

BÖLÜM 26

KANAMA DURDURUCULAR

Rezan KARAALİ¹

GİRİŞ

Hemostazın sağlanamaması, başta travma ve cerrahi işlemler olmak üzere birçok klinik durumda mortalite ve morbiditeyi artıran ciddi bir sağlık sorunu oluşturmaktadır. Acil servisler, yoğun kanama ile başvuran hastalarda hızlı ve etkili hemostatik müdahalelerin yapılması gereken en kritik alanlardan biridir. Günümüzde kanama kontrolü amacıyla kullanılan ajanlar, farmakolojik, mekanik ve biyolojik temelli çeşitli yöntemleri kapsamaktadır. Antifibrinolitik ajanlar, protrombin kompleks konsantreleri (PCC), taze donmuş plazma (TDP), topikal bitkisel ürünler, hemostatik tozlar ve fibrin yapıştırıcılar gibi çeşitli preparatlar, endikasyonlara ve hasta özelliklerine göre klinik pratikte yer bulmuştur. Bu bölümde, acil tıp pratiğinde sıkça karşılaşılan kanama tablolarında kullanılan güncel kanama durdurucu ajanların farmakodinamik özellikleri, endikasyonları, klinik etkinlikleri ve güvenlik profilleri güncel literatür eşliğinde detaylı olarak ele alınacaktır.

TRANEKSAMİK ASİT

Traneksamik asit (TXA), 1965 yılında Japonya'da Shosuke ve Utako Okamoto tarafından geliştirilmiştir (1). Pıhtı parçalanmasından sorumlu bir enzim olan plazmin oluşumunun öncüsüdür. Plazminojene geri dönüşümlü olarak bağlanır. Plazminin fibrinolitik etkilerini azaltır. Antifibrinolitik etkiye sahip olmasına rağmen prokoagülan değildir (2, 3). 1000 mg/10mL ampul formu ve 650 mg tablet formu mevcuttur. İntravenöz yoldan (iv) ve ağızdan kullanılabilir. Ağızdan alındığında en yüksek kan düzeyine 3 saatte ulaşır. %5'i metabolize edilir. %95'i metabolize edilmeden böbreklerden atılır. Tabletın yarı ömrü 11 saat ve ampul formun yarı ömrü 2 saattir (1). *Amerika Birleşik Devletleri Gıda ve İlaç Dairesi (FDA) tarafından iki endikasyon için önerilmiştir; birincisi diş çekimi yapılacak hemofili hastaları, ikincisi idiyopatik menoraji hastalarıdır. Yapılan çalışmalar sonucunda bu iki endikasyon dışında kullanılmasının önerildiği durumlar da tanımlanmıştır (1, 2).*

¹ Doç. Dr., İzmir Demokrasi Üniversitesi, rezan.karaali@idu.edu.tr, ORCID iD : 0000-0003-1831-2566

ve kontrendikasyonları iyi bilinmeli; hasta özellikleri ve klinik tablo göz önünde bulundurularak bireyselleştirilmiş bir tedavi yaklaşımı benimsenmelidir. Kanama durdurucuların uygun kullanımı, sadece akut kanama yönetiminde değil, aynı zamanda sağlık sisteminin kaynak kullanımını optimize etmede de önemli rol oynamaktadır.

