# Dişhekimliğinde Cerrahi ve Cerrahi Olmayan İşlemlerde Kanama Kontrolü: Güncelleme

Management of Hemorrhage in Surgical and Non-Surgical Dental Procedures: An Update

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## Özet

bulunan hastalardaki Kanama diyatezi müdahalesi kanama diyatezinin ciddiyetine ve işlemin girişimsel derecesine bağlı olarak değişir. Bu hastalar değişen oranda risk taşırlar. Yapılacak işlemin kanama açısından risk oranı işlem yapılacak bölgenin ulaşılabilirliği ile doğru orantılıdır. Ulaşılabilirliği düşük bölgelerde sistemik olarak uygulanacak kanama kontrol yöntemleri daha önemlidir. Cerrahi sırasında yara iyileşmesini uzatacağı için lokal kanama kontrol yöntemleri agresif olarak uygulanmamalıdır. Dişhekimi orta ve ciddi hemorajik diyatezi bulunan hastalarda, hastanın doktoruyla konsültasyon yapmalıdır. Bu gibi hastalarda dental işleme başlamadan önce kanama kontrolü konusunda yeterli bilgi ve materyale sahip olmalıdır. Cerrahi sahadaki kanamanın durması, tıkanmanın sağlanması bozulmasının engellenmesi için birçok işlem yapılabilir. Bu derlemede, topikal trombin, topikal fibrin yapıştırıcı, absorbe olabilen jelatin sünger, okside edilmiş selüloz, mikropöroz polisakkarit, fibrin yapıstırıcı, siyanoakrilat, traneksamik asit, aminokaproik asit, koterizasyon, basınç yöntemi, splint ve Ankaferd Blood Stopper değerlendirilmiştir.

**Anahtar Kelimeler:** Kanama müdahalesi, dişhekimliği, postoperatif kanama, koagülapatilerin müdahalesi

### **Abstract**

The management of patients with bleeding disorders depends on the severity of the condition and the invasiveness of the planned dental procedure. These patients have variable risks. The risk of the intervention will depend on the accessibility of the surgical site for local control of hemostasis. Systemic prevention is more important for limited access to the bleeding sites. Local hemostatic techniques must not be used too aggressively during surgery as the resulting tissue damage can prolong healing time. Clinician has to make consultation on mild and severe hemorrhagic disordered patient with patient's physician. Before managing dental surgery for these patients clinician has to have sufficient knowledge and material for controlling the hemorrhage. Various adjuncts to hemostasis can be employed at the surgical site to enhance hemostasis, aid in vascular closure and prevent clot breakdown. Topical thrombin, topical fibrin glue, absorbable gelatin sponge, oxidized cellulose, microporous polysaccharide hemispheres, fibrin sealant, n-butylcyanoacrylate, tranexamic acid, aminocaproic acid, cauterization, suturing, pressure, splint, Ankaferd Blood Stopper is the adjuncts that are evaluated in this review.

**Key Words:** Bleeding management, dentistry, postoperative bleeding, coagulopathies management

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Appropriate prophylaxis for platelet disorders will depend on both the specific defect and the nature of the planned dental surgery. Mild thrombocytopenia or mild functional disorders may require no specific systemic therapy other than the use of local hemostatic measures and antifibrinolytic agents. More severe disorders will require measures that transiently raise the platelet count or improve function. Choice of the appropriate prophylaxis should be made in consultation with the patient's haematologist<sup>1-5</sup>.

The risk of the intervention will depend on the accessibility of the surgical site for local control of hemostasis. For example, simple exodontia usually allows ready access to the potential sites of postoperative hemorrhage for application of local hemostatic measures, such as pressure or topical agents. In contrast, deep spatial or cavity (e.g., sinus) surgery and some flap surgeries may afford little or no access to the bleeding sites postoperatively. The more limited the access to these sites, the more important systemic, rather than local, measures to control postoperative hemorrhage become. Specifically, hemorrhage and hematoma formation that may cause airway obstruction must be controlled by systemic measures4.

