

1. BÖLÜM

ONKOLOJİDE ANTI-EMETİK TEDAVİ YAKLAŞIMLARI

Özlem DOĞAN¹

GİRİŞ

Bulantı ve kusma çoğu antikanser ilaçların ve radyoterapinin sık görülen yan etkilerinden birisidir. Hastanın yaşam kalitesini etkileyebilir ve daha sonraki tedaviye uyumun zayıf olmasına neden olabilir(1, 2). Ayrıca bulantı ve/veya kusma dehidratasyon, metabolik bozukluklar, besin eksikliği, anoreksiya, gastrointestinal yırtılmalar veya aspirasyon pnömonisine neden olabilir. Hasta performansını etkileyerek hastanın fonksiyonel yeteneklerin azalmasına, öz bakımının ve mental durumunun bozulmasına yol açabilir. Hepsinin de ötesinde antikanser tedaviden vazgeçme ile sonuçlanabilir (3-5). Bu nedenle bulantı ve kusmanın önlenmesi ve tedavisi oldukça önemlidir.

KEMOTERAPİ İLİŞKİLİ BULANTI- KUSMA

Kemoterapi ilişkili bulantı kusma (KİBK) akut, gecikmiş, beklenti, şiddetli ve refrakter olarak 5 sınıfa ayrılır.

Akut başlangıçlı bulantı ve/veya kusma genellikle bazı antikanser ilaçlar uygulandıktan sonra birkaç dakika ile birkaç saat içinde meydana gelir ve ilk 24 saat içinde sona erer. Yoğunluğu 5-6 saat içinde pik yapar(6).

Geç başlangıçlı bulantı ve/veya kusma antikanser ilaçlar uygulandıktan 24 saat sonra gelişir ve 2-3 günde pik yapar(7, 8). Yaygın olarak sisplatin, carboplatin, siklofosamid ve/veya antrasiklin gibi yüksek emetojenik antikanser ilaçların uygulanmasından sonra ortaya çıkar.

Kemoterapi ilişkili beklenti bulantı ve/veya kusması hastalar gelecek tedavilerini almadan önce oluşur. Daha önce KİBK deneyimleyen bir hastada

¹ Uzm. Dr., Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, Tıbbi Onkoloji Kliniği
drozlemdogan@hotmail.com

SONUÇ

KİBK birçok organ ve nörotransmitter arasında karmaşık bir etkileşim ile ortaya çıkar. Aynı şekilde bulantı ve kusma kontrolü içinde farklı yollardan etki eden birçok antiemetik ajana ihtiyaç vardır. Günümüzde kullanılan farklı tedavi kombinasyonlarına rağmen hastalarda emezis tam olarak engellenememektedir. Bu nedenle mümkün olan optimal, en uygun maliyetli antiemetik tedaviyi sağlayabilmek için araştırmalar devam etmektedir.

