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TANIM

Dispepsi toplumda oldukça sık görülen ve pek çok nedene bağlı ortaya çıkabilen heterojen semptomlar topluluğudur. Proksimal gastrointestinal sistemden kaynaklandığı düşünülen, üst abdomende lokalize epigastrik ağrı, yanma, dolgunluk ve erken doyma ile karakterizedir. Dispepsi olgularında şişkinlik, geğirme, bulantı, pirozis gibi semptomlar eşlik edebilir. Ancak bunlar dispepsi tanımı içinde yer almaz (1). Roma I ve II uzlaşma komitelerinde dispepsi üst karın bölgesinde yoğunlaşan ağrı ve rahatsızlık hissi olarak tanımlanmıştır. Şişkinlik, erken doyma, epigastrik yanma, bulantı-kusma semptomları da rahatsızlık hissi bünyesinde kabul edilmiştir. Roma II uzlaşma komitesinde farklı olarak epigastrik yanma baskın hastalar dispepsi tanımından çıkarılmış ve gastroözofageal reflü başlığında tanımlanmıştır (2). Roma III ve Roma IV uzlaşma komitelerinde dispepsiyi tanımlarken 'sadece gastroduodenal' bölgeden kaynaklanan semptomlar ele alınarak geçmişteki tanımlamaya nazaran daha kısıtlayıcı bir rapor sunulmuştur. Sadece erken doyma, postprandial dolgunluk, epigastrik yanma veya ağrının spesifik olarak gastroduodenal bölge kaynaklı olduğu kabul edilmiştir (3).

Dispepsi genel popülasyonun yaklaşık %20-32'sinde gözlenir. Popülasyon bazlı 100 çalışmayı kapsayan 312415 vakada araştırılmamış dispepsi için havuzlanmış prevalans %21 olarak saptanmıştır. Kadınlarda, H.pylori enfeksiyonunda, sigara içenlerde ve nonsteroid antiinflatuar ilaç kullananlarda dispepsi için risk artışı vardır (1). Dispepsi vakalarının yaklaşık %25'ini altta organik bir neden saptanan organik dispepsi (Tablo 1) oluştururken %75'ini ise gastroskopi dahil yapılan tüm klinik araştırmalara rağmen herhangi bir etyoloji saptanamayan fonksiyonel dispepsi oluşturmaktadır (4).

Organik Dispepsi

Peptik ülser hastalığı ve gastroözofageal reflü en sık iki organik dispepsi nedenidir. Çölyak hastalığı, üst gastrointestinal sistem(GIS) tümörleri, infiltratif hastalıklar, pankreas patolojileri, endokrin bozukluklar, ilaçlar ve gıda intoleransı diğer başlıca etyolojik nedenlerdir (Tablo 1) (5).

Peptik Ülser Hastalığı: Peptik ülser hastalarında sıklıkla yemeklerden birkaç saat sonra şiddetlenen ağrı ve yanma görülür. Ülseri olan hastalar tamamen asemptomatik olabileceği gibi dispeptik şikayetlerle de doktora başvurabilirler. Peptik ülser

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peptik semptom şiddeti ve hayat kalitesi üzerinde olumlu etki alınmıştır (92). Ancak psikososyal tedaviler ile ilgili verilerin kalitesi düşük, çalışmalar heterojen ve bias riski taşımaktadır. Bu nedenle rutin kullanıma girmesi için daha çok çalışma ve kanıtı ihtiyaç vardır.