Hemostatic techniques must not be used too aggressively during surgery as the resulting tissue damage can prolong healing time<sup>6</sup>. Devitalized tissue and foreign bodies in a healing wound forms a good environment for bacteria and shield them from the body's defenses. The dead cells and cellular debris of necrotic tissue have been shown to reduce host immune defenses and encourage active infection. A necrotic burden allowed to persist in the wound can prolong the inflammatory response, mechanically obstruct the process of wound healing, and delay reepithelialization<sup>6</sup>. Also absorbable hemostatic materials which are using for bleeding control also carry a risk of infection and may delay healing; they should therefore be avoided in immunosupressed patients<sup>1,7,8</sup>.

Various adjuncts to hemostasis can be employed at the surgical site to enhance hemostasis, aid in vascular closure and prevent clot breakdown.

Topical thrombin is an effective agent when applied directly on the bleeding wound as it converts fibrinogen to fibrin and allows rapid hemostasis in a wound<sup>1</sup>. Marjanovic reported well treated 20 patients, who were getting anticoagulant therapy, with thrombin powder<sup>9</sup>. Kovacs et al. uses thrombin with combination of fibrin and patient's venous blood for hemostasis of patients on coumarin derivative therapy and reported excellent hemostasis without occurrence of secondary hemorrhage<sup>10</sup>.

Topical fibrin glue has also been effectively used in conjunction with other hemostatic measures. It can reduce the amount of factor replacement needed when used along with antifibrinolytic agents11,12. Filho et al., reported a mandibular third molar extraction which had Von Willebrand's disease and treated with topical application of fibrin sealant and systemic administration of antifibrinolytic drugs. They reported a good hemostasis without replacement of plasma clotting fac $tor^{13}$ .

Absorbable gelatin sponge is a sterile, absorbable, water-insoluble gelatin base sponge, used to control capillary bleeding in surgical operations; it is left in situ and is absorbed in from 4 to 6 weeks. This material holds many times its weight in blood and provides a stable "scaffold" for clot formation. It is placed in tooth sockets in the form of tapered cones rolled from the sheet material. Gelatin sponge is absorbed within 4-6 weeks with little or no scar tissue formation. It should not be used under epithelial incisions or flaps because it inhibits healing of the wound's epithelial edges<sup>14</sup>. In a study, patients maintaining oral anticoagulant therapy divided into 5 groups related to their INR values and local hemostasis tried to carry out with gelatin sponge and multiple silk sutures. Gelatin sponge and sutures showed sufficient for preventing postoperative bleeding<sup>15,16</sup>.

Oxidized cellulose is a specially treated form of surgical sponge which promotes clotting and is used as a temporary dressing. Oxidized regenerated cellulose (ORC) is manufactured from regenerated cellulose derived from wood pulp containing about 50% of cellulose. To obtain purified cellulose, it is necessary to decompose it in a chemical way and subsequently put it together to make "regenerated" cellulose<sup>17,18</sup>. Petersen et al., compare the healing effect of oxidized cellulose and gelatin sponge on third molar extraction and point out that gelatin sponge has slightly more delay effect on healing<sup>18</sup>.

Microporous polysaccharide hemispheres,

dehydrate blood and accelerate clotting. It can be applied to all types of surgical sites, including tooth sockets. It has been used successfully when cones have been rolled in the dry powder and placed in sockets. There are no known contraindications for its use<sup>4</sup>. Biondo-Simoes et al., showed that microporous polysaccharide hemispheres, despite achieving hemostasis, proved to be no more favorable than n-butyl-cyanoacrylate and the fibrin adhesive<sup>19</sup>.

**Fibrin sealant,** acts both through its adhesive action and by direct contribution of fibrin to clot formation. It requires special preparation just before application. It is expensive and is probably best reserved for particularly complicated or difficult dental situations<sup>20</sup>. Fibrin sealants are either homologous or autologous products. Most used one is called Tisseel® which is composed of human fibrinogen and bovine thrombin<sup>21</sup>. Fibrin sealant has an advantage of capability for using as a slow-release drug delivery system and as a substrate for cellular growth and tissue engineering<sup>22</sup>.

