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Review Article

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Local Hemostatic Measures in Oral and Maxillofacial Surgery

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Introduction

Homeostasis is continuous process by which internal body system monitor and maintain constant internal environment. Blood is a connective tissue in fluid state closely connected to all tissues of the body. It has many roles including transport of nutrients, metabolic products, blood gases, thermal regulation hormone signaling system, heat conduction, immune response. Hemostasis is homeostasis of intravascular blood volume and is an important function of blood. It involves four major steps: vasoconstriction, platelet aggregation, coagulation and fibrinolysis [1]. The phase of vasoconstriction reduces the blood flow in preparation for platelet aggregation phase. However, the larger the size of the injured blood vessel the less possibility of vasoconstriction especially with high pressure.

Platelets adhere to exposed subendothelium with the help of released adenosine diphosphate (ADP), Von Willbrand factor (VWF) and fibrinogen. VWF also has a role in binding platelets to each other. Platelets clump to each other and degranulate releasing serotonin, ADP and thromboxane A2 which cause vasoconstriction, further platelet aggregation and degranulation. Vasoconstriction and formation of platelet plug constitutes the primary hemostasis. The purpose of coagulation phase is to stabilize the already formed plug by the addition of fibrin. Thrombin (II) acts on fibrinogen (I) to convert it to insoluble fibrin. Thrombin activation is brought by the activation of cascade of clotting factors in either the intrinsic or extrinsic pathways. The liver produces these factors and some of them are vitamin K dependent (II, VII, IX, X). Intrinsic pathway gets activated by the contact between platelets and high molecular weight kininogen, prekalkerin and plasmin. Extrinsic pathway involves the presence of tissue factor from the exposed subendothelial tissue. The common pathway involves the activation of prothrombin by factor X. The fibrinolytic phase prevents abnormal thrombus formation or propagation. The presence of fibrin activates plasminogen to plasmin which causes its proteolysis. Normal vascular endothelium produces tissue type plasminogen activator and protein C.

All surgical procedures are associated with the risk of bleeding, either intraoperatively or postoperatively, especially in the richly vascularized head and neck area. Higher blood loss was recorded in procedures that involve bone.

Primary bleeding which occurs intraoperatively is mainly due cutting a major blood vessel or into an area of large number of vessels as in vascular malformation. Significant increase in blood flow in relation to increased diameter of a blood vessel (Poiseuille's law) causes natural hemostasis to be impossible. Vasoconstrictions become ineffective in the face of high pressure and continuous wash out and dilution of the coagulation system occurs as blood leaves the vessel. Reactionary bleeding occurs few hours after the surgery and is mainly due to reversal effect of anesthesia or slippage of clips off a major vessel. Formation of pseudoaneurysm, infection or blood vessel erosion can cause secondary bleeding 1-2 weeks post operatively. Although this article describes mainly local hemostatic measures, the presence coagulopathy should be properly addressed with suitable investigation and appropriate consultations.

Rationale

Blood is lost either into the surgical field, ingested, aspirated, or accumulates in the surrounding tissue forming hematomas. Blood ingestion can cause gastric irritation, nausea and vomiting [2]. Blood in the respiratory tract can block the airway or gets aspirated. Aspiration is the inhalation of foreign material beyond the vocal cords. Altered mental status can predispose to aspiration. The consequences of aspiration include bronchial irritation, atelectasis, chemical pneumonitis, aspiration pneumonia and acute lung injury [3]. Mullane, et al. through animal study demonstrated that intratracheal injection of blood impaired the defense mechanism of lungs after 24 hours. They postulated that the presence of hemoglobin crystals inhibited the phagocytic action of immune cells. Blood also provides a good media for bacterial growth. The use of fiberoptic bronchoscope helps in the removal of aspirated blood and thus prevents associated complications [4]. Internal bleeding and hematoma formation endanger the airway by pressure effects [2]. In these cases, securing the airway is number one concern followed by monitoring and identification of the causes. Non-expanding hematomas may need only prophylactic antibiotics to prevent infection. Those that continue to expand need to be addressed with interventional radiologist or surgically.