KAYNAKLAR

1. Chauncey JM, Patel P. Tranexamic Acid. 2025 Apr 26. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. PMID: 30422504.
2. CRASH-2 trial collaborators, Shakur H, Roberts I, Afolabi A et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet*. 2010;376(9734):23-32. doi:10.1016/S0140-6736(10)60835-5
3. CRASH-2 collaborators. Roberts I, Shakur H, Afolabi A, et al. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. *Lancet*. 2011;377(9771):1096-1101.e11012. doi:10.1016/S0140-6736(11)60278-X
4. Galvagno SM Jr, Nahmias JT, Young DA. Advanced Trauma Life Support® Update 2019: Management and Applications for Adults and Special Populations. *Anesthesiol Clin*. 2019;37(1):13-32. doi: 10.1016/j.anclin.2018.09.009. Epub 2018 Dec 27. PMID: 30711226.
5. Akkan S, Çorbacıoğlu ŞK, Aytar H, et al. Evaluating Effectiveness of Nasal Compression With Tranexamic Acid Compared With Simple Nasal Compression and Merocel Packing: A Randomized Controlled Trial. *Ann Emerg Med*. 2019;74(1):72-78. doi: 10.1016/j.annemergmed.2019.03.030. Epub 2019 May 9. PMID: 31080025.
6. Amini K, Arabzadeh A, Jahed S, et al. Topical Tranexamic Acid versus Phenylephrine-lidocaine for the Treatment of Anterior Epistaxis in Patients Taking Aspirin or Clopidogrel; a Randomized Clinical Trial. *Arch Acad Emerg Med*. 2020;19:9(1):e6. doi: 10.22037/aaem.v9i1.875. PMID: 33313573;
7. Hosseinihashemi M, Jahangiri R, Faramarzi A, et al. Intranasal Topical Application of Tranexamic Acid in Atraumatic Anterior Epistaxis: A Double-Blind Randomized Clinical Trial. *Ann Emerg Med*. 2022;80(3):182-188. doi: 10.1016/j.annemergmed.2022.04.010. Epub 2022 Jun 23. PMID: 35752521.
8. Lecker I, Wang DS, Whissell PD, et al. Tranexamic acid-associated seizures: Causes and treatment. *Ann Neurol*. 2016;79(1):18-26. doi: 10.1002/ana.24558. Epub 2015 Dec 15. PMID: 26580862; PMCID: PMC4738442.
9. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet*. 2017;389(10084):2105-2116. doi: 10.1016/S0140-6736(17)30638-4. Epub 2017 Apr 26. Erratum in: *Lancet*. 2017 May 27;389(10084):2104. doi: 10.1016/S0140-6736(17)31220-5. PMID: 28456509; PMCID: PMC5446563.
10. Law ZK, England TJ, Mistri AK, et al. Incidence and predictors of early seizures in intracerebral haemorrhage and the effect of tranexamic acid. *Eur Stroke J*. 2020;5(2):123-129. doi: 10.1177/2396987320901391. Epub 2020 Jan 24. PMID: 32637645; PMCID: PMC7313371.