**n-butyl-cyanoacrylate** is an effective tissue adhesive which is hemostatic and bacteriostatic. It can be considered an alternative to conventional sutures in soft-tissue surgery. Al-Belasy and Amer evaluated the local hemostatic effect of n-butyl-2-cyanoacrylate glue in warfarin treated patients who undergo outpatient oral surgery without a change in their level of anticoagulation. They remarked the agent as an effective and easily applicable local hemostatic<sup>23</sup>. Cyanoacrylate glue also has an advantage of promoting tissue healing<sup>24</sup>.

**Antifibrinolytic agents** inhibit fibrinolysis by blocking the binding of plasminogen to fibrin and its subsequent activation to plasmin. The oral mucosa is rich in plasminogen activators, and saliva has significant fibrinolytic activity. These agents are useful in preventing clot lysis following oral surgery or dental ex-

traction. They are used as adjuncts to specific systemic therapy that corrects the coagulation factor or platelet abnormality. In hemophilia, for example, they have been shown to reduce both the risk of delayed bleeding and the amount of clotting factor replacement therapy requirement <sup>25,26</sup>.

Tranexamic acid is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin, a molecule responsible for the degradation of fibrin. It can be administered parenterally. In addition, the intravenous preparation can be diluted to a 4.8% aqueous solution and used as a mouthwash (4 times daily for 7 days) which has been used successfully in the form of a mouthwash after oral surgical procedures to inhibit postoperative bleeding episodes. In controlled trials, it markedly decreased postoperative bleeding episodes in patients on anticoagulant therapy<sup>27</sup>. Dunn and Goa emphasize the efficiency of tranexamic acid over wide range of hemorrhagic conditions such as reducing menstrual blood loss, possible alternative to surgery in menorrhagia, and successfully controlling bleeding in pregnancy<sup>28</sup>. Study comparing the effect of antifibrinolytic agents on wound healing with rat dorsal skin model shows that, unlike epsilon-aminocaproic acid, tranexamic acid has a positive effect on wound healing<sup>29</sup>. Wellington and Wagstaff point out that tranexamic acid may be considered as a first-line treatment comparing to aminocaproic acid30

**Aminocaproic acid**, a popular antifibrinolytic agent, and can be used to treat excessive postoperative bleeding. It can be used orally or intravenously. Aminocaproic acid works as an anti-fibrinolytic or antiproteolytic, like tranexamic acid. As a lysine analogue, it binds reversibly to the kringle domain of the enzymogen plasminogen. Thus plasminogen can not be activated (by its activators) to plasmin, which then can not split fibrin (anti-fibrinolytic effect)<sup>31</sup>. There are case reports of successfully controlled bleedings in patients that have bleeding disorders<sup>32,33</sup>.

**Cauterization** is a medical practice or technique of which describing the burning of part of a body to remove or close off a part of it. With this method some

tissues get damage but it is a useful tool to slow intraoperative bleeding. However, it must be used cautiously to avoid excessive tissue necrosis. Not only will the necrosis delay healing but it may also become a source of postoperative bleeding when the necrotic tissue sloughs<sup>34</sup>. Electrocautery and chemical cautery are the most used types of cauterization.

**Suturing** is worthwhile if significant apposition of soft tissue can be achieved or to protect the hemostatic pack. However, suturing may provide additional traumatic puncture points that contribute to post-operative bleeding episodes and may cause confusion over the nature and source of the hemorrhage<sup>6,34,35</sup>.

**Pressure** is the most effective method for achieving hemostasis. Pressure must be applied at the appropriate location, and moist gauze should be used to prevent the clot adhesion to it. Patients should be told that the pressure must be maintained for at least 30 minutes, and preferably for an hour, as frequent interruption of pressure will cause bleeding to continue<sup>34-36</sup>.