The hemodynamic stability is affected with massive or continuous bleeding. Loss of 30% of total blood volume leads to signs and symptoms of hypovolemia which includes flat neck veins, dry skin, tachycardia, hypotension and reduced urine output. Hypothermia and acidosis aggravate hemodynamic instability by producing coagulopathy which favors more blood loss. Estimation of blood loss (EBL), total blood volume (TBV) and allowable blood loss

(ABL) should be calculated in all surgical cases. It is better to avoid blood transfusion and its possible complications which include transfusion reactions, metabolic acidosis, hyperkalemia, hypocalcemia, hypothermia and transmission of viral diseases [5,6].

Bleeding also negatively affects the quality of the surgical field. The oral and maxillofacial surgical fields are usually difficult to access, small in size and fills rapidly with blood in the area. This may prolong the surgical time. Akinbami found that there is a significant relationship between EBL and duration of the surgery [7]. Poor operating conditions may also increase the risk of complications. Other important reasons to control surgical bleeding also include wound healing. Clot formation is the first step toward wound healing. Healing may be delayed till clot is formed and stabilized.

Hemostatic Measures and Techniques
The importance of hemostasis should always be in mind and the expected/actual blood loss being carefully calculated. Because the various hemostatic measures and techniques available have different mechanism of action, advantages and disadvantages, the surgeon is left to decide what and when to use. These mainly are classified as mechanical, chemical, energy-based, interventional radiology and surgical options. Perhaps, pressure counteracting the exist of blood from the blood stream is the single common mechanism of action of most of the modalities. For sufficient time, pressure alone can achieve hemostasis in most cases. Relatability of the circumstances or suspicion of coagulopathies makes use of hemostatic material and securing it with suture a judicious decision. However, proper patient evaluation can't be replaced by any hemostatic measure. It is the purpose of this article to bring to attention the significance of local hemostatic measures and the various options available.

Reverse Trendelenburg
In this position, the body tilted with the head elevated at about 10-30 degrees. In this position, blood is pooled in the lower part of the body. Arterial flow as detected by nasal doppler in 20-degree head elevation is reduced by 38%. In their study Hathorn, et al. found that anti-trendelenburg reduces total blood loss and improved quality of surgical field in functional endoscopic sinus surgery (FESS) [8]. Mean arterial blood pressure may not be changed due to compensatory mechanism by centers in carotid and aortic bodies. Gan, et al. [9] compared various degrees of head elevation (5°,10°,20°) and found that significant improvement in blood loss in the 20° group compared to 10°. Prolonged or excessive head elevation may cause brain ischemic events. Another concern is the aggravated negative pressure gradient between the surgical site and the right atrium which can cause air embolism.

Hypotensive Anesthesia
Hypotensive anesthesia is defined as reduction of systolic blood pressure to 80-90 mmHg or reduction of mean arterial pressure (MAP) by 30% from the base line [10]. As blood perfusion to the surgical site is reduced, the amount of bleeding is also reduced producing improved surgical field, less total blood loss and possibly shorter operating time [10,11]. For hypotensive anesthesia to be produced safely, only patients with good compensatory mechanisms are selected. Those with ischemic heart disease, atherosclerosis, carotid artery stenosis, hypertension, renal insufficiency and existing brain injury are probably not good candidates for hypotensive anesthesia. Additional contraindications to be considered include respiratory insufficiency, hemoglobinopathies and diabetes mellitus. Excessive reduction of MAP may lead to ischemic events in vital organs as brain, heart, liver and kidneys. Hypotension is achieved by deep anesthesia and heavy analgesia. Using this technique may prolong recovery time and may cause injury to the liver and kidneys. Alternative technique involves the use of direct vasodilators like nitrates and/or beta blockers. Hypotensive anesthesia requires close monitoring and a skillful anesthetist.

Energy Based Techniques
These include electrocautery and ultrasound (US) devices. They generally coagulate bleeding vessels by the use of heat. These devices help produce stable and rapid hemostasis, and also clear surgical field. It is important known the guidelines of these technologies before their use.

