Bölüm 4

KONTRAST MADDE AŞIRI DUYARLILIK REAKSİYONLARI

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Tanı ve tedavi uygulamalarındaki kullanım sıklığının giderek artmasına bağlı olarak iyotlu kontrast madde (İKM)'lere karşı yan etkiler de günlük pratikte giderek artan bir problem olarak karşımıza çıkmaktadır.

Diğer ilaç uygulamalarında olduğu gibi İKM uygulaması sonrasında görülen yan etkiler toksik reaksiyonlar (tip A reaksiyonlar) veya aşırı duyarlılık reaksiyonları (tip B reaksiyonlar) olarak sınıflandırılabilir. Toksik reaksiyonlar öngörülebilen, doza bağımlı ve kimyasal yapı ile ilişkili yan etkilerdir. Nefrotoksisite ve nörotoksisite buna örnek gösterilebilir (1-3).

Aşırı duyarlılık reaksiyonları (ADR), İKM uygulaması sonrasında semptomların başlangıç zamanına göre erken tip ve erken olmayan veya gecikmiş tip aşırı ADR olarak ikiye ayrılır. Erken tip ADR, kontrast madde uygulanması sonrasında ilk 1 saat (<6 saat) içinde ortaya çıkarken, erken olmayan tip ADR 1 saatten sonra genellikle 24-48 saat sonra hatta bazen daha geç dönemde ortaya çıkabilir (1-4).

İKM Sınıflandırılması ve Fizyokimyasal Özellikleri

İKM'ler basit kimyasal yapısı bir benzen halkası ve en az 3 iyot atomundan (triiyodobenzen) oluşan iyotlu tuzlardır. Her moleküldeki iyot atomlarının sayısı radyoopasite üretiminden sorumludur. İKM'ler bir benzen halkasına sahipse monomerik yapıda, benzoik nükleus kovalan bağlı ise dimerik yapıdadır. Ben-

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KAYNAKLAR

1. Costantino MT, Romanini L, Gaeta F, et al. SIRM-SIAAIC consensus, an Italian document on management of patients at risk of hypersensitivity reactions to contrast media. *Clinical and Molecular Allergy.* 2020;18:13. doi: 10.1186/s12948-020-00128-3
2. Torres MJ, Trautmann A, Bohm I, et al. Practice parameters for diagnosing and managing iodinated contrast media hypersensitivity. *Allergy.* 2021;76(5):1325-1339. doi: 10.1111/all.14656
3. Brockow K**.** Immediate and delayed cutaneous reactions to radiocontrast media. *Chemical Immunology and Allergy*. 2012;97:180-190. doi: 10.1159/000335631
4. Ingelmo AR DI, Moreno RC et al. Clinical practice guidelines for diagnosis and management of hypersensitivity reactions to contrast media. *Journal of Investigational Allergology and Clinical Immunology* 2016;26(3):144-55. doi: 10.18176/jiaci.0058
5. Brockow K, Sanchez-Borges M**.** Hypersensitivity to contrast media and dyes. *Immunology Allergy Clinics of North America*. 2014;34(3):547-564. doi: 10.1016/j.iac.2014.04.002
6. Sanchez-Borges M, Aberer W, Brockow K, et al. Controversies in Drug Allergy: Radiographic Contrast Media. The *Journal of Allergy and Clinical Immunology: In Practice*. 2019;7(1):61-65. doi: 10.1016/j.jaip.2018.06.030
7. Newmark JL, Mehra A, Singla AK**.** Radiocontrast media allergic reactions and interventional pain practice--a review. *Pain Physician.* 2012;15(5):665-675.
8. Cochran ST**.** Anaphylactoid reactions to radiocontrast media. *Current Allergy and Asthma Reports*. 2005;5(1):28-31. doi: 10.1007/s11882-005-0051-7
9. International Collaborative Study of Severe A**.** Risk of anaphylaxis in a hospital population in relation to the use of various drugs: an international study. *Pharmacoepidemiology and Drug Safety*. 2003;12(3):195-202. doi: 10.1002/pds.822
10. Brockow K, Ring J**.** Classification and pathophysiology of radiocontrast media hypersensitivity. *Chemical Immunology and Allergy.* 2010;95:157-169. doi: 10.1159/000315949
11. Katayama H, Yamaguchi K, Kozuka T, et al**.** Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. *Radiology.* 1990;175(3):621-628. doi: 10.1148/radiology.175.3.2343107
12. Palmer FJ**.** The RACR survey of intravenous contrast media reactions. Final report. *Australasian Radiology.* 1988;32(4):426-428. doi: 10.1111/j.1440-1673.1988.tb02770.x
13. Wolf GL, Arenson RL, Cross AP**.** A prospective trial of ionic vs nonionic contrast agents in routine clinical practice: comparison of adverse effects. *AJR American Journal of Roentgenology.* 1989;152(5):939-944. doi: 10.2214/ajr.152.5.939
14. Caro JJ, Trindade E, McGregor M**.** The risks of death and of severe nonfatal reactions with high- vs low-osmolality contrast media: a meta-analysis. *AJR American Journal of Roentgenology*. 1991;156(4):825-832. doi: 10.2214/ajr.156.4.1825900
15. Dona I, Barrionuevo E, Blanca-Lopez N, et al. Trends in hypersensitivity drug reactions: more drugs, more response patterns, more heterogeneity. *Journal of Investigational Allergology and Clinical Immunology*. 2014;24(3):143-153
16. Gomez E, Ariza A, Blanca-Lopez N, et al**.** Nonimmediate hypersensitivity reactions to iodinated contrast media. *Current Opinion in Allergy and Clinical Immunology*. 2013;13(4):345-353. doi: 10.1097/ACI.0b013e328362b926
17. Bohm I, Speck U, Schild HH**.** Pilot study on basophil activation induced by contrast medium. *Fundamental & Clinical Pharmacology*. 2011;25(2):267-276. doi: 10.1111/j.1472-8206.2010.00826.x