**Splint**: The use of preformed splints to protect and enhance the placement of pressure on sockets is a valuable adjunct in multiple extraction procedures. It is a technique that should be considered for complicated situations where systemic management is required, but is difficult or expensive to deliver. The most popular material is soft, mouth guard type material. Splints enhance the formation of firm, well organized clots and prevent them from being dislodged or traumatized. Splints also shield the clots or medication packs from saliva and the fibrinolytic substances it contains. They are quick and simple to fabricate. They must be removed and cleaned once a day. It is recommended that they be worn for 4–7 days<sup>35,37,38</sup>.

Ankaferd Blood Stopper (ABS) is a standardized mixture of five plants that has been used historically as a hemostatic agent but its mechanism of action remains unknown. The basic mechanism of action for ABS appears to be the formation of an encapsulated protein network that provides focal points for erythrocyte aggregation. ABS, induced formation of the protein network affected the entire physiological hemostatic process without unequally affecting any individual clotting factor. Therefore, ABS thought to be effective both in individuals with normal hemostatic parameters and in patients with deficient primary hemostasis and/ or secondary hemostasis<sup>39</sup>. Laboratory study to evaluate in vivo hemostatic effect of ABS in rats pretreated with warfarin shows ABS can provide a therapeutic potential for the management of patients with deficient primary hemostasis in clinical medicine<sup>40</sup>. Efficiency of ABS for superficial and deep skin lacerations and minor/moderate trauma injuries in a porcine bleeding model was also demonstrated<sup>41</sup>. There are clinical case reports showing successful bleeding management of ABS topically over uncontrolled bleedings with known methods<sup>42-44</sup>. Akkoç et al., studied the antibacterial effect of ABS and indicated that anti-infective properties of ABS adds a new value to its hemostatic effect in the healing of infected hemorrhagic wounds, as well as opening new avenues for its potential use for antiinfective actions and food preservation<sup>45</sup>.

**Conclusion:** There are various materials that can be used for local bleeding control procedures. All of materials which are using for bleeding control have some disadvantages like; high prices, delayed wound healing and foreign body reaction. It is the clinicians' success to choose the most appropriate method for the patient's local management of the bleeding. Therefore, before managing dental surgery for these patients, clinician has to have sufficient knowledge and material for controlling the hemorrhage.

#### Kaynaklar

- Gupta A., Epstein JB., Cabay RJ. Bleeding disorders of importance in dental care and related patient management. JCDA. 73(1):77-83, 2007.
- Little JW, Falace DA, Miller CS, Rhodus NL. Dental management of the medically compromised patient. 5th ed. St. Louis: CV Mosby Co. 1997 p. 681-742.
- Gomez-Moreno G., Cutando-Soriano A, Arana C, Scully C. Hereditary blood coagulation disorders: management and dental treatment. J Dent Res. 84(11):978-985, 2005.
- Israels S., Schwetz N., Boyar R., McNicol A. Bleeding disorders: Characterization, dental consideration and management. J Can Dent Assoc. 72(9): 827. 2006.
- Kumar JN, Kumar RA, Varadarajan R, Sharma N. Specialty dentistry for the hemophiliac: is there a protocol in place? Indian J Dent Res. 18(2):48-54, 2007.
- Shetty V., Bertolami CN. Wound Healing In. Miloro M. ed. Peterson's Princinles of oral and Maxillofacial Surgery. 2nd ed. Hamilton London 2004. p. 10.
- Mitchell R. An evaluation of bone healing in cavities in the jaws implanted with a collagen matrix. Br J Oral Maxillofac Surg. 30(3);180-2, 1992.
- Mattsson T., Anderssen K., Koendell PA., Lindskog S. A longitudinal comparative histometric study of the biocompability of threee local hemostatic agents. Int J Oral Maxillofac Surg. 19(1);47-50, 1990.
- Marjanovic M. Use of thrombin powder after tooth extraction in patients receiving anticoagulant therapy. Vojnosanit Pregl. 59(4):389-392, 2002.
- Kovacs B, Tóth K, Kerenyi GPost-extraction hemostasis during coumarin anticoagulant therapy with a locally applied coagulation-active substance. Int J Oral Surg. 5(1):3-7, 1976.
- Rackoz M, Mazar A, Varon D, Spierer S, Blinder D, Martinowitz U. Dental extractions in patients with bleeding disorders. The use of fibrin glue. Oral Surg Oral Med Oral Pathol. 75(3):280– 282, 1993.
- 12. Martinowitz U, Schulman S, Horoszowski H, Heim M. Role of fibrin sealants in surgical procedures on patients with hemostatic disorders. Clin Orthop Relat Res. 328(2):65–75, 1996.