SONUÇ

Dispepsi, toplumda oldukça sık görülen bir semptom olup öncelikle organik- fonksiyonel ayırımı yapılmalıdır. Dispepsi vakalarının büyük kısmını oluşturan fonksiyonel dispepsi hastalar, sağlık kuruluşları ve toplum için önemli mali etkilere sahiptir. Bu nedenle hekimlerin fonksiyonel dispepsiyi tanıyabilmeleri, araştırmaları ve tanı testlerini dikkatli bir şekilde kullanabilmeleri ve etkili tedaviler önerebilmeleri önemlidir. Semptomlara ve müdahalelere verilen yanıtlara dayalı bireyselleştirilmiş tedavi çok önemlidir. FD'nin anlaşılmasını iyileştirmek ve etkili tedavilerin geliştirilmesini sağlamak için daha fazla araştırmaya ihtiyaç vardır. Günümüzde fonksiyonel dispepside semptom bazlı tanı konulmakta ve hastalara semptomaya yönelik tedavi verilmektedir. Ne yazık ki mevcut seçenekler ile tedavi başarısının yeterli olmadığı önemli bir hasta grubu bulunmaktadır. Gelecekte geliştirilecek olan mekanizma bazlı stratejiler ile patofizyolojiyi hedef alan tedavi seçenekleri ile daha etkin ve başarılı sonuçlar elde edilmesi olasıdır.

KAYNAKLAR

1. Tack J, Bisschops R, Sarnelli G. Pathophysiology and treatment of functional dyspepsia. *Gastroenterology*. 2004;127(4):1239-1255. doi: 10.1053/j.
2. Drossman DA, Thompson GW, Talley NJ, et al. Identification of subgroups of functional gastrointestinal disorders. *Gastroenterology International*. 1990;3:159-172.
3. Schmulson MJ, Drossman DA. What Is New in Rome IV. *Journal of Neurogastroenterology and Motility*. 2017;23(2):151-163. doi: 10.5056/jnm16214.
4. Ford AC, Marwaha A, Lim A, Moayyedi P. What is the prevalence of clinically significant endoscopic findings in subjects with dyspepsia? Systematic review and meta-analysis. *Clinical Gastroenterology and Hepatology*. 2010;8(10): 830-837, doi: 10.1016/j.cgh.2010.05.031.
5. Sayuk GS, Gyawali CP. Functional Dyspepsia: Diagnostic and Therapeutic Approaches. *Drugs*. 2020;80(13): 1319-1336. doi: 10.1007/s40265-020-01362-4.
6. Moayyedi P, Talley NJ, Fennerty MB, et al. Can the clinical history distinguish between organic and functional dyspepsia? *JAMA*. 2006;5;295(13): 1566-1576. doi: 10.1001/jama.295.13.1566.
7. Vakil N, Moayyedi P, Fennerty MB, et al. Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy: systematic review and meta-analysis. *Gastroenterology*. 2006;131(2): 390-401;doi: 10.1053/j.gastro.2006.04.029.
8. Sleisenger's and Fordtrans's Gastrointestinal and liver disease, 10th Edirion, 2016
9. Feinle-Bisset C, Vozzo R, Horowitz M, et al. Diet, food intake, and disturbed physiology in the pathogenesis of symptoms in functional dyspepsia. *American Journal of Gastroenterology*. 2004;99(1): 170-81. doi: 10.1111/j.1572-0241.2004.04003.x.
10. Bytzer P. Dyspepsia as an adverse effect of drugs. *Best Pract Res Best practice & research. Clinical gastroenterology*. 2010;24(2): 109-20. doi: 10.1016/j.bpg.2009.11.006.
11. Ofman JJ, MacLean CH, Straus WL, et al. Meta-analysis of dyspepsia and nonsteroidal anti-inflammatory drugs. *Arthritis and rheumatism*. 2003;49:508-518. doi: 10.1002/art.11192.
12. Eisen GM, Goldstein JL, Hanna DB, et al. Meta-analysis: upper gastrointestinal tolerability of valdecoxib, a cyclooxygenase-2-specific inhibitor, compared with nonspecific nonsteroidal anti-inflammatory drugs among patients with osteoarthritis and rheumatoid arthritis. *Alimentary pharmacology & therapeutics*. 2005.;21(5): 591-598. doi: 10.1111/j.1365-2036.2005.02383.x.
13. Oustamanolakis P, Tack J. Dyspepsia: organic versus functional. *Journal of clinical gastroenterology*. 2012;46(3):175-90. doi: 10.1097/MCG.0b013e318241b335.
14. Caballero-Mateos AM, Redondo Cerezo E. Dyspepsia, functional dyspepsia and Rome IV criteria. *Revista española de enfermedades digestivas*. 2018;110(8):530-531. doi: 10.17235/reed.2018.5599/2018.
15. Vanheel H, Carbone F, Valvekens L, et al. Pathophysiological Abnormalities in Functional Dyspepsia Subgroups According to the Rome III Criteria. *The American journal of gastroenterology*. 2017 ;112(1): 132-140. doi: 10.1038/ajg.2016.499.
16. Goodoory VC, Houghton LA, Black CJ, et al. Characteristics of, and natural history among, individuals with Rome IV functional bowel disorders. *Journal of neurogastroenterology and motility*. 2022 ;34(5):e14268. doi: 10.1111/nmo.14268.
17. Aziz I, Palsson OS, Törnblom H, et al. Epidemiology, clinical characteristics, and associations for symptom-based Rome IV functional dyspepsia in adults in the USA, Canada, and the UK: a cross-sectional population-based study. *he lancet. Gastroenterology & hepatology*. 2018;3(4):252-262. doi: 10.1016/S2468-1253(18)30003-
18. Palsson OS, Whitehead WE, van Tilburg MA, et al. Rome IV Diagnostic Questionnaires and Tables for Investigators and Clinicians. *Gastroenterology*. 2016;13:S0016-5085(16)00180-3. doi: 10.1053/j.gastro.2016.02.014.