18. Brockow K, Romano A, Aberer W, et al. Skin testing in patients with hypersensitivity reactions to iodinated contrast media - a European multicenter study. *Allergy.* 2009;64(2):234-241. doi: 10.1111/j.1398-9995.2008.01832.x

19. Goksel O, Aydin O, Atasoy C, et al. Hypersensitivity reactions to contrast media: prevalence, risk factors and the role of skin tests in diagnosis--a cross-sectional survey. I*nternational Archieves of Allergy and Immunology*. 2011;155(3):297-305. doi: 10.1159/000320760

20. Laroche D, Aimone-Gastin I, Dubois F, et al. Mechanisms of severe, immediate reactions to iodinated contrast material. *Radiology.* 1998;209(1):183-190. doi: 10.1148/radiology.209.1.9769830

21. Mita H, Tadokoro K, Akiyama K**.** Detection of IgE antibody to a radiocontrast medium. *Allergy.* 1998;53(12):1133-1140. doi: 10.1111/j.1398-9995.1998.tb03832.x

22. Pinnobphun P, Buranapraditkun S, Kampitak T, et al**.** The diagnostic value of basophil activation test in patients with an immediate hypersensitivity reaction to radiocontrast media. *Annals of Allergy Asthma & Immunol*. 2011;106(5):387-393. doi: 10.1016/j.anai.2010.12.020

23. Salas M, Gomez F, Fernandez TD, et al. Diagnosis of immediate hypersensitivity reactions to radiocontrast media. *Allergy*. 2013;68(9):1203-1206. doi: 10.1111/all.12214

24. Laroche D**.** Immediate reactions to contrast media: mediator release and value of diagnostic testing. *Toxicology.* 2005;209(2):193-194. doi: 10.1016/j.tox.2005.01.010

25. Trcka J, Schmidt C, Seitz CS, et al. Anaphylaxis to iodinated contrast material: nonallergic hypersensitivity or IgE-mediated allergy? *AJR American Journal of Roentgenology.* 2008;190(3):666-670. doi: 10.2214/AJR.07.2872

26. Brockow K, Christiansen C, Kanny G, et al. Management of hypersensitivity reactions to iodinated contrast media. *Allergy*. 2005;60(2):150-158. doi: 10.1111/j.1398-9995.2005.00745.x

27. Brockow K, Ring J**.** Anaphylaxis to radiographic contrast media. *Current Opinion in Allergy and Clinical Immunology.* 2011;11(4):326-331. doi: 10.1097/ACI.0b013e32834877c3

28. Ring J, Arroyave CM, Frizler MJ, et al**.** In vitro histamine and serotonin release by radiographic contrast media (RCM). Complement-dependent and -independent release reaction and changes in ultrastructure of human blood cells. *Clinical & Experimental Immunology*. 1978;32(1):105-118.