Electrocautery (bipolar and monopolar) is commonly used. The first electrosurgical unit (ESU) was introduced by the biophysist Bovie in 1928 [12]. Electrocautery is based on the principle that high frequency waves (400 kHz to 10 MHz) concentration and conduction through a tissue causes increased temperature at that tissue. Frictional heat is produced by the passage of electromagnetic field through the cellular cytoplasm causing rapid oscillation of cytoplasmic cations and anions. The cutting mode is intended to vaporize tissue and is achieved by fully rectified low voltage waveform with a narrow tip held near but not in contact with the tissue. Bulky tip and partially rectified high voltage waves produce the coagulation mode. Monopolar units disperse the current through the patient into a dispersion patch while in bipolar only the tissue to be cut or coagulated is involved in the circuit. Bipolar devices have the advantage of lesser burn injuries and lateral heat production. With regard to coagulation, up to 2 mm and 7 mm is possible with use of monopolar and bipolar units, respectively.

Disadvantages expected from the use of electrocautery include smoke production which creates unpleasant odor and obstructs the surgical field. Tissue damage from charring and lateral heat production is another concern. Cooling period of 8 and 15 seconds is recommended between repeated monopolar incisions and coagulation, respectively. Interference with pacemakers by monopolar unit has been reported [13].

Ultrasonic devices, like harmonic scalpel, are other modality that uses heat to control bleeding. Rather than inducing intracellular heat in the targeted tissue, ultrasonic devices produce heat in the instrument tip via vibration. Early generations where able to seal vessels up to 3mm diameter only. Newer Harmonic ACE®+ shear7 can seal vessels with diameter up to 7mm with significantly less heat production and greater seal stability when compared to bipolar devices [14]. Other advantages are no smoke production and no interference with pacemaker function. He, et al. compared harmonic to electrocautery in axillary node dissection for breast cancer patients and concluded that harmonic group had reduced operative time, blood loss, post-operative drain and total hospital stay [15]. Reduced post-operative pain in the harmonic group is possibly related to less lateral heat production. Energy based techniques provide fast hemostasis when compared to topically applied materials but the resultant lateral heat and tissue injury possibly increase the patient discomfort postoperatively [16,17].

Topical Agents

Bone Wax

Introduced in 1886, bone wax is probably the oldest hemostatic material. It is commonly used by neurosurgeons and orthopedic surgeons. It is a mix between bees wax and Vaseline. After molding with gloved hands, bone wax is applied directly to bleeding bone and it acts as a mechanical plug. A major drawback is being non-resorbable. This precludes its use in areas of future dental implants or in contaminated fields. Haward, et al. found that bone wax has inhibitory effect on bone formation as it isolates the created bone defect [18]. For the same reason, it also reduces microbial elimination from the surgical site. Finn, et al. compared different hemostatic materials effect on bone formation in created osseous defects in dogs [19]. Materials used were bone wax, oxidized cellulose, gel foam, and microfibrillar collagen and concluded that all materials can be used in bone except for bone wax. Additional concerns include allergic reaction, bone wax granuloma and embolism [20].

Oxidized Cellulose (Surgical®)

Oxidized cellulose and oxidized regenerated cellulose were first introduced in 1942 and 1960, respectively. The reason for regeneration of oxidized cellulose is to eliminate impurities [20]. Cellulose basically acts by plugging bleeding surface and providing a scaffold trapping platelets and erythrocytes. It also swells about 10 times its weight which adds tamponade effects.

Due to its low pH, caustic effect is believed to be responsible for the initial artificial clot. The brownish coloration of cellulose after its application to bleeding site is due to hemolysis and release of hemoglobin from erythrocytes. Hemoglobin is converted to the brownish-colored acid hematin by the acidic medium. Possible antimicrobial effects were suggested and its use is probably justified in contaminated sites [21]. It best is applied to large oozing surface. Reports on resorption time vary and it is related mainly to the amount applied, but generally it takes about 4 to 8 months [22].

Merzaei, et al. compared ChitoHem to electrocautery and concluded that less postoperative pain was experienced in the ChitoHem group possibly due to less tissue damage [17]. Drawbacks of cellulose are mainly due to its swelling and low pH which can cause nerve injury. Alkan, et al. showed that cellulose induced immediate nerve injury when applied to rat sciatic nerve [23]. Low pH inactivates thrombin and this prevents the combination of both materials. Cellulose use should not be used in excessive amount and or tightly packed.