11. Nesek Adam V, Bošan-Kilibarda I. Prothrombin Complex Concentrate In Emergency Department. *Acta Clin Croat.* 2022;61(Suppl 1):53-58. doi: 10.20471/acc.2022.61.s1.09. PMID: 36304807; PMCID: PMC9536167.
12. Baskaran J, Lopez RA, Cassagnol M. Prothrombin Complex Concentrate. 2024 Oct 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. PMID: 30969538.
13. Tanaka KA, Shettar S, Vandyck K, et al. Roles of Four-Factor Prothrombin Complex Concentrate in the Management of Critical Bleeding. *Transfus Med Rev.* 2021;35(4):96-103. doi: 10.1016/j.tmr.2021.06.007. Epub 2021 Aug 26. PMID: 34551881.
14. Sarode R, Milling TJ Jr, Refaai MA, et al. Efficacy and safety of a 4-factor prothrombin complex concentrate in patients on vitamin K antagonists presenting with major bleeding: a randomized, plasma-controlled, phase IIb study. *Circulation.* 2013;10;128(11):1234-43. doi: 10.1161/CIRCULATIONAHA.113.002283. Epub 2013 Aug 9. PMID: 23935011; PMCID: PMC6701181.
15. Refaai MA, Goldstein JN, Lee ML, et al. Increased risk of volume overload with plasma compared with four-factor prothrombin complex concentrate for urgent vitamin K antagonist reversal. *Transfusion.* 2015;55(11):2722-9. doi: 10.1111/trf.13191. Epub 2015 Jul 1. PMID: 26135740; PMCID: PMC4755192.
16. Frontera JA, Lewin JJ 3rd, Rabinstein AA, et al. Guideline for Reversal of Antithrombotics in Intracranial Hemorrhage: Executive Summary. A Statement for Healthcare Professionals From the Neurocritical Care Society and the Society of Critical Care Medicine. *Crit Care Med.* 2016;44(12):2251-2257. doi: 10.1097/CCM.0000000000002057. PMID: 27858808.
17. Greenberg SM, Ziai WC, Cordonnier C, Dowlathshahi D, et al. American Heart Association/American Stroke Association. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke.* 2022;53(7):e282-e361. doi: 10.1161/STR.0000000000000407. Epub 2022 May 17. PMID: 35579034.
18. Spahn DR, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. *Crit Care.* 2019;27;23(1):98. doi: 10.1186/s13054-019-2347-3. PMID: 30917843; PMCID: PMC6436241.
19. Steiner T, Poli S, Griebel M, et al. Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial. *Lancet Neurol.* 2016;15(6):566-73. doi: 10.1016/S1474-4422(16)00110-1. Epub 2016 Apr 11. PMID: 27302126.
20. Dzik WH. Reversal of oral factor Xa inhibitors by prothrombin complex concentrates: a re-appraisal. *J Thromb Haemost.* 2015;13 Suppl 1:S187-94. doi: 10.1111/jth.12949. PMID: 26149022.
21. Eikelboom JW, Kozek-Langenecker S, Exadaktylos A, et al. Emergency care of patients receiving non-vitamin K antagonist oral anticoagulants. *Br J Anaesth.* 2018;120(4):645-656. doi: 10.1016/j.bja.2017.11.082. Epub 2017 Dec 1. PMID: 29576106.
22. Chaudhary R, Singh A, Chaudhary R, et al. Evaluation of Direct Oral Anticoagulant Reversal Agents in Intracranial Hemorrhage: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2022;5(11):e2240145. doi: 10.1001/jamanetworkopen.2022.40145. PMID: 36331504; PMCID: PMC9636520.
23. Gómez-Outes A, Alcubilla P, Calvo-Rojas G, et al. Meta-Analysis of Reversal Agents for Severe Bleeding Associated With Direct Oral Anticoagulants. *J Am Coll Cardiol.* 2021;77(24):2987-3001. doi: 10.1016/j.jacc.2021.04.061. PMID: 34140101.
24. Majeed A, Ågren A, Holmström M, et al. Management of rivaroxaban- or apixaban-associated major bleeding with prothrombin complex concentrates: a cohort study. *Blood.*

