

## Yoğun Bakımda Hematolojik Sorunlara Yaklaşım

Ayşe KARATAŞ<sup>1</sup>

Bu bölümde yoğun bakımda karşılaşılabileceğimiz hematoloji alanına özgü hızlı tanı ve tedavi gerektiren başlıca konulara yer verilmiştir.

Yoğun bakım hastalarında sıklıkla hemostaz testlerine ihtiyaç duyulmaktadır ve bunların doğru yorumlanması aşırı ve eksik tedavi ihtimalini azaltmaktadır. Bu nedenle öncelikle sık kullanılan hemostaz testlerinin yorumlanması ele alınmıştır. Takiben, mortalitesinin yüksek olması ve yönetiminin oldukça güç olması nedeniyle kritik hastalarda özel bir öneme sahip olan dissemine intravasküler koagülasyon tanı ve tedavisine değinilmiştir.

Tromboembolik olaylar, yoğun bakımda yatan hastalarda en önemli morbidite ve mortalite nedenleri arasındadırlar. Bu nedenle tromboz profilaksisi ve gerektiğinde tedavi edilmesi, kritik önem taşımaktadır. Yoğun bakımda antikoagülan tedavi konu başlığı altında antikoagülan tedavide kullanılan ajanlara ve tedavide dikkat edilmesi gereken noktalar yer almaktadır. Klinik pratiğimizde en sık kullandığımız antikoagülan ajanlar olan heparinlere bağlı gelişen bir komplikasyon olan heparin ilişkili trombositopeni ayrı bir konu başlığında ele alınmıştır.

Son olarak nadir görülen ancak erken dönemde tedavi başlanmadığında %90 ölümcül seyreden hematolojik bir acil olan trombotik trombositopenik purpura tanı ve tedavisine yer verilmiştir.

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### ► Rituksimab

Son yıllarda akut atak tedavisine TTP'ye rituksimab eklenmesi önerilmektedir (60).

TTP'de hayatı tehdit eden kanama ya da kanama riski olan girişimler dışında, sadece trombositopeni endikasyonu ile trombosit transfüzyonu önerilmemektedir.

Refrakter ya da relaps vakalarda tedavi seçenekleri; siklofosamid, vinkristin, splenektomi ya da başlangıçta tedaviye eklenmediyse rituksimabdır (61).

Bir monoklonal anti-von Willebrand faktör antikoru olan kaplasizumabın bazı ülkelerde TTP tedavisinde kullanımı onaylanmıştır (62).

### | Kaynaklar

1. van Ommen CH, Peters M. The bleeding child. Part I: primary hemostatic disorders. *European journal of pediatrics*. 2012;171(1):1-10. doi: 10.1007/s00431-011-1532-4
2. van Herrewegen F, Meijers JC, Peters M, et al. The bleeding child. Part II: disorders of secondary hemostasis and fibrinolysis. *European journal of pediatrics*. 2012;171(2):207-214. doi: 10.1007/s00431-011-1571-x
3. Dahlbäck B. Blood coagulation. *The Lancet*. 2000;355(9215):1627-1632. doi: 0.1016/S0140-6736(00)02225-X
4. Bates SM, Weitz JJ. Coagulation assays. *Circulation*. 2005;112(4):e53-e60. doi: 10.1161/CIRCULATIONAHA.104.478222
5. Zürcher M, Sulzer I, Barizzi G, et al. Stability of coagulation assays performed in plasma from citrated whole blood transported at ambient temperature. *Thrombosis and haemostasis*. 2008;99(2):416-426. doi: 10.1160/TH07-07-0448
6. Kershaw G, Orellana D, editors. Mixing tests: diagnostic aides in the investigation of prolonged prothrombin times and activated partial thromboplastin times. *Seminars in thrombosis and hemostasis*; 2013; 39(3): 283–290. doi: 10.1055/s-0033-1336832
7. Kamal AH, Tefferi A, Pruthi RK. How to interpret and pursue an abnormal prothrombin time, activated partial thromboplastin time, and bleeding time in adults. *Mayo Clinic proceedings*. 2007;82(7):864-873. doi: 10.4065/82.7.864
8. Van Cott EM, Smith EY, Galanakis DK. Elevated fibrinogen in an acute phase reaction prolongs the reptilase time but typically not the thrombin time. *American journal of clinical pathology*. 2002;118(2):263-268. doi: 10.1309/WUB3-72JT-E50M-EU8J
9. Lowe GD, Rumley A, Mackie IJ. Plasma fibrinogen. *Annals of Clinical Biochemistry*. 2004;41(6):430-440. doi: 10.1258/0004563042466884
10. Johnson ED, Schell JC, Rodgers GM. The D-dimer assay. *American journal of hematology*. 2019;94(7):833-839. doi: 10.1002/ajh.25482
11. Gando S, Levi M, Toh C-H. Disseminated intravascular coagulation. *Nature reviews Disease primers*. 2016;2(1):1-16. doi: 10.1038/nrdp.2016.37
12. Levi M, Scully M. How I treat disseminated intravascular coagulation. *Blood*. 2018;131(8):845-854. doi: 10.1182/blood-2017-10-804096
13. Benjamin RJ, McLaughlin LS. Plasma components: properties, differences, and uses. *Transfusion*. 2012;52:9S-19S. doi: 10.1111/j.1537-2995.2012.03622.x

