherent costs associated with physician time to suture, bandaging, and repeat visit for suture removal [32]. In a busy and unpredictable emergency department, this time saving is essential.

Unlike topical hemostatic agents, which are often natural polymers, tissue adhesives used for wound closure in the emergency department are primarily synthetic polymers [33]. This is largely due to their high tensile strength, flexibility, and ability to form mechanical bonds [33]. The three primary classes of tissue adhesives used for wound closure are polyurethane-based tissue adhesives, polyethylene glycol-based tissue adhesives, and cyanoacrylate synthetic glues [33].

3.1 Polyurethane-based tissue adhesives

Polyurethane-based tissue adhesives are not commonly used in emergency practice, although they do have applications in surgical practice. The isocyanate prepolymers in the adhesive bond to the amines in tissue proteins, forming a urea bond [3]. Historically, there have been issues with polyurethane-based tissue adhesive toxicity (including thrombosis and hemolysis) and long setup time [3], but they are undergoing development currently using various concentrations of castor oil and other additives to optimize their surgical adhesive properties [34, 35]. Although there is currently some application of these adhesives in the operating theater in renal, plastics, and orthopedic surgery, they are not currently used for traumatic injuries typically seen in the emergency department. As they have shown promise in reducing seroma formation in surgical wounds, they may have applications for larger traumatic wounds in the future.

3.2 Polyethylene-based tissue adhesives

Polyethylene-based adhesives are not currently typically used in emergency practice. Like polyurethane-based adhesives, they are primarily used inside the body, with current uses most commonly related to sealing lung surgical sites and preventing dural leaks after neurosurgery [36]. These adhesives have a very fast setup time and are strong and biodegradable [36]. They have potential for emergency department application in the future.

3.3 Cyanoacrylate synthetic glues (Dermabond® [Ethicon Inc., Somerville, NJ, USA], Histoacryl® [BBraun, Melsungen, Germany], SurgiSeal® [Adhezion Biomedical LLC., Reading, PA, USA], Periacryl® [GluStitch, Delta, BC, Canada], Glu-Stitch® [GluStitch, Delta, BC, Canada], Indermil® [Surgical Specialties, Frenchs Forest, NSW, Australia])

Cyanoacrylate synthetic glues are by far the most common tissue adhesives used for wound repair in emergency departments (**Table 2**). These glues were initially developed during attempts to make a clear plastic. Initially, they were too brittle and caused significant inflammation to tissue but subsequently underwent tremendous redesign over the course of decades prior to their final approval by the FDA in the form of 2-octyl cyanoacrylate in the late 1990s [3, 30]. Cyanoacrylate glues are monomers that react upon contact with water on tissue in an exothermic reaction, causing them to polymerize across the wound edges, allowing healing to take place below. These agents are also antimicrobial, which is an additional advantage [3, 30, 32].

Cyanoacrylate glues have the tensile strength of 5-0 suture, and they reach their maximal bonding strength 2.5 min after application [30]. Given these properties, it stands to reason that wounds most appropriate for glue repair are wounds that would require a suture strength of 5-0 or 6-0. Therefore, cyanoacrylate synthetic glues are not recommended for wounds under tension such as those crossing joint lines, highly gaping wounds, or wounds in very moist areas of the body [30, 32]. It is acceptable to use tissue adhesive glue on wounds that require deep sutures to reduce tension and gaping on the wound, so long as after those sutures are placed, the wound would be appropriate for closure with 5-0 or 6-0 suture. Cosmetically, cyanoacrylate has similar outcomes to standard sutures in appropriately chosen lacerations but a slightly higher risk of dehiscence [30, 31].

Tissue adhesive should be applied to an appropriately cleaned and dry wound. The wound edges should be approximated, and the adhesive should be applied over the approximated edges three to four times [30]. The hydroxyl ions in the wound edges activate the adhesive and seal the wound. The adhesive should never be introduced into the wound. In addition to causing an exothermic reaction because of the amount of moisture, it creates a foreign body reaction, with tissue inflammation and poor healing [30, 32]. Tissue adhesives should therefore not be used on heavily contaminated wounds, bites, macerated wounds, or wounds that are complex and difficult to approximate [30–32].