29. Szebeni J**.** Hypersensitivity reactions to radiocontrast media: the role of complement activation. *Current Allergy and Asthma Reports*. 2004;4(1):25-30. doi: 10.1007/s11882-004-0038-9

30. Brockow K, Vieluf D, Puschel K, et al**.** Increased postmortem serum mast cell tryptase in a fatal anaphylactoid reaction to nonionic radiocontrast medium. *Journal of Allergy and Clinical Immunology.* 1999;104(1):237-238. doi: 10.1016/s0091-6749(99)70141-7

31. Clement O, Dewachter P, Mouton-Faivre C, et al. Immediate Hypersensitivity to Contrast Agents: The French 5-year CIRTACI Study. *EClinicalMedicin*e. 2018;1:51-61. doi: 10.1016/j.eclinm.2018.07.002

32. Schrijvers R, Breynaert C, Ahmedali Y, et al**.** Skin Testing for Suspected Iodinated Contrast Media Hypersensitivity. *Journal of Allergy and Clinical Immunology: In Practice.* 2018;6(4):1246-1254. doi: 10.1016/j.jaip.2017.10.040.

33. Antunez C, Barbaud A, Gomez E, et al. Recognition of iodixanol by dendritic cells increases the cellular response in delayed allergic reactions to contrast media. *Clinical and Experimental Allergy.* 2011;41(5):657-664. doi: 10.1111/j.1365-2222.2010.03693.x.

34. Torres MJ, Gomez F, Dona I, et al. Diagnostic evaluation of patients with nonimmediate cutaneous hypersensitivity reactions to iodinated contrast media. *Allergy.* 2012;67(7):929-935. doi: 10.1111/j.1398-9995.2012.02840.x.
35. Torres MJ, Mayorga C, Cornejo-Garcia JA, et al. Monitoring non-immediate allergic reactions to iodine contrast media. *Clinical and Experimental Immunology*. 2008;152(2):233-238. doi: 10.1111/j.1365-2249.2008.03627.x
36. Kanny G, Pichler W, Morisset M, et al. T cell-mediated reactions to iodinated contrast media: evaluation by skin and lymphocyte activation tests. *Journal of Allergy and Clinical Immunology.* 2005;115(1):179-185. doi: 10.1016/j.jaci.2004.09.012.
37. Vernassiere C, Trechot P, Commun N, et al. Low negative predictive value of skin tests in investigating delayed reactions to radio-contrast media. *Contact Dermatitis.* 2004;50(6):359-366. doi: 10.1111/j.0105-1873.2004.00367.x.
38. Bohm I, Heverhagen JT, Klose KJ**.** Classification of acute and delayed contrast media-induced reactions: proposal of a three-step system. *Contrast Media & Molecular Imaging*. 2012;7(6):537-541. doi: 10.1002/cmmi.1475.
39. Brockow K**.** Medical algorithm: Diagnosis and treatment of radiocontrast media hypersensitivity. *Allergy.* 2020;75(5):1278-1280. doi: 10.1111/all.14147.
40. Brockow K, Ardern-Jones MR, Mockenhaupt M, et al. EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity. *Allergy*. 2019;74(1):14-27. doi: 10.1111/all.13562
41. Wang CL, Cohan RH, Ellis JH, et al**.** Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reactions. *AJR American Journal of Roentgenology.* 2008;191(2):409-415. doi: 10.2214/AJR.07.3421.
42. Ring J, Messmer K**.** Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *The Lancet.* 1977;1(8009):466-469. doi: 10.1016/s0140-6736(77)91953-5.
43. Brown SG**.** Clinical features and severity grading of anaphylaxis. *Journal of Allergy and Clinical Immunology.* 2004;114(2):371-376. doi: 10.1016/j.jaci.2004.04.029
44. Pradubpongsa P, Dhana N, Jongjarearnprasert K, et al**.** Adverse reactions to iodinated contrast media: prevalence, risk factors and outcome-the results of a 3-year period. *Asian Pacific Journal of Allergy Immunology.* 2013;31(4):299-306. doi: 10.12932/AP0297.31.4.2013
45. Webb JA, Stacul F, Thomsen HS, et al. Members Of The Contrast Media Safety Committee Of The European Society Of Urogenital R**.** Late adverse reactions to intravascular iodinated contrast media. *European Radiology.* 2003;13(1):181-184. doi: 10.1007/s00330-002-1650-5.
46. Bellin MF, Stacul F, Webb JA, et al. Late adverse reactions to intravascular iodine based contrast media: an update. *European Radiology*. 2011;21(11):2305-2310. doi: 10.1007/s00330-011-2200-9
47. Bohm I, Schild HH**.** A practical guide to diagnose lesser-known immediate and delayed contrast media-induced adverse cutaneous reactions. *European Radiology*. 2006;16(7):1570-1579. doi: 10.1007/s00330-006-0202-9.
48. Schonmann C, Brockow K**.** Adverse reactions during procedures: Hypersensitivity to contrast agents and dyes. *Annals of Allergy Asthma & Immunology.* 2020;124(2):156-164. doi: 10.1016/j.anai.2019.11.022
49. Hosoya T, Yamaguchi K, Akutsu T, et al. Delayed adverse reactions to iodinated contrast media and their risk factors. *Radiation Medicine.* 2000;18(1):39-45.
50. Katayama H, Yamaguchi K, Kozuka T, et al. Full-scale investigation into adverse reaction in Japan. Risk factor analysis. The Japanese Committee on the Safety of Contrast Media. *Investigational Radiology.* 1991;26 (1):S33-36. doi: 10.1097/00004424-199111001-00010