KAYNAKLAR

1. Navari RM, Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. *New England Journal of Medicine*. 2016;374:1356-1367.
2. McDonagh M, Peterson K, Thakurta S. Consideration of evidence on antiemetic drugs for nausea and vomiting associated with chemotherapy or radiation therapy in adults. 2014.
3. Laszlo J. Emesis as limiting toxicity in cancer chemotherapy. Williams & Wilkins, Baltimore. 1983.
4. Ettinger DS, Armstrong DK, Barbour S, et al. Antiemesis. *Journal of the National Comprehensive Cancer Network*. 2012;10:456-485.
5. Richardson JL, Marks G, Levine A. The influence of symptoms of disease and side effects of treatment on compliance with cancer therapy. *Journal of Clinical Oncology*. 1988;6:1746-1752.
6. Warr DG, Street JC, Carides AD. Evaluation of risk factors predictive of nausea and vomiting with current standard-of-care antiemetic treatment: analysis of phase 3 trial of aprepitant in patients receiving adriamycin-cyclophosphamide-based chemotherapy. *Supportive Care in Cancer*. 2011;19:807-813.
7. Kris MG, Gralla RJ, Clark RA, et al. Incidence, course, and severity of delayed nausea and vomiting following the administration of high-dose cisplatin. *Journal of Clinical Oncology*. 1985;3:1379-1384.
8. Roila F, Boschetti E, Tonato M, et al. Predictive factors of delayed emesis in cisplatin-treated patients and antiemetic activity and tolerability of metoclopramide or dexamethasone. A randomized single-blind study. *American journal of clinical oncology*. 1991;14:238-242.
9. Moher D, Arthur AZ, Pater JL. Anticipatory nausea and/or vomiting. *Cancer treatment reviews*. 1984;11:257-264.
10. Jacobsen PB, Redd WH. The development and management of chemotherapy-related anticipatory nausea and vomiting. *Cancer investigation*. 1988;6:329-336.
11. Morrow GR. Clinical characteristics associated with the development of anticipatory nausea and vomiting in cancer patients undergoing chemotherapy treatment. *Journal of Clinical Oncology*. 1984;2:1170-1176.
12. Roila F, Molassiotis A, Herrstedt J, et al. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy-and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. *Annals of Oncology*. 2016;27:119-133.
13. Roila F, Hesketh PJ, Herrstedt J. Prevention of chemotherapy-and radiotherapy-induced emesis: results of the 2004 Perugia International Antiemetic Consensus Conference. *Annals of oncology: official journal of the European Society for Medical Oncology*. 2005;17:20-28.
14. Janelins MC, Tejani MA, Kamen C, et al. Current pharmacotherapy for chemotherapy-induced nausea and vomiting in cancer patients. *Expert opinion on pharmacotherapy*. 2013;14:757-766.
15. Darmani NA. Mechanisms of broad-spectrum antiemetic efficacy of cannabinoids against chemotherapy-induced acute and delayed vomiting. *Pharmaceuticals*. 2010;3:2930-2955.