Gelatin

Gelatin is made from sheep or equine dermis and tendons. It binds to surfaces and stops bleeding by providing a scaffold for plug formation. Gelatin swells about 200% and 40 times its original volume and weight, respectively. This adds tamponade effect in its mechanism of action and adverse reaction. It gets resorbed in 4-6 weeks and this makes it a better choice than bone wax [20]. Another advantage is its neutral pH which allows combination with thrombin for enhanced effects. Helito, et al. compared Floseal® to electrocautery and found that it is equally effective with the advantage of not interfering with cardiac pacemaker and lesser chances of wound healing complications. However, it is better to avoid gelatin in infected sites, closed cavities, adjacent to vital structures and in bone defects. Although it doesn't inhibit osteogenesis, gelatin delays bone formation. Other concerns include allergy to porcine products and granuloma formation [21].

Collagen

Similar to gelatin, collagen is also of animal source. Collagen has several advantages over the mentioned materials in that it has fast hemostasis, fast resorption, less swelling, and less reaction [20]. It promotes platelet aggregation, adheres to injured surfaces and activates the intrinsic pathway [21]. Bovine collagen was found to be the most suitable agent placed next to nerves in animal studies and the best material among bone wax, gelatin and cellulose in terms of bone healing [23]. Similar to other material from animals, allergic and foreign body reactions as well as infection are possible. Its use should be avoided in contaminated sites.

Platelet Poor Plasma

Because platelet poor plasma (PPP) byproduct from the preparation of platelet rich plasma (PRP) and is rich in coagulation factors. The addition of 0.5 ml solution of 1:1 calcium chloride and bovine thrombin produces the gel state of PPP. Cillo, et al. compared hemostatic effect of PPP with microfibrillar collagen applied to areas of posterior iliac crest harvesting sites [24]. They concluded that PPP gel is equally effective to microfibrillar collagen. Being cheap and of autologous source, PPP gel is an attractive hemostatic option. Its use should be planned for before the procedure, however.

Thrombin

Thrombin converts fibrinogen to fibrin, activates platelet and causes vasoconstriction. Thrombin is supplied in powder, solution or spray. It can be applied alone over the bleeding surface or combined with gelatin or collagen Bovine source causes immune reaction with the subsequent formation of antibodies to prothrombin, thrombin and factor V (cardiolipin) causing severe coagulopathy [25]. Direct injection into a blood vessel may result in extensive intravascular clotting [22].

Tranexamic Acid

The role of plasmin is to degrade already formed blood clot by proteolytic action. It gets activated by the attachment to the formed fibrin. Tranexamic acid binds to plasminogen and prevents is attachment to fibrin and subsequent activation. Its use in major surgeries like total knee or hip replacement, cardiac and trauma conditions is widely established [26]. It should be used with caution in patients with renal impairment (possible toxicity), pregnancy (as it crosses placenta) and in patients known to have seizures. Contraindications to its use include active thrombosis, color vision disturbance, subarachnoid hemorrhage and allergy. Systemic use of tranexamic acid is effective in cases of hyperfibrinolytic states associated with tissue injury, shock and hypoxia (as in severe trauma).

Pedersen evaluated the fibrinolytic environment of the oral cavity and concluded that initially there is reduction of fibrinolysis followed by increased fibrinolysis after bleeding stops. This was correlated with the present of salivary plasminogen and tissue plasminogen activator form oral epithelial cells [27].

Basso, et al. studied the effect of oral health on the level of fibrinolytic activity [28]. Increased fibrinolytic activity after oral surgeries was also linked to saliva. In addition, patients with poor oral health index had increased fibrinolytic activity in alveolar blood compared to peripheral blood. This increased activity is possibly triggered by inflammation and bacterial degradation of fibrinogen.

Mithiborwala, et al. evaluated the effectiveness of tranexamic acid in patients with anticoagulant and antiplatelet therapy and concluded that topical use of tranexamic acid as a pressure pack can be used to reduce bleeding without discontinuing antithrombotic medications [29].

Sealants

These are active hemostatic agents that usually contain either fibrin or collagen along with thrombin and clot stabilizer. They have the advantage of flow and adhesion. These are usually used over large bleeding surface as in head and neck surgeries [30]. Fibrin-based sealants like Tisseel® consist of fibrinogen (human), thrombin (bovine) and antifibrinolytic (aprotinin or tranexamic acid). These are the final activated coagulation factors. Thrombin acts on fibrinogen to produce fibrin and aprotinin increases clot stability. This would provide a source of fibrin for patients with insufficient fibrinogen level. Use of sealants requires dry filed and mixing of the components at the time of application usually by double syringe technique. It is important to avoid excessive use as this creates a thick layer interferes with healing. Other concerns include possible thrombus formation if introduced through intravascular route and hypersensitivity to bovine products or aprotinin. Crosseal® avoided the use of bovine products and contains human thrombin and fibrinogen with tranexamic acid.