19. Stanghellini V, Talley NJ, Chan F, et al. Rome IV—gastrointestinal disorders. *Gastroenterology* 2016;150:1380–1392. doi: 10.1053/j.gastro.2016.02.011.
20. Corsetti M, Caenepeel P, Fischler B, et al. Impact of coexisting irritable bowel syndrome on symptoms and pathophysiological mechanisms in functional dyspepsia. *The American journal of gastroenterology*. 2004;99: 1152–1159. doi: 10.1111/j.1572-0241.2004.30040.x.
21. Malt EA, Berle JE, Olafsson S, et al. Fibromyalgia is associated with panic disorder and functional dyspepsia with mood disorders. A study of women with random sample population controls. *Journal of psychosomatic research*. 2000;49(5): 285–289. doi: 10.1016/s0022-3999(00)00139-2. P
22. Ford AC, Marwaha A, Sood R, et al. Global prevalence of, and risk factors for, uninvestigated dyspepsia: a meta-analysis. *Gut*. 2015;64(7):1049–1057. doi: 10.1136/gutjnl-2014-307843.
23. Piessevaux H, De Winter B, Louis E, et al. Dyspeptic symptoms in the general population: a factor and cluster analysis of symptom groupings. *Neurogastroenterology & Motility*. 2009;21:378–388. doi: 10.1111/j.1365-2982.2009.01262.x.
24. Koloski NA, Talley NJ, Boyce PM. Predictors of health care seeking for irritable bowel syndrome and nonulcer dyspepsia: a critical review of the literature on symptom and psychosocial factors. *The American journal of gastroenterology*. 2001;96(5):1340–9. doi: 10.1111/j.1572-0241.2001.03789.x.
25. Lacy BE, Weiser KT, Kennedy AT. Functional dyspepsia: the economic impact to patients. *Alimentary pharmacology & therapeutics*. 2013;38(2):170–177. doi: 10.1111/apt.12355.
26. Pleyer C, Bittner H, Locke GR, et al. Overdiagnosis of gastroesophageal reflux disease and underdiagnosis of functional dyspepsia in a USA community. *Neurogastroenterology & Motility* 2014;26: 1163–1171. doi: 10.1111/nmo.12377.
27. Shajib Y, El-Serag HB. The prevalence and risk factors of functional dyspepsia in a multiethnic population in the United States. *The American journal of gastroenterology*. 2004 Nov;99(11):2210–1216. doi: 10.1111/j.1572-0241.2004.40052.x.
28. Kim SE, Park HK, Kim N, et al. Prevalence and risk factors of functional dyspepsia: a nationwide multicenter prospective study in Korea. *Journal of clinical gastroenterology*. 2014 ;48(2):e12–18. doi: 10.1097/MCG.0b013e31828f4bc9.
29. Delgado-Aros S, Camilleri M, Cremonini F, et al. Contributions of gastric volumes and gastric emptying to meal size and postmeal symptoms in functional dyspepsia. *Gastroenterology*. 2004;127:1685–1694. doi: 10.1053/j.gastro.2004.09.006.
30. Kindt S, Tack J. Impaired gastric accommodation and its role in dyspepsia. *Gut*. 2006;55(12):1685–1691. doi: 10.1136/gut.2005.085365.
31. Tack J, Demedts I, Meulemans A, et al. Role of nitric oxide in the gastric accommodation reflex and in meal induced satiety in humans. *Gut*. 2002;51(2):219–224. doi: 10.1136/gut.51.2.219.
