

ANTİDEPRESAN İLAÇ ZEHİRLENMELERİ

İrfan BASMACI¹

Giriş

Antidepresan ilaçlar birçok endikasyonla yaygın olarak reçete edilmektedir. Antidepresan ilaçlar; selektif serotonin reuptake inhibitörleri (SSRI), trisiklik antidepresanlar (TSA), monoamin oksidaz inhibitörleri (MAOI), atipik antidepresanlar (heterosiklikler) olmak üzere dört grupta incelenebilirler (1). Lityum bu sınıflandırmanın dışındadır. Bu bölümde bipolar bozuklukta atak ve idame tedavisinde kullanılan bir duygudurum dengeleyici olan lityum zehirlenmesine de yer verilmiştir.

Amerika Zehir Danışma Merkezleri Birliğinin (American Association of Poison Control Centers; AAPCC) 2018 yılında yayınladığı raporda; antidepresan ilaçlarla zehirlenme oranı %5.22 vaka sayısı 132,807 olarak beşinci sırada bildirilmiştir. Son 10 yılda maruziyet artışı en hızlı olan grubun yılda 1.887 vaka ile antidepresanlar olduğu raporlanmıştır (2). Antidepresan ilaçlarla olan zehirlenmelerde risk değerlendirilmesi ADORA(Antidepressant Overdose Risk Assessment) kriterleri ile yapılmaktadır (Tablo 1'de). Zehirlenmeden sonraki altı saat içinde bir ve üzerindeki sayılarda kriterin varlığı morbidite ve mortalite açısından yüksek riskli, Hiç kriter olmaması düşük riskli olarak kabul edilmektedir (3).

¹ Uzm. Dr. İrfan BASMACI, Yedikule Surp Pırgiç Ermeni Hastanesi, Ruh Sağlığı ve Hastalıkları Bölümü, irfanbasmaci@gmail.com

Lityum terapötik aralığı dar bir ilaçtır, zehirlenme durumlarında hidrasyon ve hemodiyaliz en etkili tedavi yöntemleridir.

KAYNAKLAR

1. Baldessarini RJ. Drug therapy of depression and anxiety disorders. In: Brunton LL, Lazo JS, Parker K, eds. Goodman & Gilman's, The Pharmacological Basis of Therapeutics 11th ed. USA: McGraw-Hill Companies; 2005. p.429-59.
2. Gummin DD, Mowry JB, Spyker DA et al. 2018 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 36th Annual Report. Clin Toxicol (Phila). 2019 Dec;57(12):1220-1413. doi: 10.1080/15563650.2019.1677022. Epub 2019 Nov 21. Erratum in: Clin Toxicol (Phila). 2019 Dec;57(12):e1. PMID: 31752545.
3. Açıkalın A, Gülen M, Acehan S ve ark. Her Supraventriküler Taşikardi Kardiyojenik Değildir: Olgu Sunumu. Akademik Acil Tıp Olgu Sunumları Dergisi. 2011;2(4):39-42.
4. Small GW. Treatment of Geriatric Depression. Depress Anxiety. 1998;8 Suppl 1:32-42. PMID: 9809212.
5. Baldessarini RJ. Drugs and the treatment of psychiatric disorders. In: Hardman JG, Limbird LE, Molinoff PB, et al. editors. Goodman and Gilman's the pharmacological basis of therapeutics. 9th ed. New York: McGraw-Hill Press, 1996. p. 431-59.
6. Gareri P, De Fazio P, De Fazio S et al. Adverse effects of atypical antipsychotics in the elderly: a review. Drugs Aging. 2006;23(12):937-56. doi: 10.2165/00002512-200623120-00002. PMID: 17154659.
7. Baldessarini RJ. Current status of antidepressants: clinical pharmacology and therapy. J Clin Psychiatry 1989; 50: 117-26.
8. Ellenhorn EL, Francis PD. Cyclic Antidepressants. In: Goldfrank LR, Flomenbaum NM, Lewin NA, Howland MA, Hoffman RS, Nelson LS, eds. Goldfrank's Toxicology Emergencies. 7th ed. USA: McGraw-Hill Companies; 2002. p.847-64.
9. Ellenhorn MJ. Cyclic Antidepressants. In: Ellenhorn MJ, Schonwald S, Ordog G, Wasserberger J, eds. Ellenhorn's Medical Toxicology. 2nd ed. USA: Williams and Wilkins; 1997. p.624-36.
10. Benowitz NL. Antidepressants, Tricyclic. In: Olson KR, editors. Poisoning and Drug Overdose. 4th ed. USA: USA: Connecticut; 2004. p.90-3.
11. Ellenhorn MJ. Antidepressant agents. In: Ellenhorn MJ, Schonwald S, Ordog G, Wasserberger J, eds. Ellenhorn's Medical Toxicology. 2nd ed. USA: Williams and Wilkins; 1997. p.615-23.
12. Kalkan Ş. Antidepressanlarla zehirlenme. Türk Farmakoloji Derneği, 20. Ulusal Farmakoloji Kongresi, 3. Klinik Toksikoloji Sempozyumu, 4.Klinik Farmakoloji Sempozyumu Kongre Programı ve Bildiri Özet Kitabı. Antalya. 2009: 28-35
13. Newton EH, Shih RD, Hoffman RS. Cyclic antidepressant overdose: a review of current management strategies. Am J Emerg Med. 1994 May;12(3):376-9. doi: 10.1016/0735-6757(94)90165-1. PMID: 8179756.