- 13. Filho Ade M, dos Santos RS, Costa JR, Puppin AA, de Rezende RA, Beltrão GC. Oral surgery with fibrin sealants in patients with bleeding disorders: a case report. J Contemp Dent Pract. 7(3):106-112, 2006.
- 14. Abada HT, Golzarian J. Gelatine sponge particles: handling characteristics for endovascular use. Tech Vasc Interv Radiol. 10(4):257-260, 2007.
- 15. Blinder D, Manor Y, Martinowitz U, Taicher S. Dental extractions in patients maintained on oral anticoagulant therapy: comparison of INR value with occurrence of postoperative bleeding. Int J Oral Maxillofac Surg. 30(6):518–521, 2001.
- Blinder D, Manor Y, Martinowitz U, Taicher S, Hashomer T. Dental extractions in patients maintained on continued oral anticoagulant: comparison of local hemostatic modalities. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 88(2):137-140, 1999.
- Kollár P, Such P, Muselík J, Bajerová M, Havelka P, Sopuch T. Hemostatic effects of oxidized cellulose Ceska Slov Farm. 57(1):11-16, 2008.
- Petersen JK, Krogsgaard J, Nielsen KM, Nørgaard EB. A comparison between 2 absorbable hemostatic agents: gelatin sponge (Spongostan) and oxidized regenerated cellulose (Surgicel). Int J Oral Surg. 13(5):406-410, 1984.
- Biondo-Simões Mde L, Petrauskas R, Dobrowolski AG, Godoy G, Kaiber F, Ioshii SO. Validity of microporous polysaccharide hemispheres as a hemostatic agent in hepatic injuries: an experimental study in rats. Acta Cir Bras. 22(1):29-33, 2007.
- 20. Zusman SP, Lustig JP, Baston I. Postextraction hemostasis in patients on anticoagulant therapy: the use of a fibrin sealant. Quintessence Int. 23(10):713–716, 1992.
- 21. Davis BR, Sándor GK. Use of fibrin glue in maxillofacial surgery. J Otolaryngol. 27(2):107-112, 1998.
- 22. Spotnitz WD, Prabhu R. Fibrin sealant tissue adhesive-review and update. J Long Term Eff Med Implants. 15(3):245-270, 2005.
- 23. Al-Belasy FA, Amer MZ. Hemostatic effect of n-butyl-2-cyanoacrylate (histoacryl) glue in warfarin-treated patients undergoing oral surgery. J Oral Maxillofac Surg. 61(12):1405-1409, 2003.
- 24. Kulkarni SS, Chava VK. Comparison of cyanoacrylate and silk sutures on healing of oral