32. Sarnelli G, Vandenberghe J, Tack J. Visceral hypersensitivity in functional disorders of the upper gastrointestinal tract. *Digestive and liver disease*. 2004;36(6):371–376. doi: 10.1016/j.dld.2004.01.018.
33. Keohane J, Quigley EM. Functional dyspepsia: the role of visceral hypersensitivity in its pathogenesis. *World journal of gastroenterology*. 2006;12(17):2672–2676. doi: 10.3748/wjg.v12.i17.2672.
34. Oshima T, Okugawa T, Tomita T, et al. Generation of dyspeptic symptoms by direct acid and water infusion into the stomachs of functional dyspepsia patients and healthy subjects. *Alimentary pharmacology & therapeutics*. 2012;35(1):175–182. doi: 10.1111/j.1365-2036.2011.04918.x.
35. Simren M, Tornblom H, Palsson OS, et al. Visceral hypersensitivity is associated with GI symptom severity in functional GI disorders: consistent findings from five different patient cohorts. *Gut*. 2018;67(2): 255–262. doi: 10.1136/gutjnl-2016-312361.
36. Vanheel H, Vicario M, Vanuytsel T, et al. Impaired duodenal mucosal integrity and low-grade inflammation in functional dyspepsia. *Gut*. 2014;63(2):262–271. doi: 10.1136/gutjnl-2012-303857.
37. Du L, Shen J, Kim JJ, et al. Increased Duodenal Eosinophil Degranulation in Patients with Functional Dyspepsia: A Prospective Study. *Scientific reports*. 2016;6:34305. doi: 10.1038/srep34305.
38. Vanheel H, Vicario M, Vanuytsel T, et al. Impaired duodenal mucosal integrity and low-grade inflammation in functional dyspepsia. *Gut* 2014;63:262–271. doi: 10.1136/gutjnl-2012-303857.
39. di Stefano M, Vos R, Vanuytsel T, et al. Prolonged duodenal acid perfusion and dyspeptic symptom occurrence in healthy volunteers. *Neurogastroenterology & Motility* 2009;21:712. doi: 10.1111/j.1365-2982.2009.01274.x.
40. Locke 3rd GR, Zinsmeister AR, Talley NJ, et al. Familial association in adults with functional gastrointestinal disorders. *Mayo Clinic proceedings*. 2000;75:907–912. doi: 10.4065/75.9.907
41. Chung HA, Lee SY, Lee HJ, et al. G protein $\beta 3$ subunit polymorphism and long-term prognosis of functional dyspepsia. *Gut Liver*. 2014 ;8(3):271–276. doi: 10.5009/gnl.2014.8.3.271.
42. Bercik P, De Giorgio R, Blennerhassett P, et al. Immune-mediated neural dysfunction in a murine model of chronic *Helicobacter pylori* infection. *Gastroenterology*. 2002;123(4):1205–1215. doi: 10.1053/gast.2002.36024.
43. Tornblom H, Holmvall P, Svenungsson B, et al. Gastrointestinal symptoms after infectious diarrhea: a 5-year follow-up in a Swedish cohort of adults. *Clinical gastroenterology and hepatology*. 2007;5:461–464. doi: 10.1016/j.cgh.2007.01.007.
44. Mearin F, Perez-Oliveras M, Perello A, et al. Dyspepsia and irritable bowel syndrome after a *Salmonella* gastroenteritis outbreak: one-year follow-up cohort study. *Gastroenterology* 2005;129:98–104. doi: 10.1053/j.gastro.2005.04.012.
45. Cervantes J, Michael M, Hong BY, et al. Investigation of oral, gastric, and duodenal microbiota in patients with upper gastrointestinal symptoms. *Journal of investigative medicine*. 2021;69(4):870–877. doi: 10.1136/jim-2020-001642.