- 2017;130(15):1706-1712. doi: 10.1182/blood-2017-05-782060. Epub 2017 Aug 23. PMID: 28835439.
25. Schulman S, Gross PL, Ritchie B, et al. Study Investigators. Prothrombin Complex Concentrate for Major Bleeding on Factor Xa Inhibitors: A Prospective Cohort Study. *Thromb Haemost.* 2018;118(5):842-851. doi: 10.1055/s-0038-1636541. Epub 2018 Mar 21. Erratum in: *Thromb Haemost.* 2018 Dec;118(12):2188. doi: 10.1055/s-0038-1675417. PMID: 29564837.
 26. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al. American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* 2015;46(7):2032-60. doi: 10.1161/STR.0000000000000069. Epub 2015 May 28. PMID: 26022637.
 27. Nienaber U, Innerhofer P, Westermann I, et al. The impact of fresh frozen plasma vs coagulation factor concentrates on morbidity and mortality in trauma-associated haemorrhage and massive transfusion. *Injury.* 2011;42(7):697-701. doi: 10.1016/j.injury.2010.12.015. Epub 2011 Mar 9. PMID: 21392760.
 28. Innerhofer P, Fries D, Mittermayr M, et al. Reversal of trauma-induced coagulopathy using first-line coagulation factor concentrates or fresh frozen plasma (RETIC): a single-centre, parallel-group, open-label, randomised trial. *Lancet Haematol.* 2017 Jun;4(6):e258-e271. doi: 10.1016/S2352-3026(17)30077-7. Epub 2017 Apr 28. Erratum in: *Lancet Haematol.* 2017;4(6):e257. doi: 10.1016/S2352-3026(17)30084-4. PMID: 28457980.
 29. Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. *Blood.* 2010;116(6):878-85. doi: 10.1182/blood-2010-02-261891. Epub 2010 Apr 16. PMID: 20400681.
 30. Verbeek TA, Stine JG, Saner FH, et al. Hypercoagulability in End-stage Liver Disease: Review of Epidemiology, Etiology, and Management. *Transplant Direct.* 2018;4(11):e403. doi: 10.1097/TXD.0000000000000843. PMID: 30534594; PMCID: PMC6233657.
 31. Bharadwaj MS, Bora V. Managing Fresh-Frozen Plasma Transfusion Adverse Effects: Allergic Reactions, TACO, and TRALI. [Updated 2023 Nov 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK597370/>
 32. Watson JJ, Pati S, Schreiber MA. Plasma Transfusion: History, Current Realities, and Novel Improvements. *Shock.* 2016;46(5):468-479. doi: 10.1097/SHK.0000000000000663. PMID: 27380536.
 33. Khawar H, Patel P, Stevens JB, Guzman N. Fresh Frozen Plasma (FFP). 2025 Feb 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. PMID: 30020719.
 34. The Lancet Haematology. Updates on blood transfusion guidelines. *Lancet Haematol.* 2016;3(12):e547. doi: 10.1016/S2352-3026(16)30172-7. PMID: 27890071.
 35. Greenberg SM, Ziai WC, Cordonnier C, et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke.* 2022;53(7):e282-e361. doi:10.1161/STR.0000000000000407
 36. Runyon BA., AASLD Practice Guidelines Committee. Management of adult patients with ascites due to cirrhosis: an update. *Hepatology.* 2009;49(6):2087-107
 37. Escobar MF, Nassar AH, Theron G, et al. FIGO Safe Motherhood and Newborn Health Committee. FIGO recommendations on the management of postpartum hemorrhage 2022. *Int J*