14. Harrigan RA, Brady WJ. ECG abnormalities in tricyclic antidepressant ingestion. *Am J Emerg Med.* 1999 Jul;17(4):387-93. doi: 10.1016/s0735-6757(99)90094-3. PMID: 10452441.
15. Liebelt, EL. Cyclic antidepressants. In Goldfrank's Toxicology Emergencies. 8th ed. (Eds NE Flomenbaum, LR Goldfrank, RS Hoffman, MA Howland, NA Lewin, LS Nelson):1083-98. New York, McGraw-Hill, 2006.
16. İçme F. Kalp etkilenmesine sebep olan antikolinergik ilaç zehirlenmelerinde sodyum bikarbonat tedavisinin etkinliğinin karşılaştırılması (Tıpta uzmanlık tezi). Adana, Çukurova Üniversitesi. 2006.
17. Klasco RK, ed: POISINDEX® System. Thomson Micromedex, Greenwood Village, Colorado Vol. 129, expires 9/2006.
18. Aslan Ş, Emet M, Çakır Z ve ark. Suicide attempts with amitriptyline in adults: A prospective, demographic, clinical study. *Turk J Med Sci.* 2011;41:243-9.
19. Kerr GW, McGuffie AC, Wilkie S. Tricyclic antidepressant overdose: a review. *Emerg Med J.* 2001;18:236-41.
20. Ünverir P. Acil serviste trisiklik antidepresan zehirlenmeleri: Kritik hastalar. *Türkiye Acil Tıp Dergisi.* 2007;7:86-95.
21. Şahin G, Giray B, Erkekoğlu P. Trisiklik antidepresanlarla zehirlenmelerde tedavi yaklaşımları. *Türkiye Klinikleri J Med Sci.* 2008;28:533-43.
22. Tran TP, Panacek EA, Rhee KJ et al. Response to dopamine vs norepinephrine in tricyclic antidepressant-induced hypotension. *Acad Emerg Med.* 1997 Sep;4(9):864-8. doi: 10.1111/j.1553-2712.1997.tb03811.x. PMID: 9305427.
23. Wyse DG, Waldo AL, DiMarco JP et al. Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med.* 2002 Dec 5;347(23):1825-33. doi: 10.1056/NEJMoa021328. PMID: 12466506.
24. Nichol G, McAlister F, Pham B et al. Meta-analysis of randomised controlled trials of the effectiveness of antiarrhythmic agents at promoting sinus rhythm in patients with atrial fibrillation. *Heart.* 2002 Jun;87(6):535-43. doi: 10.1136/heart.87.6.535. PMID: 12010934; PMCID: PMC1767130.
25. Mills KC. Tricyclic antidepressants. In *Emergency Medicine A Comprehensive Study Guide*, 6th ed (Eds JE Tintinalli, G Kelen, JS Stapczynski):1025-33. New York, McGraw-Hill, 2004.
26. Bigwood B, Galler D, Amir N et al. Brugada syndrome following tricyclic antidepressant overdose. *Anaesth Intensive Care.* 2005 Apr;33(2):266-70. doi: 10.1177/0310057X0503300219. PMID: 15960413.
27. Denizbaşı A. Kokain zehirlenmesi ve intravenöz lipid emülsiyon tedavisi. Erişim Adresi: <http://www.acilci.net/denizbasi-kokain-zehirlenmesi-ve-intravenoz-lipid-emulsiyon-tedavisi/> (Erişim Tarihi: 27.12.2020)
28. Hendron D, Menagh G, Sandilands EA et al. Tricyclic antidepressant overdose in a toddler treated with intravenous lipid emulsion. *Pediatrics.* 2011 Dec;128(6):e1628-32. doi: 10.1542/peds.2011-0867. Epub 2011 Nov 7. PMID: 22065274.