51. Namasivayam S, Kalra MK, Torres WE, et al**.** Adverse reactions to intravenous iodinated contrast media: an update. *Current Problems in Diagnostic Radiology.* 2006;35(4):164-169. doi: 10.1067/j.cpradiol.2006.04.001.

52. Fujiwara N, Tateishi R, Akahane M, et al. Changes in risk of immediate adverse reactions to iodinated contrast media by repeated administrations in patients with hepatocellular carcinoma. *PLoS One*. 2013;8(10):e76018. doi: 10.1371/journal.pone.0076018

53. Kobayashi D, Takahashi O, Ueda T, et al**.** Asthma severity is a risk factor for acute hypersensitivity reactions to contrast agents: a large-scale cohort study. *Chest.* 2012;141(5):1367-1368. doi: 10.1378/chest.11-3143.

54. Bansie RD, Karim AF, van Maaren MS, et al. Assessment of immediate and non-immediate hypersensitivity contrast reactions by skin tests and provocation tests: A review. *International Journal of Immunopathology and Pharmacology.* 2021;35:20587384211015061. doi: 10.1177/20587384211015061

55. Choyke PL, Miller DL, Lotze MT, et al**.** Delayed reactions to contrast media after interleukin-2 immunotherapy. *Radiology.* 1992;183(1):111-114. doi: 10.1148/radiology.183.1.1549655.

56. Yoon SH, Lee SY, Kang HR, et al. Skin tests in patients with hypersensitivity reaction to iodinated contrast media: a meta-analysis. *Allergy.* 2015;70(6):625-637. doi: 10.1111/all.12589

57. Brockow K, Romano A, Blanca M, et al**.** General considerations for skin test procedures in the diagnosis of drug hypersensitivity. *Allergy.* 2002;57(1):45-51.

58. Kim SH, Jo EJ, Kim MY, et al. Clinical value of radiocontrast media skin tests as a prescreening and diagnostic tool in hypersensitivity reactions. *Annals of Allergy Asthma & Immunology*. 2013;110(4):258-262. doi: 10.1016/j.anai.2013.01.004.

59. Greenberger PA, Patterson R**.** The prevention of immediate generalized reactions to radiocontrast media in high-risk patients. *Journal of Allergy and Clinical Immunology.* 1991;87(4):867-872. doi: 10.1016/0091-6749(91)90135-b.

60. Joint Task Force on Practice P, American Academy of Allergy A, Immunology, American College of Allergy A, Immunology, Joint Council of Allergy A, et al. Drug allergy: an updated practice parameter. *Annals of Allergy Asthma & Immunology.* 2010;105(4):259-273. doi: 10.1016/j.anai.2010.08.002.

61. Hasdenteufel F, Waton J, Cordebar V, et al. Delayed hypersensitivity reactions caused by iodixanol: an assessment of cross-reactivity in 22 patients. *Journal of Allergy and Clinical Immunology.* 2011;128(6):1356-1357. doi: 10.1016/j.jaci.2011.05.034.

62. Lerch M, Keller M, Britschgi M, et al. Cross-reactivity patterns of T cells specific for iodinated contrast media. *Journal of Allergy and Clinical Immunology.* 2007;119(6):1529-1536. doi: 10.1016/j.jaci.2007.02.007.