- Gynaecol Obstet. 2022;157 Suppl 1(Suppl 1):3-50.
38. Baş B, Küçükdemirci Ö, Ustaoglu M. Ankaferd blood stopper: A novel additional strategy for less experienced gastroenterologists in gastrointestinal bleeding treatment. *Medicine (Baltimore)*. 2024;103(22):e38319. doi:10.1097/MD.00000000000038319
 39. Kurt M, Onal I, Akdogan M, et al. Ankaferd Blood Stopper for controlling gastrointestinal bleeding due to distinct benign lesions refractory to conventional antihemorrhagic measures. *Can J Gastroenterol*. 2010;24:380-4.
 40. Ozaslan E, Purnak T, Yildiz A, et al. A new practical alternative for tumoural gastrointestinal bleeding: Ankaferd Blood Stopper. *Dig Liver Dis*. 2010;42:594-5.
 41. Koyuncu N. The Effectiveness of Ankaferd Blood Stopper in the Management of Traumatic Bleeding. *Adv Ther*. 2019;36(5):1143-1149. doi:10.1007/s12325-019-00935-4
 42. Teker MA, Korkut AY, Kahya V, et al. Prospective randomized controlled clinical trial of ABS in patients with acute anterior epistaxis. *Eur Arch Otorhinolaryngol*. 2010;267(9):1377-81.
 43. Yılmaz AÇ, Aygün D. Evaluation of the effects of three natural products and a hemostatic agent on wound healing: an experimental study. *Turkish Journal of Medical Sciences*, 2023; 53.1: 58-67.
 44. Simsek C, Selek S, Koca M, et al. Proteomic and transcriptomic analyses to explain the pleiotropic effects of Ankaferd blood stopper. *SAGE Open Med*. 2017;5:2050312117722569. Published 2017 Jul 27. doi:10.1177/2050312117722569
 45. Koluman A, Akar N, Haznedaroglu IC. Antibacterial activities of Ankaferd hemostat (ABS) on "Shiga toxin producing *Escherichia coli*" and other pathogens significant in Foodborne diseases. *Turk J Haematol* 2017; 34(1): 93-98.
 46. Akalin I, Okur FV, Haznedaroglu IC, et al. Acute in vitro effects of ABS (Ankaferd Hemostat) on the lymphoid neoplastic cells (B-CLL and RAJI Tumor Cell Lines). *Int J Hematol Oncol* 2014; 24: 253-259.
 47. Jiang SX, Chahal D, Ali-Mohamad N et al. Hemostatic powders for gastrointestinal bleeding: a review of old, new, and emerging agents in a rapidly advancing field. *Endosc Int Open*. 2022;10(8):E1136-E1146. Published 2022 Aug 15. doi:10.1055/a-1836-8962.
 48. Barkun AN, Adam V, Lu Y et al. Using Hemospray improves the cost- effectiveness ratio in the management of upper gastrointestinal non-variceal bleeding. *J Clin Gastroenterol* 2018; 52: 36-44.
 49. Laine L, Barkun AN, Saltzman JR et al. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. *Am J Gastroenterol* 2021; 116: 899-917.
 50. Holster IL, Maat MPD, Ducharme R et al. Sa1671 In vitro examination of the effects of the hemostatic powder (HemosprayTM) on coagulation and thrombus formation in humans. *Gastrointest Endosc* 2012;75: AB240.
 51. Rodríguez de Santiago E, Burgos-Santamaría D, Pérez-Carazo L et al. Hemostatic spray powder TC-325 for GI bleeding in a nationwide study: survival and predictors of failure via competing risks analysis. *Gastrointest Endosc* 2019; 90: 581-590.e6.
 52. EndoClot new GI therapeutic solutions [online]. <http://endoclot.com/products.html> [accessed 24 June 2025].
 53. Prei JC, Barmeyer C, Bürgel N et al. EndoClot polysaccharide hemostatic system in nonvariceal gastrointestinal bleeding: results of a prospective multicenter observational pilot study. *J Clin Gastroenterol* 2016; 50: e95-e100
 54. Bang B, Lee E, Maeng J et al. Efficacy of a novel endoscopically deliverable muco-adhesive hemostatic powder in an acute gastric bleeding porcine model. *PLoS One* 2019; 14: e0216829.

55. Medtronic. Nexpowder TM* Endoscopic Hemostasis System. [https:// www.medtronic.com/covidien/en-gb/products/therapeutic-endoscopy/nexpowder-endoscopic-hemostasis-system.html](https://www.medtronic.com/covidien/en-gb/products/therapeutic-endoscopy/nexpowder-endoscopic-hemostasis-system.html)
56. Spotnitz WD, Burks S. Hemostats, sealants, and adhesives: components of the surgical toolbox. *Transfusion* 2008; 48:1502.
57. Beudert M, Gutmann M, Lühmann T, et al. Fibrin Sealants: Challenges and Solutions. *ACS Biomater Sci Eng.* 2022;8(6):2220-2231. doi:10.1021/acsbiomaterials.1c01437.
58. Daud A, Kaur B, McClure GR, et al. Fibrin and Thrombin Sealants in Vascular and Cardiac Surgery: A Systematic Review and Meta-analysis. *Eur J Vasc Endovasc Surg.* 2020;60(3):469-478. doi:10.1016/j.ejvs.2020.05.016.
59. Mandell SP, Gibran NS. Fibrin sealants: surgical hemostat, sealant and adhesive. *Expert Opin Biol Ther.* 2014;14(6):821-830. doi:10.1517/14712598.2014.897323.
60. Nervi C, Gamelli RL, Greenhalgh DG, et al. A multicenter clinical trial to evaluate the topical hemostatic efficacy of fibrin sealant in burn patients. *J Burn Care Rehabil* 2001; 22:99.