Chitosan (HemCon®)

This material is known for its use by solders to rapidly stop bleeding in battlefields. Chitosan is derived from shrimp shell chitin and conversion to gel form occurs by deacetylation. It works by attracting and red blood cells and formation of artificial clot independent of both the intrinsic or extrinsic pathways. This is achieved by electrostatic attraction between the positively charged N-acetylglucosamine polymer forming chitin and the negatively charged red blood cells. If the coagulation pathways are intact, they get activated by this process. Among the advantages of this material is that it achieves fast hemostasis (less than one minute), activates the release of platelet growth factors and some bacteriostatic effects. Although from shrimp chitin, no adverse reaction was reported when used in patients with shell-fish allergy. Malmaquist, et al. evaluated HemCon in subjects whether anticoagulated or not and showed significantly better hemostatic effect (less than one minute) when compared to control sites (9.5 minutes) [31]. In addition, better healing and lower pain scores although insignificant, were reported. Due to the fact that it acts directly on RBCs, its efficiency in cases with low hematocrit is not known. Samama, et al. concluded that RBCs are essential proper platelet adhesion which is affected by hematocrit values less than 20% [32].

Advanced Hemostatic Techniques

Interventional Radiology

Sometimes the local measures mentioned fail in the face of severe or intractable hemorrhage. These are possible in certain cases like vascular malformation, aneurysm or pseudoaneurysm, injuries involving major vessels and oncologic lesions [33-35]. In such severe hemorrhage, the facility of interventional radiology (IVR) is lifesaving.

The aim of Trans Arterial Embolization (TAE) is to stop bleeding by only targeting the causative vessel. Contrast enhanced CT allows the identification of the bleeding vessel, possible collaterals and abnormalities like malformation, aneurysm/pseudoaneurysm or arteriovenous fistula. Access to the bleeding vessel is achieved by catheterization through the femoral artery and by the delivery of embolic material like Embospheres®, or occlusive device like coils, the vessel is occluded and bleeding is controlled.

The advantages of TAE are the high selectivity, minimal invasiveness and ability to reach inaccessible locations. Persistent bleeding from collateral circulation can be accounted for in the same or in subsequent session. Noy, et al. found that 78.5% of the cases respond to only one TAE session [36]. Although highly selective and successful, TAE may not be possible in cases of vasospasm or torturous vessels. In addition, IVR demands stabilized patient condition which needs pressure pack, secured airway, the presence of a senior surgeon beside the interventional radiologist.

External Carotid Artery Ligation

This procedure involves ligation of the external carotid artery (ECA) after coming out from the common carotid artery (CCA). It is an effective method to control severe hemorrhage especially when the facility of IVR is not available or ineffective. The option of external carotid artery (ECA) is selected as one of the last resorts to control bleeding.

The common carotid sheath is accessed from incision at the anterior border of the sternocleidomastoid muscle. The advantage of ECA ligation lies in the speed of the procedure especially to be performed by the same surgeon on the operating table. The ECA is identified and ligated. One or more branches of the ECA may also be ligated to manage blood coming from collateral circulation. Nasr described a case of severe hemorrhage caused by self-inflected gunshot which was managed by bilateral ECA ligation. ECA can be also be done prophylactically before surgical procedures involving extensively vascularized area as in oncological procedures [37-39].

Choice between IVR versus ECA ligation is based on the presence of skillful radiologist and trained surgeon. If both facilities are available, it may be prudent to start with the TAE as the initial step. Performing ligation of the ECA precludes subsequent TAE to any of its branches. Bouloux described a case where TRE failed to manage bleeding from vascular malformation and ECA ligation was needed [40].