14. Bick RL, Arun B, Frenkel EP. Disseminated intravascular coagulation. clinical and pathophysiological mechanisms and manifestations. *Haemostasis*. 1999;29(2-3):111-134. doi: 10.1159/000022493
15. Wada H, Thachil J, Di Nisio M, et al. Guidance for diagnosis and treatment of DIC from harmonization of the recommendations from three guidelines. The Scientific Standardization Committee on DIC of the International Society on Thrombosis Haemostasis. *Journal of thrombosis and haemostasis*. 2013; 11(1): 761-767. doi: 10.1111/jth.12155
16. Levi M, Toh C, Thachil J, et al. Guidelines for the diagnosis and management of disseminated intravascular coagulation. *British journal of haematology*. 2009;145(1):24-33. doi: 10.1111/j.1365-2141.2009.07600.x
17. Gross P, Weitz J. New Antithrombotic Drugs. *Clinical Pharmacology & Therapeutics*. 2009;86(2):139-146. doi: 10.1038/clpt.2009.98
18. Hirsh J. Heparin. *New England Journal of Medicine*. 1991;324(22):1565-1574. doi: 10.1056/NEJM199105303242206
19. Hirsh J, Warkentin TE, Shaughnessy SG, et al. Heparin and low-molecular-weight heparin mechanisms of action, pharmacokinetics, dosing, monitoring, efficacy, and safety. *Chest*. 2001;119(1):64S-94S. doi: 10.1378/chest.119.1\_suppl.64s
20. Hirsh J, Raschke R. Heparin and low-molecular-weight heparin: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004;126(3):188S-203S. doi: 10.1378/chest.126.3\_suppl.188S
21. Monagle P, Bannow BS. Thrombosis and thrombophilia. In: Altman JK, Mandernach MW, Naik RP et al. (eds) *American Society of Hematology Self-Assessment Program*. 8th ed. Washington, DC: American Society of Hematology; 2022. p. 219-248. doi: 10.1182/ashsap8.chapter09
22. Raschke RA, Gollihare B, Peirce JC. The effectiveness of implementing the weight-based heparin nomogram as a practice guideline. *Archives of internal medicine*. 1996;156(15):1645-1649. doi: 10.1001/archinte.1996.00440140067006
23. Schulman S, Bijsterveld NR. Anticoagulants and their reversal. *Transfusion medicine reviews*. 2007;21(1):37-48. doi: 10.1016/j.tmr.2006.08.002
24. Girolami B, Girolami A. Heparin-induced thrombocytopenia: a review. *Seminars in thrombosis and hemostasis*; 2006;32(8):803-9. doi: 10.1055/s-2006-955463
25. Hao C, Sun M, Wang H, et al. Low molecular weight heparins and their clinical applications. *Progress in molecular biology and translational science*. 2019;(163):21-39. doi: 10.1016/bs.pmbts.2019.02.003
26. Zhang Y, Zhang M, Tan L, et al. The clinical use of Fondaparinux: A synthetic heparin pentasaccharide. *Progress in molecular biology and translational science*. 2019;163:41-53. doi: 10.1016/bs.pmbts.2019.02.004
27. Walenga JM, Jeske WP, Frapaise FX, et al. Fondaparinux: a synthetic heparin pentasaccharide as a new antithrombotic agent. *Expert opinion on investigational drugs*. 2002;11(3):397-407. doi: 10.1517/13543784.11.3.397
28. Nagler M, Haslauer M, Wuillemin WA. Fondaparinux—data on efficacy and safety in special situations. *Thrombosis research*. 2012;129(4):407-417. doi: 10.1016/j.thromres.2011.10.037
29. Baker WL, Johnson SG. Pharmacogenetics and oral antithrombotic drugs. *Current opinion in pharmacology*. 2016;27:38-42. doi: 10.1016/j.coph.2016.01.008
30. Harter K, Levine M, Henderson SO. Anticoagulation drug therapy: a review. *The western journal of emergency medicine*. 2015;16(1):11-17. doi: 10.5811/westjem.2014.12.22933
31. Kuruvilla M, Gurk-Turner C. A review of warfarin dosing and monitoring. *Baylor University Medical Center Proceedings*. 2001;14(3):305-306. doi: 10.1080/08998280.2001.11927781
32. Haznedaroğlu İC. Antikoagulan tedavi: genel bakış. *Dahili Tıp Bilimleri Dergisi*. 2005;12(2):4-10.