29. Yates C, Galvao T, Sowinski KM et al. EXTRIP workgroup. Extracorporeal treatment for tricyclic antidepressant poisoning: recommendations from the EXTRIP Workgroup. *Semin Dial.* 2014 Jul-Aug;27(4):381-9. doi: 10.1111/sdi.12227. Epub 2014 Apr 9. PMID: 24712820; PMCID: PMC4282541.
30. Stork CM. Serotonin reuptake inhibitors and atypical antidepressants. In: Goldfrank LR, Flomenbaum NM, Lewin NA, Howland MA, Hoffman RS, Nelson LS, eds. *Goldfrank's Toxicology Emergencies*, 7th ed. USA: McGraw-Hill Companies; 2002. p. 847-64.
31. Thorsson B, Snook C, Thorgeirsson G. Survival after prolonged cardiac arrest from venlafaxine (abstract), European Association of Poisons Centres and Clinical Toxicologists. XX International Congress, Amsterdam, The Netherlands, 2000.
32. Shaw MW, Sheard JDH Fatal venlafaxine overdose with acinar zone 3 liver cell necrosis. *Am J Forensic Med Pathol* 2005;26:367-8.
33. Benowitz NL. Antidepressants, general (noncyclic). In: Olson, KR, eds. *Poisoning and Drug Overdose*. 4th ed. USA: Connecticut; 2004. p.88-90.
34. Engebretsen KM, Harris CR, Wodd JE. Cardiotoxicity and late onset seizures with citalopram overdose. *J Emerg Med* 2003;25:163-6.
35. Rothenhausler HB, Haberl C, Ehrentroust S et al. Suicide attempt by pure citalopram overdose causing long-lasting severe sinus bradycardia, hypotension and syncope: successful therapy with a temporary pacemaker. *Pharmacopsychiatry* 2000;33:150-2.
36. Isbister GK, Bowe SJ, Dawson A et al. Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose. *J Toxicol Clin Toxicol.* 2004;42(3):277-85. doi: 10.1081/clt-120037428. PMID: 15362595
37. Mason PJ, Morris VA, Balczak TJ Serotonin syndrome. Presentation of 2 cases and review of the literature. *Medicine (Baltimore)* 2000; 79: 201-209
38. Dunkley EJ, Isbister GK, Sibbritt D et al. The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *QJM.* 2003 Sep;96(9):635-42. doi: 10.1093/qjmed/hcg109. PMID: 12925718.
39. Sternbach H. The serotonin syndrome. *Am J Psychiatry.* 1991 Jun;148(6):705-13. doi: 10.1176/ajp.148.6.705. PMID: 2035713.
40. Gillman PK. The serotonin syndrome and its treatment. *J Psychopharmacol.*1999;13(1):100-9. doi: 10.1177/026988119901300111. PMID: 10221364.
41. Nisijima K, Yoshino T, Yui K, et al. Potent serotonin (5-HT)(2A) receptor antagonists completely prevent the development of hyperthermia in an animal model of the 5-HT syndrome. *Brain Res.* 2001 Jan 26;890(1):23-31. doi:10.1016/s0006-8993(00)03020-1. PMID: 11164765
42. Brown TM, Skop BP, Mareth TR. Pathophysiology and management of the serotonin syndrome. *Ann Pharmacother.* 1996 May;30(5):527-33. doi: 10.1177/106002809603000517. PMID: 8740336.
43. Martin TG. Serotonin syndrome. *Ann Emerg Med.* 1996 Nov;28(5):520-6. doi: 10.1016/s0196-0644(96)70116-6. PMID: 8909274.