Conclusion

Hemostasis is an important aspect of any surgical procedure. Good hemostasis allows better surgical quality, reduces possibility of complications and patient discomfort. Surgeons should have basic knowledge of various hemostatic modalities. The preparation of cautery or US devices should be planned before the operation. Some modalities involve anesthetists or interventional radiologists, so proper communication is mandatory.

References

1. G Chacon, C Uglade (2006) Perioperative management of the patient with hematologic disorders. Oral Maxillofacial Surg Clin N Am 18: 161-171.
2. Moghadam H, Caminiti M (2002) Life-threatening hemorrhage after extraction of third molars: case report and management protocol. J Can Dent Assoc 68: 670-674.
3. Ryu T, Kim D, Byun S (2018) Fiberoptic bronchoscopic treatment of blood aspiration and use of Sugammadex in a patient with epistaxis. Medicine 97: 15.
4. Mullane J, Huber L, Popovic N (1974) Aspiration of blood and

pulmonary host defense mechanisms. Ann Surg 180: 236-242.
5. Giannakoploulos H, Carrasco L, Alabakoff J, Quinn P (2006) Fluid and electrolyte management and blood product usage. Oral Maxillofacial Surg Clin N Am 18: 7-17.
6. Zuluaga Giraldo M (2013) Management of perioperative bleeding in children. Step by step review. Rev Colomb Anestesiol 41: 50-56.
7. Akinbami B, Obembe B (2014) Assessment of intraoperative blood loss during oral and maxillofacial surgical procedures in a Nigerian tertiary health care center. Journal of Blood Transfusion 2014: 8.
8. Hathorn I, Habib R, Manji J, Javer A (2013) Comparing the reverse Trendelenburg and Horizonal position for Endoscopic sinus surgery: A randomized controlled trial. Otolaryngology head and neck Surgery 148: 308-313.
9. Gan E, Habib R, Rajwani A, Javer A (2014) Five-degree, 10-degree, and 20-degree reverse trendelenburg position during functional endoscopic sinus surgery: a double-blind randomized controlled trial. International Forum of Allergy and Rhinology 4: 61-68.
10. Shaban B, Attar A, Eshghpour M (2016) Concepts, applications and efficacy of hypotensive anesthesia in maxillofacial and orthognathic surgeries: review of literature. Journal of Dental and Medical Sciences 15: 92-96.
11. Barak M, Yoav L, Abu el-Naaj I (2015) Hypotensive anesthesia versus normotensive anesthesia during major maxillofacial surgery: a review of the literature. The scientific world journal 2015: 7.
12. Munro M (2012) Fundamentals of electrosurgery Part I: principles of radiofrequency energy for surgery. The SAGES Manual on the fundamental use of surgical energy (FUSE) p 15-59.
13. Mangar D, Atlas G, Kane P (1991) Electrocautery induced pacemaker malfunction during surgery. Can J Anaesth 38: 616-618.
14. Ethicon US, LLC. Intelligent Ultrasonic Energy Delivered by HARMONIC® devices with Adaptive Tissue Technology: 018618-140721. Springer Healthcare LLC.
15. He Q, Zhaung D, Zheng L, Fan Z, Zhou P, et al. (2012) Harmonic focus versus electrocautery in axillary lymph node dissection for breast cancer: a randomized clinical study. Clinical Breast Cancer 12: 454-458.
16. Mirzaei R, Mahjoobi B, Kordestani SS, Habib F, Mohammadi S (2016) ChitoHem hemostatic powder compared with electrocautery anorectal surgery: a randomized controlled trial. J Integr Cardilo 3: 1-3.
17. Helito CP, Gobbi RG, Castrillon LM, Hinkel BB, Pecora JR, et al. (2013) Comparison of Floseal® and electrocautery in hemostasis after total knee arthroplasty. Acta Ortop Bras 21: 320-322.
18. Howard TC, Kelley RR (1969) The effect of bone wax on the healing of experimental rat tibial lesions. Clin Orthop 63: 226-232.
19. Finn MD, Schow SR, Schneiderman ED (1992) Osseous regeneration in the presence of four common hemostatic agents. J Oral Maxillofac Surg 50: 608-612.
20. Brightmore TGJ (1975) Haemostasis and healing following median sternotomy. Br J Surg 62: 152.