46. Pavlidis P, Powell N, Vincent RP, et al. Systematic review: bile acids and intestinal inflammation-luminal aggressors or regulators of mucosal defence? *Alimentary pharmacology & therapeutics*. 2015;42(7):802-17. doi: 10.1111/apt.13333.
47. Van Oudenhove L, Aziz Q. The role of psychosocial factors and psychiatric disorders in functional dyspepsia. *Nat Rev Gastroenterol Hepatol* 2013;10:58-67. doi: 10.1038/nrgastro.2013.10.
48. Lee HS, An YS, Kang J, et al. Effect of acute auditory stress on gastric motor responses to a meal in healthy volunteers. *Journal of gastroenterology and hepatology*. 2013;28(11): 1699-16704. doi: 10.1111/jgh.12309.
49. Aro P, Talley NJ, Johansson SE, et al. Anxiety is linked to new-onset dyspepsia in the Swedish population: a 10-year follow-up study. *Gastroenterology* 2015;148:928-937. doi: 10.1053/j.gastro.2015.01.039.
50. Jones MP, Tack J, Van Oudenhove L, et al. Mood and anxiety disorders precede development of functional gastrointestinal disorders in patients but not in the population. *Clinical gastroenterology and hepatology*. 2017;15:1014-20. doi: 10.1016/j.cgh.2016.12.032.
51. NICE. Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. 2019. Available from: www.nice.org.uk/guidance/CG184.
52. Black CJ, Paine PA, Agrawal A, et al. British Society of Gastroenterology guidelines on the management of functional dyspepsia. *Gut*. 2022;71:1697-1723. doi: 10.1136/gutjnl-2022-327737.
53. Masuy I, Van Oudenhove L, Tack J. Review article: treatment options for functional dyspepsia. *Alimentary pharmacology & therapeutics*. 2019 May;49(9):1134-1172. doi: 10.1111/apt.15191.
54. Rabeneck L, Wristers K, Soucek J, et al. Impact of upper endoscopy on satisfaction in patients with previously uninvestigated dyspepsia. *Gastrointestinal endoscopy*. 2003;57:295-299. doi: 10.1067/mge.2003.122.
55. Mitchell RM, Collins JS, Watson RG, et al. Differences in the diagnostic yield of upper gastrointestinal endoscopy in dyspeptic patients receiving proton-pump inhibitors and H2-receptor antagonists. *Endoscopy* 2002;34:524-526. doi: 10.1055/s-2002-33230.
56. Canga III C, Vakil N. Upper GI malignancy, uncomplicated dyspepsia, and the age threshold for early endoscopy. *The American journal of gastroenterology*. 2002;97:600-603. doi: 10.1111/j.1572-0241.2002.05536.x.
57. Moayyedi P, Lacy BE, Andrews CN, et al. ACG and CAG Clinical Guideline: management of dyspepsia. *The American journal of gastroenterology*. 2017;112:988-1013. doi: 10.1038/ajg.2017.154
58. Mahadeva S, Chia YC, Vinothini A, et al. Cost-effectiveness of and satisfaction with a *Helicobacter pylori* "test and treat" strategy compared with prompt endoscopy in young Asians with dyspepsia. *Gut*. 2008;57:1214-1220. doi: 10.1136/gut.2007.147728.
59. Mazzoleni LE, Sander GB, Francesconi CF, et al. *Helicobacter pylori* eradication in functional dyspepsia: HEROES trial. *Archives of internal medicine*. 2011;171:1929-36. doi: 10.1001/archinternmed.2011.533.