16. Borison HL. Physiology and pharmacology of vomiting. *Pharmacol Rev.* 1953;5:193-230.
17. Seigel LJ, Longo DL. The control of chemotherapy-induced emesis. *Annals of Internal Medicine.* 1981;95:352-359.
18. Dodds LJ. The control of cancer chemotherapy-induced nausea and vomiting. *Journal of Clinical Pharmacy and Therapeutics.* 1985;10(2):143-66.
19. Rapoport BL. Delayed chemotherapy-induced nausea and vomiting: pathogenesis, incidence, and current management. *Frontiers in pharmacology.* 2017;8:19.
20. Ahrari S, Chow R, Goodall S, DeAngelis C. Anticipatory nausea: current landscape and future directions. 2017.
21. Roscoe JA, Morrow GR, Aapro MS, Molassiotis A, Olver I. Anticipatory nausea and vomiting. *Supportive Care in Cancer.* 2011;19(10):1533-8.
22. Molassiotis A, Aapro M, Dicato M, Gascon P, Novoa SA, Isambert N, et al. Evaluation of risk factors predicting chemotherapy-related nausea and vomiting: results from a European prospective observational study. *Journal of pain and symptom management.* 2014;47(5):839-48. e4.
23. Hesketh PJ, Aapro M, Street JC, Carides AD. Evaluation of risk factors predictive of nausea and vomiting with current standard-of-care antiemetic treatment: analysis of two phase III trials of aprepitant in patients receiving cisplatin-based chemotherapy. *Supportive care in cancer.* 2010;18(9):1171-7.
24. Craig JB, Powell BL. The management of nausea and vomiting in clinical oncology. *The American journal of the medical sciences.* 1987;293(1):34-44.
25. Laszlo J. Treatment of nausea and vomiting caused by cancer chemotherapy. *Cancer treatment reviews.* 1982;9:3-9.
26. Grunberg SM, Osoba D, Hesketh PJ, Gralla RJ, Borjeson S, Rapoport BL, et al. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity—an update. *Supportive care in cancer.* 2005;13(2):80-4.
27. Rao KV, Faso A. Chemotherapy-induced nausea and vomiting: optimizing prevention and management. *American health & drug benefits.* 2012;5(4):232.
28. Aapro M, Grunberg S, Manikhas G, Olivares G, Suarez T, Tjulandin S, et al. A phase III, double-blind, randomized trial of palonosetron compared with ondansetron in preventing chemotherapy-induced nausea and vomiting following highly emetogenic chemotherapy. *Annals of oncology.* 2006;17(9):1441-9.
29. Roila F. Ondansetron versus granisetron, both combined with dexamethasone, in the prevention of cisplatin-induced emesis. *Annals of Oncology.* 1995;6(8):805-10.
30. Ruff P, Paska W, Goedhals L, et al. Ondansetron Compared with Granisetron in the Prophylaxis of Cisplatin-Induced Acute Emesis: A Multicentre Double-Blind, Randomised, Parallel-Group Study. *Oncology.* 1994;51:113-118.
31. Geling O, Eichler H-G. Should 5-hydroxytryptamine-3 receptor antagonists be administered beyond 24 hours after chemotherapy to prevent delayed emesis? Systematic re-evaluation of clinical evidence and drug cost implications. *Journal of Clinical Oncology.* 2005;23:1289-1294.
32. Hickok JT, Roscoe JA, Morrow GR, et al. 5-Hydroxytryptamine-receptor antagonists versus prochlorperazine for control of delayed nausea caused by doxorubicin: a URCC CCOP randomised controlled trial. *The lancet oncology.* 2005;6:765-772.
33. Jordan K, Hinke A, Grothey A, et al. A meta-analysis comparing the efficacy of four 5-HT₃-receptor antagonists for acute chemotherapy-induced emesis. *Supportive Care in Cancer.* 2007;15:1023-1033.
34. Billio A, Morello E, Clarke MJ. Serotonin receptor antagonists for highly emetogenic chemotherapy in adults. *Cochrane Database of Systematic Reviews.* 2010.
35. Botrel TEA, Clark OAC, Clark L, et al. Efficacy of palonosetron (PAL) compared to other serotonin inhibitors (5-HT₃ R) in preventing chemotherapy-induced nausea and vomiting