21. Bruno M Pereira, JoSé B Bortoto, GuStavo P FraGa (2018) Topical hemostatic agents in surgery: review and prospects. Rev Col Bras Cir 45: e1900.
22. Kumar S (2016) Local hemostatic agents in the management of bleeding in oral surgery. Asian Journal of pharmaceutical and clinical research 9.
23. Alkan A, Inal S, Yildirinm M, Bas B, Agar E (2007) The effects of hemostatic agents on peripheral nerve function: an experimental study. J Oral Maxillofac Surg 65: 630-634.
24. Cillo J, Marx R, Stevens M (2007) Evaluation of autologous platelet-poor plasma gel as a hemostatic adjunct after posterior iliac crest bone harvest. J Oral Maxillofac Surg 65: 1734-1738.
25. Semple E, Speck E, Aslam R, Kim M, Kumar V, et al. (2008) Evaluation of platelet gel characteristics using thrombin produced by thrombin processing device: a comparative study. J Oral Maxillofac Surg 66: 632-638.
26. Crash-2 Trial Collaborators, Shakur H, Roberts I, Bautista R, Caballero J, et al. (2010) Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): A randomized, placebo-controlled trial. The Lancet 376: 23-32.
27. Pedersen S (1991) Hemostasis in oral surgery-the possible pathogenetic implications of oral fibrinolysis on bleeding. Experimental and clinical studies of the hemostatic balance in the oral cavity, with particular reference to patients with acquired and congenital defects of the coagulation system. Danish medical bulletin 38: 427-443.
28. Basso FG, Annichino-Bizzacchi JM, de Souza Medina S, Boer CC, Pizzigatti Correa ME (2017) Oral Health plays a role on Oral Fibrinolytic Activity. Ann Pediatr Child Health 5: 1123.
29. Mithiborwala A, Shah N, Mahajan A, Bagga IK, Doshi D, et al. (2016) Control of post extraction hemorrhage by tranexamic acid pressure pack in patients on anticoagulant and antiplatelet therapy: a prospective clinical study. Journal of Craniofacial Research 01901: 6-10.
30. Buckley MJ, Beckman EJ (2010) Adhesive use in oral and maxillofacial surgery. Oral Maxillofacial Surg Clin N Am 22: 195-199.
31. Malmaquest JP, Clemens SC, Oien HJ, Wilson SL (2008) Hemostasis of oral surgery wounds with HemCon dental dressing. J Oral Maxillofac Surg 66: 1177-1183.
32. Samama CM (1995) Traumatic emergencies and hemostasis. Cah anesthesiol 43: 479.
33. Ghanem AA, Hadidi YN (2017) Management of a life-threatening bleeding following extraction of deciduous second molar related to capillary haemagnioma. Craniomaxillofac Trauma Reconstruction 10: 166-170.
34. Stiefel MF, Park MS, McDougall CG, Albuquerque FC (2010) Endovascular treatment of hemorrhagic alveolar artery pseudoaneurysm after tooth extraction: a case report. J Oral Maxillofac Surg 68: 2325-2328.
35. Oh JS, Kim SG, Kim HK, Moon SY (2009) Massive hemorrhage following bilateral sagittal split ramus osteotomy: a case report. J Oral Maxillofac Surg 67: 895-898.
36. Noy D, Rachmiel A, Emodi O, Amsalem Y, Israel Y, et al. (2017) Transarterial embolization in maxillofacial intractable potentially life-threatening hemorrhage. J Oral Maxillofac Surgery 75: 1223-1231.
37. Nasr MM (2015) Bilateral external carotid artery ligation: a life-saving procedure in severe maxillofacial trauma. International journal of surgery case reports 8: 81-83.
38. Kumar RV, Chakravarthy C, Sekhar GR, Devireddy SK, Kumaravelu C, et al. (2010) Metastatic thyroid carcinoma presenting as hypervascular lesion of the mandible: a case report

and review of literature. J Oral Maxillofac Surg 68: 2613-2616.
39. Sultana J, Bashar A, Moro S (2017) External carotid artery ligation an elective procedure of controlling inadvertent bleeding from oral malignancies: experience of Dhaka dental college and hospital. Cancer Sci 3.
40. Bouloux GF, Perciaccante V (2009) Massive hemorrhage during oral and maxillofacial surgery: ligation of the external carotid artery or embolization? J Oral Maxillofac Surg 67: 1547-1551.