33. Hirsh J, Dalen JE, Anderson DR, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. *Chest*. 1998;114(5):445S-469S. doi: 10.1378/chest.119.1\_suppl.8S
34. Baker RI, Coughlin PB, Salem HH, et al. Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis. *The Medical Journal of Australia*. 2004;181(9):492-497. doi: 10.5694/j.1326-5377.2004.tb06407.x
35. Lee LH. DOACs . Advances and limitations in real world. *Thrombosis Journal*. 2016;14(1):17. doi: 10.1186/s12959-016-0111-3
36. Tekin G. Klinik Pratikte Yeni Oral Antikoagülanların Kullanımı. *MN Kardiyoloji Dergisi*. 2015;22(3):167-173.
37. Connors JM. Testing and monitoring direct oral anticoagulants. *Blood*. 2018;132(19):2009-2015. doi: 10.1182/blood-2018-04-791541
38. Hapgood G, Butler J, Malan E, et al. The effect of dabigatran on the activated partial thromboplastin time and thrombin time as determined by the Hemoclot thrombin inhibitor assay in patient plasma samples. *Thrombosis and haemostasis*. 2013;110(08):308-315. doi: 10.1160/TH13-04-0301
39. Cuker A, Siegal D. Monitoring and reversal of direct oral anticoagulants. *Hematology*. 2015;2015(1):117-124. doi: 10.1182/asheducation.V2015.1.117.3916182
40. Steiner T, Böhm M, Dichgans M, et al. Recommendations for the emergency management of complications associated with the new direct oral anticoagulants (DOACs), apixaban, dabigatran and rivaroxaban. *Clinical Research in Cardiology*. 2013;102(6):399-412. doi: 10.1007/s00392-013-0560-7
41. Burnett AE, Mahan CE, Vazquez SR, et al. Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment. *Journal of Thrombosis and Thrombolysis*. 2016;41(1):206-232. doi:10.1007/s11239-015-1310-7
42. Warkentin TE. Bivalent direct thrombin inhibitors: hirudin and bivalirudin. *Best Practice & Research Clinical Haematology*. 2004;17(1):105-125. doi: 10.1016/j.beha.2004.02.002
43. LaMonte MP, Nash ML, Wang DZ, et al. Argatroban anticoagulation in patients with acute ischemic stroke (ARGIS-1) A randomized, placebo-controlled safety study. *Stroke*. 2004;35(7):1677-1682. doi: 10.1161/01.STR.0000131549.20581.ba
44. McKeage K, Plosker GL. Argatroban. *Drugs*. 2001;61(4):515-522. doi: 10.2165/00003495-200161040-00005
45. Warkentin TE, Kelton JG. Temporal aspects of heparin-induced thrombocytopenia. *New England journal of medicine*. 2001;344(17):1286-1292. doi:10.1056/NEJM200104263441704
46. Cuker A, Cines DB. How I treat heparin-induced thrombocytopenia. *Blood*. 2012;119(10):2209-2218. doi: 10.1182/blood-2011-11-376293
47. Hogan M, Berger JS. Heparin-induced thrombocytopenia (HIT): Review of incidence, diagnosis, and management. *Vascular Medicine*. 2020;25(2):160-173. doi:10.1177/1358863X19898253
48. Lo GK, Juhl D, Warkentin TE, et al. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *Journal of thrombosis and haemostasis*. 2006;4(4):759-765. doi: 10.1111/j.1538-7836.2006.01787.x
49. Minet V, Dogné J-M, Mullier F. Functional assays in the diagnosis of heparin-induced thrombocytopenia: a review. *Molecules*. 2017;22(4):617. doi: 10.3390/molecules22040617
50. Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. *Blood Advances*. 2018;2(22):3360-3392. doi: 10.1182/bloodadvances.2018024489
51. Arepally GM. Heparin-induced thrombocytopenia. *Blood*. 2017;129(21):2864-2872. doi: 10.1182/blood-2016-11-709873

52. Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e495S-e530S. doi: 10.1378/chest.11-2303
53. Blombery P, Scully M. Management of thrombotic thrombocytopenic purpura: current perspectives. *Journal of blood medicine*. 2014;5:15-23. doi: 10.2147/JBM.S46458
54. Joly BS, Coppo P, Veyradier A. Thrombotic thrombocytopenic purpura. *Blood*. 2017;129(21):2836-2846. doi: 10.1182/blood-2016-10-709857
55. Kremer Hovinga JA, Coppo P, Lämmle B, et al. Thrombotic thrombocytopenic purpura. *Nature reviews Disease primers*. 2017;3(1):1-17. doi: 10.1038/nrdp.2017.20
56. Sayani FA, Abrams CS. How I treat refractory thrombotic thrombocytopenic purpura. *Blood*. 2015;125(25):3860-3867. doi: 10.1182/blood-2014-11-551580
57. Scully M, Cataland S, Coppo P, et al. Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies. *Journal of thrombosis and haemostasis*. 2017;15(2):312-322. doi: 10.1111/jth.13571
58. Paydary K, Banwell E, Tong J, et al. Diagnostic accuracy of the PLASMIC score in patients with suspected thrombotic thrombocytopenic purpura: a systematic review and meta-analysis. *Transfusion*. 2020;60(9):2047-2057. doi: 10.1111/trf.15954
59. Balduini CL, Gugliotta L, Luppi M, et al. High versus standard dose methylprednisolone in the acute phase of idiopathic thrombotic thrombocytopenic purpura: a randomized study. *Annals of hematology*. 2010;89(6):591-596. doi: 10.1007/s00277-009-0877-5
60. Scully M, McDonald V, Cavenagh J, et al. A phase 2 study of the safety and efficacy of rituximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. *Blood*. 2011;118(7):1746-1753. doi: 10.1182/blood-2011-03-341131
61. George JN. How I treat patients with thrombotic thrombocytopenic purpura: 2010. *Blood*. 2010;116(20):4060-4069. doi: 10.1182/blood-2010-07-271445
62. Peyvandi F, Scully M, Kremer Hovinga JA, et al. Caplacizumab for acquired thrombotic thrombocytopenic purpura. *New England Journal of Medicine*. 2016;374(6):511-522. doi: 10.1056/NEJMoa1505533