44. Sporer KA. The serotonin syndrome. Implicated drugs, pathophysiology and management. *Drug Saf.* 1995 Aug;13(2):94-104. doi: 10.2165/00002018-199513020-00004. PMID: 7576268.
45. Lappin RI, Auchincloss EL Treatment of the serotonin syndrome with cyproheptadine. *N Engl J Med.* 1994 Oct 13;331(15):1021-2. doi: 10.1056/NEJM199410133311514. PMID: 8084345.
46. Parrott AC. Recreational Ecstasy/MDMA, the serotonin syndrome, and serotonergic neurotoxicity. *Pharmacol Biochem Behav.* 2002 Apr;71(4):837-44. doi: 10.1016/s0091-3057(01)00711-0. PMID: 11888574
47. Benowitz NL. Monoamin oxidase inhibitors In: Olson KR, eds. *Poisoning and Drug Overdose.* 4th ed. USA: Connecticut; 2004. p.269-71.
48. Meltzer E, Steinlauf S. The clinical manifestations of lithium intoxication. *Isr Med Assoc J* 2002; 4:265-267.
49. Peces R, Fernández EJ, Regidor D et al. Tratamiento de la intoxicación aguda por litio mediante hemodiálisis con dializadores de alta eficiencia [Treatment of acute lithium intoxication with high-flux haemodialysis membranes]. *Nefrologia.* 2006;26(3):372-8.
50. De Haro L, Roelandt J, Pommier P et al. Aetiologies of lithium overdose: 10-year experience of Marseille poison centre. *Ann Fr Anesth Reanim* 2003; 22:514-519.
51. Oakley PW, Whyte IM, Carter GL. Lithium toxicity: an iatrogenic problem in susceptible individuals. *Austr N Z J Psychiatry* 2001; 35:833-840.
52. Schou M. The recognition and management of lithium intoxication. In *Handbook of Lithium Therapy* (Ed M Schou):394-402. Lancaster, England, MTP Press, 1980.
53. Shopsin B, Gershon S. Pharmacology-toxicology of the lithium ion. In *Lithium: Its Role in Psychiatric Research and Treatment* (Eds S Gershon, B Shopsin):107-146. New York, Plenum, 1973.
54. S, Akdeniz F, Vahip S. Lityum zehirlenmesi. *Psikiyatri, Psikoloji, Psikofarmakoloji Dergisi* 2003;11:316-324.
55. Chakrabarti S, Chand PK. Lithium - induced tardive dystonia. *Neurol India* 2002; 50:473-475.
56. Porto FH, Leite MA, Fontenelle LF, et al. The Syndrome of Irreversible Lithium-Effectuated Neurotoxicity (SILENT): one-year follow-up of a single case. *J Neurol Sci.* 2009 Feb 15;277(1-2):172-3. doi: 10.1016/j.jns.2008.10.010. Epub 2008 Nov 30. PMID: 19046589.
57. Jefferson JW, Greist JH, Ackerman DL *Lithium Encyclopedia for Clinical Practice.* 2nd ed. Washington DC, American Psychiatric Press, 1987.
58. Serinken M, Karcioğlu O, Korkmaz A. Rarely seen cardiotoxicity of lithium overdose: complete heart block. *Int J Cardiol* 2009; 132:276-278.
59. Hansen HE, Amdisen A. Lithium intoxication. (Report of 23 cases and review of 100 cases from the literature). *Q J Med* 1978; 47:123-144.
60. Hauger RL, O'Connor KA, Yudofsky S. Lithium Toxicity: When is hemodialysis necessary? *Acta Psychiatr Scand* 1990; 81:515-517.

61. Apte SN, Langston JW. Permanent neurological deficits due to lithium toxicity. *Ann Neurol* 1983; 13:453-455.
62. Camus M, Hennere G, Baron G et al. Comparison of lithium concentrations in red blood cells and plasma in samples collected for TDM, acute toxicity, or acute-on-chronic toxicity. *Eur J Clin Pharmacol* 2003; 59:583-587.
63. Schou M, Amedisim A, Trap-Jensen J. Lithium poisoning. *Am J Psychiatry* 1968; 125:520-527.
64. Derinoz O, Unlusoy A, Kanburođlu K. Etkili sıvı tedavisine yanıt veren lityum zehirlenmesi. *Türkiye Çocuk Hastalıkları Dergisi* 2009; 3(4):53-56.
65. Scharman EJ. Methods used to decrease lithium absorption or enhance elimination. *Clin Toxicol* 1997; 35:601-608.
66. Teece S, Crawford I. Best evidence topic report: no clinical evidence for gastric lavage in lithium overdose. *Emerg Med J* 2005; 22:43-44.
67. Nielsen JB, Vestergaard P. Lithium intoxication: assessment, treatment and prevention. *Ugeskr Laeger* 2007; 169:522.
68. Kes P, Basić Jukić N. New experiences with the therapy of acute kidney injury. *Pri-lozi* 2008; 29:119-153.
69. Meertens JH, Jagernath DR, Eleveld DJ. Haemodialysis followed by continuous veno-venous haemodiafiltration in lithium intoxication; a model and a case. *Eur J Intern Med* 2009; 20:70-73.