3.3.1 Novel uses for cyanoacrylate tissue glue

Cyanoacrylate glues are used in oral surgery practice, but their use for dental injuries in the emergency department is currently off-label. Nevertheless, tissue

	Product	Manufacturer
Cyanoacrylate synthetic glues	Dermabond®	Ethicon Inc., Somerville, NJ, USA
	Histoacryl®	BBraun, Melsungen, Germany
	SurgiSeal®	Adhezion Biomedical LLC., Reading, PA, USA
	Periacryl®	GluStitch, Delta, BC, Canada
	Glu-Stitch®	GluStitch, Delta, BC, Canada
	Indermil®	Surgical Specialties, Frenchs Forest, NSW, Australia

Table 2.
Tissue adhesives.

adhesives have found a niche in emergency department management of dental injuries. In the setting of an acutely fractured tooth involving exposed dentin (which is extremely painful), standard of care is to cover the exposed fracture site with calcium hydroxide paste. If this is unavailable, some providers advocate for using cyanoacrylate glue to cover the exposed dentin, as it controls pain and can be removed without difficulty using a solvent in the dentist's office [37, 38]. One study also evaluated the use of cyanoacrylate for pain control in carious teeth, which found it effective for pain control [38]. Cyanoacrylate has antimicrobial properties, which provides theoretical benefits in these settings. However, cyanoacrylate has not been studied for safety in these scenarios, nor has it been assessed for adverse events, only for pain control. Therefore, the physician needs to be aware that any use of cyanoacrylate in treatment of dental fractures in the emergency department setting is not evidence-based.

In patients with avulsed and replanted teeth or in those with subluxed teeth, cyanoacrylate can be useful in splinting the injured tooth.

4. Adverse effects and complications of topical hemostatic agents

Topical hemostatic agents, tissue adhesives, and sealants may have adverse effects usually related to the composition of the agent, location of placement of the agent, and the absorption times of the agent. Slowly degrading products can serve as a nidus for infection especially if excessive amounts are used. In many cases, these agents are used in confined places and can then lead to compression of surrounding structures. Many of the complications associated with these agents are related to surgical uses rather than emergency department applications [39].

4.1 Air embolism

Air embolism is a rare complication that has been reported with the use of injectable agents such as spray thrombin or fibrin sealant. Care must be taken when spraying these objects so as not to exceed recommended pressures and to spray at an appropriate distance from the affected tissue. There are no reported cases of air embolism secondary to use of an atomizer, as may be used with TXA [40–42].

4.2 Wound infection

Wound infection may be associated with the use of topical hemostatic agents. It is difficult to analyze the risk of infection due solely to hemostatic agents versus due to confounding factors. Adverse factors, such as type and location of wound, foreign body material in the wound, and etiology of the wound, all play a role in development of wound infection. If a patient has other systemic symptoms that need to be addressed and needs urgent or emergent wound closure, that too can play a role in development of wound infection. The risk of infection, as it relates to hemostatic agents, can be minimized by cleaning the wound thoroughly and removing excess topical agent after hemostasis is achieved.

4.3 Impaired wound healing

Impaired wound healing may be due to failure to effectively close the wound, dehiscence of the wound repair, and excessive amounts of hemostatic agent

being used. When excessive amount of agent is used, as in cyanoacrylate closure, increased metabolites can form and cause an inflammatory response in the surrounding tissue which leads to poor wound healing [43].

4.4 Hypotension

Hypotension has been reported in some individuals receiving injections of bovine-derived products, such as thrombin. The hypotension is believed to occur with higher than normal concentrations of bovine thrombin but has been noted to be mostly transient lasting less than a minute. The hypotension does respond to epinephrine, if needed, and can be avoided by reducing the amount of bovine thrombin used and compression of injection sites [44–46].

4.5 Allergic reactions and anaphylaxis

Anaphylaxis and allergic reactions are also mostly related to bovine-derived products. These products must be avoided in individuals with a history of prior anaphylactic reactions to plasma products or IgA deficiency [47].