60. Malfertheiner P, Megraud F, Rokkas T, et al. European *Helicobacter* and Microbiota Study group. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut*. 2022-327745. doi: 10.1136/gutjnl-2022-327745.
61. Chey WD, Leontiadis GI, Howden CW, et al. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection. *The American journal of gastroenterology*. 2017;112(2):212-239. doi: 10.1038/ajg.2016.563.
62. Ford AC, Mahadeva S, Carbone et al. Functional dyspepsia. *Lancet*. 2020;396(10263):1689-1702. doi: 10.1016/S0140-
63. Sugano K, Tack J, Kuipers EJ, et al. Kyoto global consensus report on *Helicobacter pylori* gastritis. *Gut*. 2015;64:1353-1367. doi: 10.1136/gutjnl-2015-309252.
64. Armstrong D, Veldhuyzen van Zanten SJ, Barkun AN, et al. CADET-HR Study Group. Heartburn-dominant, uninvestigated dyspepsia: a comparison of 'PPI-start' and 'H2-RA-start' management strategies in primary care--the CADET-HR Study. *Alimentary pharmacology & therapeutics*. 2005;21(10):1189-202. doi: 10.1111/j.1365-2036.2005.02466.x.
65. Reimer C, Søndergaard B, Hilsted L, et al. Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy. *Gastroenterology* 2009;137:80-87. doi: 10.1053/j.gastro.2009.03.058.
66. Lacy BE, Chase RC, Cangemi DJ. The treatment of functional dyspepsia: present and future. *Expert review of gastroenterology & hepatology*. 2023;17(1):9-20. doi: 10.1080/17474124.2023.2162877.
67. Standacher HM, Nevin AN, Duff C, et al. Epigastric symptom response to low FODMAP dietary advice compared with standard dietetic advice in individuals with functional dyspepsia. *Journal of neurogastroenterology and motility* 2021;33(11):e14148. doi: 10.1111/nmo.14148.
68. Basnayake C, Kamm MA, Stanley A, et al. Standard gastroenterologist versus multidisciplinary treatment for functional gastrointestinal disorders (MANTRA): an open-label, singlecentre, randomised controlled trial. *The lancet. Gastroenterology & hepatology*. 2020;5(10):890-899. doi: 10.1016/S2468-1253(20)30215-6.
69. Pinto-Sanchez MI, Yuan Y, Hassan A, et al. Proton pump inhibitors for functional dyspepsia. *The Cochrane database of systematic reviews*. 2017;11(11):CD011194. doi: 10.1002/14651858.CD011194.pub3.
70. Wauters L, Ceulemans M, Frings D, et al. Proton pump inhibitors reduce duodenal eosinophilia, mast cells, and permeability in patients with functional dyspepsia. *Gastroenterology*. 2021;160(5):1521-31.e9. doi: 10.1053/j.gastro.2020.12.016.
71. Du LJ, Chen BR, Kim JJ, et al. *Helicobacter pylori* eradication therapy for functional dyspepsia: Systematic review and meta-analysis. *World journal of gastroenterology*. 2016;22(12):3486-95. doi: 10.3748/wjg.v22.i12.3486.
72. Pittayanon R, Yuan Y, Bollegala NP, et al. Prokinetics for functional dyspepsia: a systematic review and meta-analysis of randomized control trials. *American Journal of Gastroenterology*. 2019;114:233-43. doi: 10.1038/s41395-018-0258-6.
73. Tack J, Camilleri M, Chang L, et al. Systematic review: cardiovascular safety profile of 5-HT(4) agonists developed for gastrointestinal disorders. *Alimentary pharmacology & therapeutics*. 2012;35:745-67. doi: 10.1111/j.1365-