- wounds-an animal model study. Indian J Dent Res. 14(4):254-258, 2003.
- 25. Mannucci PM. Hemostatic drugs. N Engl J Med. 339(4):245-253, 1998.
- 26. Sindet-Pedersen S, Stenbjerg S. Effect of local antifibrinolytic treatment with tranexamic acid in hemophiliacs undergoing oral surgery. J Oral Maxillofac Surg. 44(9):703-707,1986.
- 27. Sindet-Pedersen S, Ramstrom G, Bernvil S, Blomback M. Hemostatic effect of tranexamic mouthwash in anticoagulant-treated patients undergoing oral surgery. N Engl J Med. 320(12):840-843,1989.
- 28. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. Drugs. 57(6):1005-1032,1999.
- 29. Björlin G, Nilsson IM. The effect of antifibrinolytic agents on wound healing. Int J Oral Maxillofac Surg, 17(4):275-276,1988.
- 30. Wellington K, Wagstaff AJ. Tranexamic acid: a review of its use in the management of menorrhagia. Drugs. 63(13):1417-1433,2003.
- 31. Lucas ON, Albert TW. Epsilon aminocaproic acid in hemophiliacs undergoing dental extractions: a concise review. Oral Surg Oral Med Oral Pathol. 51(2):115-120,1981.
- 32. Gardner FH, Helmer RE 3rd. Aminocaproic acid. Use in control of hemorrhage in patients with amegakaryocytic thrombocytopenia. 243(1):35-37,1980.
- 33. Ziccardi VB, Saini J, Demas PN, Braun TW. Management of the oral and maxillofacial surgery patient with end-stage renal disease. J Oral Maxillofac Surg. 50(11):1207-1212,1992.
- 34. Lockhart PB, Gibson J, Pond SH, Leitch J. Dental management considerations for the patient with an acquired coagulopathy. Part 2: Coagulopathies from drugs. Br Dent J. 195(9):495-401,2003.
- 35. Lockhart PB, Gibson J, Pond SH, Leitch J. Dental management considerations for the patient with an acquired coagulopathy. Part 1: Coagulopathies from systemic disease. Br Dent J. 195(8):439-445,2003.
- 36. Ness Gm, Peterson JL. Impacted Teeth In: Miloro M. ed. Peterson's Principles of oral and

- Maxillofacial Surgery 2nd ed Hamilton London. 2004: p.150.
- 37. Kaddour Brahim A, Stieltjes N, Roussel-Robert V, Yung F, Ginisty D. Dental extractions in children with congenital coagulation disorders: therapeutic protocol and results. Rev Stomatol Chir Maxillofac. 107(5):331-337,2006.
- 38. Adornato MC, Penna KJ. Hemostatic technique. Using a splint in oral bleeding. N Y State Dent J. 67(6):24-25,2001.
- 39. Goker H, Haznedaroglu IC, Ercetin S, Kirazli S, Akman U, Ozturk Y, et al. Hemostatic actions of the folkloric medicinal plant extract Ankaferd Blood Stopper. J Int Med Res. 36(1):163-1*7*0,2008.
- 40. Cipil H, Kosar A, Kaya A, Uz B, Haznedaroglu IC, Goker H, et al. In Vivo Hemostatic Effect of the Medicinal Plant Extract Ankaferd Blood Stopper in Rats Pretreated With Warfarin. Clin Appl Thromb Hemost. 15(3):270-276,2009.
- 41. Bilgili H, Kosar A, Kurt M, Onal IK, Goker H, Captug O, et al. Hemostatic efficacy of Ankaferd Blood Stopper in a swine bleeding model. Med Princ Pract. 18(3):165-169,2009.
- 42. Ibis M, Kurt M, Onal IK, Haznedaroglu IC. Successful management of bleeding due to solitary rectal ulcer via topical application of Ankaferd blood stopper. J Altern Complement Med. 14(9):1073-1074,2008.
- 43. Kurt M, Kacar S, Onal IK, Akdogan M, Haznedaroglu IC. Ankaferd Blood Stopper as an effective adjunctive hemostatic agent for the management of life-threatening arterial bleeding of the digestive tract. Endoscopy 40(2):E262,2008.
- 44. Kurt M, Disibeyaz S, Akdogan M, Sasmaz N, Aksu S, Haznedaroglu IC. Endoscopic application of ankaferd blood stopper as a novel experimental treatment modality for upper gastrointestinal bleeding: a case report. Am J Gastroenterol. 103(8):2156-2158,2008.
- 45. Akkoc N., Akcelik M., Haznedaroglu IC., Göker H., Turgut M., Aksu S., Kirazlı S., Fırat HC. In vitro anti-bacterial activities of Ankaferd medicinal plant extract. Turk Klinik J Med Sci. 29(2):410-415,2009.

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