4.6 Infectious disease transmission

Infectious disease transmission is a potential complication when any products using blood components are used, and transmission may be more likely when hemostatic agents are used in an aerosolized form. Though there is a theoretical risk of viral transmission, including HIV and hepatitis, with topical hemostatic agents, there have been no reported cases in the last 20 years [48].

4.7 Vascular thrombosis

Vascular thrombosis is also a theoretical risk; however, there is no increased rate of vascular or graft thrombosis with the use of topical hemostatic agents. Great care must be taken not to inject these agents into a blood vessel or opened vessel [49, 50].

4.8 Immune-mediated bleeding

An immune-mediated bleeding diathesis can occur with the use of bovine thrombin preparations. The diathesis occurs due to development of a factor V deficiency secondary to an antibovine factor V antibody that cross-reacts with endogenous factor V. The risk of this complication can be reduced by using human thrombin. If patients have prior exposure to a bovine thrombin, antibodies may persist for years, and if known bovine thrombin should be avoided [51, 52].

5. Bleeding scenarios

Much of the literature found on uses of topical hemostatic agents for bleeding involves surgical and perioperative indications. However, different bleeding scenarios may present to the emergency department where topical adhesives and hemostatic agents may be of benefit. We will discuss some of these indications, including cutaneous bleeding, varicosity bleeding, AV fistula bleeding, post-tooth extraction bleeding, and epistaxis.

5.1 Bleeding wounds

Approximately 6 million minor wounds are treated in emergency departments in the United States every year. Most cutaneous bleeding occurs due to lacerations of the skin. These lacerations can be caused by blunt or penetrating trauma to the epidermal and dermal layers. Management of these minor wounds has three goals: control of bleeding, avoidance of infection, and cosmetically acceptable, functional scars. Many factors contribute to management of these wounds. The wound must be assessed, and factors such as age of injury, mechanism of injury, extent of wound, neurovascular injury, and location of wound all play a role in determining the type of closure employed. Hemostasis of these wounds must be accomplished, and most times simple pressure for 10–15 min can achieve this. Persistent bleeding may require lidocaine with epinephrine injected or applied to the wound. In those cases where bleeding is difficult to stop, the direct application of surgical absorbable gelatin foam (Gelfoam®) to the wound is an alternative method of achieving hemostasis. Gelfoam®, however, should not be used in infected wounds or at the skin closure site because it may delay healing. After achieving hemostasis, wounds may require debridement, irrigation, and foreign body removal. Once the wound has been adequately assessed and prepared, primary closure with suture, staples, skin tape, or topical adhesive may be utilized. The most common topical adhesives used in the emergency department are cyanoacrylate synthetic glues. These offer tensile strength equivalent to 5-0 sutures. They have similar cosmetic outcomes to sutures but do have a slightly higher risk of dehiscence [53–55].

5.2 Bleeding varicosities

Varicose veins are dilated, elongated, tortuous, subcutaneous veins 3 mm or greater in diameter. They may involve the saphenous veins, saphenous tributaries, or superficial leg veins. Complications of varicose veins most commonly include superficial vein thrombosis and bleeding and, though uncommon, may require immediate attention. Varicose veins located near bony prominences are more prone to hemorrhage, and bleeding is usually due to minor trauma. Hemorrhage, in most cases, can be controlled with direct pressure and elevation of the leg. When these measures fail to sufficiently control bleeding, injections with lidocaine with epinephrine, suturing, and topical hemostatic agents may be helpful. Though no formal studies have specifically looked at topical agents to help with varicose bleeding, anecdotally, the use of topical thrombin, TXA, and absorbable gelatin foam may stop bleeding or control it until more definitive surgical interventions can be performed [56, 57].

5.3 Bleeding arteriovenous fistula

Arteriovenous (AV) fistula is the vascular access preferred for long-term hemodialysis in patients with end-stage renal disease. Hemodialysis accesses are subject to complications such as clotting, stenosis, infection, and hemorrhage. Access complications are common among hemodialysis patients, but they are usually not life-threatening. Fatal vascular access hemorrhage is very rare with an incidence of only 0.4%, but when these patients present to the emergency department, various measures can be employed in order to control the bleeding until definitive measures can be taken, usually by a vascular surgeon. Most of the literature regarding fistula bleeding is related to intraoperative bleeding which can be controlled with suturing, topical thrombin, and cellulose gelatin foam. Extrapolating this data, one could conclude that emergency department management of AV fistula bleeding should

involve direct pressure to the site of bleeding with the aid of topical thrombin products and gelatin foam products. Definitive treatment usually will involve suture repair done by a vascular surgeon either in the emergency department or operating room [58].