63. Keller M, Lerch M, Britschgi M, et al. Processing-dependent and -independent pathways for recognition of iodinated contrast media by specific human T cells. *Clinical and Experimental Allergy.* 2010;40(2):257-268. doi: 10.1111/j.1365-2222.2009.03425.x

64. Lerondeau B, Trechot P, Waton J, et al. Analysis of cross-reactivity among radiocontrast media in 97 hypersensitivity reactions. *Journal of Allergy and Clinical Immunology*. 2016;137(2):633-635 doi: 10.1016/j.jaci.2015.07.035

65. Brockow K**.** Immediate and delayed reactions to radiocontrast media: is there an allergic mechanism? *Immunology and Allergy Clinics of North America*. 2009;29(3):453-468. doi: 10.1016/j.iac.2009.04.001.

66. Gracia-Bara MT, Moreno E, Laffond E, et al. Tolerability of iobitridol in patients with non-immediate hypersensitivity reactions to iodinated contrast media. *Allergy.* 2019;74(1):195-197. doi: 10.1111/all.13603.

67. Torres MJ**.** Basophil activation test (BAT) in the diagnosis of immediate hypersensitivity reactions to radiocontrast media--reply. *Allergy*. 2013;68(12):1628-1629.

68. Dona I, Bogas G, Salas M, et al. Hypersensitivity Reactions to Multiple Iodinated Contrast Media. *Frontiers in Pharmacology.* 2020;11:575437. doi: 10.3389/fphar.2020.575437

69. Meucci E, Radice A, Fassio F, et al. Diagnostic approach to hypersensitivity reactions to iodinated contrast media: a single-center experience on 98 patients. *European Annals of Allergy and Clinical Immunology.* 2020;52(5):220-229. doi: 10.23822/EurAnnACI.1764-1489.129.

70. Kwon OY, Lee JH, Park SY, et al. Novel Strategy for the Prevention of Recurrent Hypersensitivity Reactions to Radiocontrast Media Based on Skin Testing. *The Journal of Allergy and Clinical Immunology: In Practice.* 2019;7(8):2707-2713. doi: 10.1016/j.jaip.2019.04.036.

71. Ahn YH, Koh YI, Kim JH, et al. The potential utility of iodinated contrast media (ICM) skin testing in patients with ICM hypersensitivity. *Journal of Korean Medical Science.* 2015;30(3):245-251. doi: 10.3346/jkms.2015.30.3.245

72. Trautmann A, Brockow K, Behle V, et al**.** Radiocontrast Media Hypersensitivity: Skin Testing Differentiates Allergy From Nonallergic Reactions and Identifies a Safe Alternative as Proven by Intravenous Provocation. *The Journal of Allergy and Clinical Immunology: In Practice. 2019;7(7):2218-2124.* doi: 10.1016/j.jaip.2019.04.005.

73. Mirakian R, Ewan PW, Durham SR, et al. BSACI guidelines for the management of drug allergy. *Clinical and Experimental Allergy.* 2009;39(1):43-61. doi: 10.1111/j.1365-2222.2008.03155.x.

74. Lasser EC, Berry CC, Mishkin MM, et al**.** Pretreatment with corticosteroids to prevent adverse reactions to nonionic contrast media. *AJR American Journal of Roentgenology.* 1994;162(3):523-6. doi: 10.2214/ajr.162.3.8109489.

75. Demoly P, Adkinson NF, Brockow K, et al. International Consensus on drug allergy. *Allergy*. 2014;69(4):420-437. doi: 10.1111/all.12350.

76. Lee SY, Yang MS, Choi YH, et al. Stratified premedication strategy for the prevention of contrast media hypersensitivity in high-risk patients. *Annals of Allergy Asthma & Immunology.* 2017;118(3):339-344. doi: 10.1016/j.anai.2016.11.027

77. Park SJ, Kang DY, Sohn KH, et al. Immediate Mild Reactions to CT with Iodinated Contrast Media: Strategy of Contrast Media Readministration without Corticosteroids. *Radiology.* 2018;288(3):710-716. doi: 10.1148/radiol.2018172524.

78. Abe S, Fukuda H, Tobe K, et al**.** Protective effect against repeat adverse reactions to iodinated contrast medium: Premedication vs. changing the contrast medium. *European Radiology.* 2016;26(7):2148-2154. doi: 10.1007/s00330-015-4028-1

79. Romano A, Artesani MC, Andriolo M, et al**.** Effective prophylactic protocol in delayed hypersensitivity to contrast media: report of a case involving lymphocyte transformation studies with different compounds. *Radiology*. 2002;225(2):466-470. doi: 10.1148/radiol.2251011654.