- (CINV) in patients receiving moderately or highly emetogenic (MoHE) treatment: systematic review and meta-analysis. *Supportive Care in Cancer*. 2011;19:823-832.
36. Spartinou A, Nyktari V, Papaioannou A. Granisetron: a review of pharmacokinetics and clinical experience in chemotherapy induced-nausea and vomiting. *Expert opinion on drug metabolism & toxicology*. 2017;13:1289-1297.
 37. Brygger L, Herrstedt J, Research AoGC. 5-Hydroxytryptamine₃ receptor antagonists and cardiac side effects. *Expert opinion on drug safety*. 2014;13:1407-1422.
 38. Charbit B, Albaladejo P, Funck-Brentano C, et al. Prolongation of QTc interval after postoperative nausea and vomiting treatment by droperidol or ondansetron. *The Journal of the American Society of Anesthesiologists*. 2005;102:1094-1100.
 39. Freedman SB, Uleryk E, Rumantir M, et al. Ondansetron and the risk of cardiac arrhythmias: a systematic review and postmarketing analysis. *Annals of emergency medicine*. 2014;64:19-25.
 40. Tricco AC, Soobiah C, Antony J, et al. Safety of serotonin (5-HT₃) receptor antagonists in patients undergoing surgery and chemotherapy: protocol for a systematic review and network meta-analysis. *Systematic reviews*. 2013;2:1-5.
 41. Diemunsch P, Grélot L. Potential of substance P antagonists as antiemetics. *Drugs*. 2000;60:533-546.
 42. Rapoport B, Schwartzberg L, Chasen M, et al. Efficacy and safety of rolapitant for prevention of chemotherapy-induced nausea and vomiting over multiple cycles of moderately or highly emetogenic chemotherapy. *European Journal of Cancer*. 2016;57:23-30.
 43. Gralla RJ, De Wit R, Herrstedt J, et al. Antiemetic efficacy of the neurokinin-1 antagonist, aprepitant, plus a 5HT₃ antagonist and a corticosteroid in patients receiving anthracyclines or cyclophosphamide in addition to high-dose cisplatin: analysis of combined data from two phase III randomized clinical trials. *Cancer*. 2005;104:864-868.
 44. Hesketh PJ, Grunberg SM, Gralla RJ, et al. The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a multinational, randomized, double-blind, placebo-controlled trial in patients receiving high-dose cisplatin—the Aprepitant Protocol 052 Study Group. *Journal of Clinical Oncology*. 2003;21:4112-4119.
 45. Zhang L, Lu S, Feng J, et al. A randomized phase III study evaluating the efficacy of single-dose NEPA, a fixed antiemetic combination of netupitant and palonosetron, versus an aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC). *Annals of Oncology*. 2018;29:452-458.
 46. Rapoport B, Chua D, Poma A, et al. Study of rolapitant, a novel, long-acting, NK-1 receptor antagonist, for the prevention of chemotherapy-induced nausea and vomiting (CINV) due to highly emetogenic chemotherapy (HEC). *Supportive Care in Cancer*. 2015;23:3281-3288.
 47. Poli-Bigelli S, Rodrigues-Pereira J, Carides AD, et al. Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting: results from a randomized, double-blind, placebo-controlled trial in Latin America. *Cancer*. 2003;97:3090-3098.
 48. Chawla SP, Grunberg SM, Gralla RJ, et al. Establishing the dose of the oral NK1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2003;97:2290-2300.
 49. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. *Journal of Clinical Oncology*. 2011;29:4189.
 50. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. *Journal of Clinical Oncology*. 2017;35:3240-3261.
 51. Navari RM, Qin R, Ruddy KJ, et al. Olanzapine for the prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC): Alliance A221301, a randomized, double-blind, placebo-controlled trial. *American Society of Clinical Oncology*; 2015.

52. Muench J, Hamer AM. Adverse effects of antipsychotic medications. *American family physician*. 2010;81:617-622.
53. Mustian KM, Darling TV, Janelins MC, et al. Chemotherapy-induced nausea and vomiting. *US oncology*. 2008;4:19.
54. Marx W, Isenring EA, Lohning AE. Determination of the concentration of major active anti-emetic constituents within commercial ginger food products and dietary supplements. *European Journal of Integrative Medicine*. 2017;10:19-24.
55. Mustian KM, Devine K, Ryan JL, et al. Treatment of nausea and vomiting during chemotherapy. *US oncology & hematology*. 2011;7:91.
56. Feyer PC, Maranzano E, Molassiotis A, et al. Radiotherapy-induced nausea and vomiting (RINV): MASCC/ESMO guideline for antiemetics in radiotherapy: update 2009. *Supportive Care in Cancer*. 2011;19:5-14.
57. McKenzie E, Zaki P, Raman S, et al. Radiation-induced nausea and vomiting: a comparison between MASCC/ESMO, ASCO, and NCCN antiemetic guidelines. *Supportive Care in Cancer*. 2019;27:783-791.
58. Ruhlmann CH, Jahn F, Jordan K, et al. 2016 updated MASCC/ESMO consensus recommendations: prevention of radiotherapy-induced nausea and vomiting. *Supportive Care in Cancer*. 2017;25:309-316.
59. Roila F, Herrstedt J, Aapro M, et al. ESMO/MASCC Guidelines Working Group: Guideline update for MASCC and ESMO in the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting: results of the Perugia consensus conference. *Ann Oncol*. 2010;21:232-243.