5.4 Bleeding from dental extraction

Post-extraction bleeding is a recognized, frequently encountered complication in dental practices. It is defined as bleeding that continues beyond 8–12 hours after dental extraction. The incidence of post-extraction bleeding varies from 0 to 26%. If post-extraction bleeding is not managed, complications can range from soft tissue hematomas to severe blood loss. Local causes of bleeding include soft tissue and bone bleeding. Systemic causes include platelet problems, coagulation disorders, or excessive fibrinolysis. There is a wide array of techniques suggested for the treatment of post-extraction bleeding, which include interventions aimed at both local and systemic causes. Many of these patients will present to the emergency department with their bleeding complications. In addition to treating systemic causes, many techniques can be employed to control the local etiologies of the bleeding. Surgical interventions mainly involve suturing of the site. In addition, nonsurgical hemostatic measures can be employed as well as combination therapy with surgical and nonsurgical techniques. Nonsurgical measures commonly include hemostatic agents such as oxidized cellulose, gel foam, thrombin, collagen fleeces, cyanoacrylate glue, acrylic or surgical splints, and local antifibrinolytic solutions, such as tranexamic acid mouthwash [59].

5.5 Epistaxis

Epistaxis is a common problem encountered in the emergency department. It occurs in up to 60% of the general population; however, 10% or fewer seek medical attention. Epistaxis can be classified as anterior with the common source of bleeding being Kiesselbach's plexus or posterior with the source being the sphenopalatine artery. Initial treatment at home or in the emergency department include conservative measures such as blowing the nose to remove clots, using vasoconstrictive sprays such as oxymetazoline, applying steady pressure for 10 minutes, placing cold compresses on the bridge of the nose, placing a cotton pledget in the nostril, and having the patient bend forward so as not to accumulate blood in the oropharynx. When these measures fail, more invasive measures can be used such as cautery, nasal packing with tampons, gauze, or balloon catheters. There has recently been more literature regarding the use of thrombogenic foams and gels as well as the use of TXA as an adjunct to these measures. Fibrin glue is a safe and effective addition and has been shown to be as effective as cautery and packing [60]. Thrombin gel, such as Floseal, was associated with an absolute 26% lower rebleeding rate compared with nasal packing and was easier to insert and judged more satisfactory by both providers and patients in a randomized trial of 70 patients with acute anterior nosebleeds [14]. In another prospective study, FloSeal® effectively controlled posterior bleeds in 8 of 10 patients whose initial packing failed [61]. Surgicel® and Gelfoam® are common conformable hemostatic materials and have been described in reviews or small case series as useful in nasal bleeding refractory to cautery [62]. These materials can be trimmed to an appropriate size and then applied directly to the bleeding source. Tranexamic acid has been studied for epistaxis and has shown some benefit in both short-term cessation of bleeding and decreasing rates of rebleeding. There was also a trend towards improved control of bleeding when directly compared to nasal packing alone. The delivery of TXA can be done by using

an atomizer and/or saturating nasal tampons with topical application of 500 mg of the IV formulation (TXA 100 mg/ml). Care must be taken in patients with higher risk of systemic thrombosis as systemic absorption may be variable when TXA is applied to the nasal mucosa [63].

6. Conclusion

A number of products are available to assist in topical hemostasis. The choice of which product to use is based partly on availability as well as the particular application. Similarly, there are multiple tissue adhesives available on the market, but the provider will likely be limited to one or two different products.

Conflict of interest

The authors declare no conflicts of interest to disclose.

Author details

Donald Jeanmonod, Guhan Rammohan and Rebecca Jeanmonod*
Department of Emergency Medicine, St. Luke's University Hospital, Bethlehem, PA, USA

*Address all correspondence to: rebeccajeanmonod@yahoo.com

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