- 2036.2012.05011.x.
74. Al-Saffar A, Lennernas H, Hellstrom PM. Gastroparesis, metoclopramide, and tardive dyskinesia: risk revisited. *Journal of neurogastroenterology and motility*. 2019;e13617. doi: 10.1111/nmo.13617.
 75. Francis P, Zavala SR. Functional Dyspepsia. 2024. In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing; 2024.
 76. Nennstiel S, Bajbouj M, Schmid RM, et al. Prucalopride reduces the number of reflux episodes and improves subjective symptoms in gastroesophageal reflux disease: a case series. *Journal of medical case reports*. 2014;8:34. doi: 10.1186/1752-1947-8-34.
 77. Carbone F, Vandenberghe A, Holvoet L, et al. A double-blind randomized, multicenter, placebo-controlled study of itopride in functional dyspepsia postprandial distress syndrome. *Journal of neurogastroenterology and motility* 2022; 34(8):e14337. doi: 10.1111/nmo.14337.
 78. Tack J, Janssen P, Masaoka T, et al. Efficacy of busiprone, a fundus-relaxing drug, in patients with functional dyspepsia. *Clinical gastroenterology and hepatology*. 2012;10:1239-1245. doi: 10.1016/j.cgh.2012.06.036.
 79. Taghvaei T, Elyasi F, Rahbar Z, et al. Effectiveness of Busiprone in Patients with Functional Dyspepsia: A Randomized, Double-Blind, Placebo-Controlled Study. *Middle East journal of digestive diseases*. 2021 t;13(4):302-313. doi: 10.34172/mejdd.2021.239
 80. Shrestha DB, Budhathoki P, Subedi P, et al. Acotiamide and Functional Dyspepsia: A Systematic Review and Meta-Analysis. *Cureus*. 2021;13(12):e20532. doi: 10.7759/cureus.20532.
 81. Drossman DA, Tack J, Ford AC, et al. Neuromodulators for functional gastrointestinal disorders (disorders of gut-brain interaction): a Rome Foundation working team report. *Gastroenterology* 2018;154:1140-1171. doi: 10.1053/j.gastro.2017.11.279.
 82. Liu J, Jia L, Jiang S, et al. Effects of Low-Dose Amitriptyline on Epigastric Pain Syndrome in Functional Dyspepsia Patients. *Digestive diseases and sciences*. 2021;66(2):521-525. doi: 10.1007/s10620-020-06191-9.
 83. Jiang SM, Jia L, Liu J, et al. Beneficial effects of antidepressant mirtazapine in functional dyspepsia patients with weight loss. *World journal of gastroenterology*. 2016;22(22):5260-5266. doi: 10.3748/wjg.v22.i22.5260.
 84. Ford AC, Luthra P, Tack J, et al. Efficacy of psychotropic drugs in functional dyspepsia: systematic review and meta-analysis. *Gut*. 2017;66:411-420. doi: 10.1136/gutjnl-2015-310721.
 85. van Kerkhoven LA, Laheij RJ, Aparicio N, et al. Effect of the antidepressant venlafaxine in functional dyspepsia: a randomized, double-blind, placebo-controlled trial. *Clinical gastroenterology and hepatology*. 2008;6:746-752. doi: 10.1016/j.cgh.2008.02.051.
 86. Carbone F, Vanuytsel T, Tack J. The effect of mirtazapine on gastric accommodation, gastric sensitivity to distention, and nutrient tolerance in healthy subjects. *Journal of neurogastroenterology and motility* 2017;29. doi: 10.1111/nmo.13146.
 87. Tan VP, Liu KS, Lam FY, et al. Randomised clinical trial: rifaximin versus placebo for the treatment of functional dyspepsia. *Alimentary pharmacology & therapeutics* 2017;45:767-776. doi: 10.1111/apt.13945.
 88. Tziatzios G, Gkolfakis P, Leite G, et al. Probiotics in Functional Dyspepsia. *Microorganisms*. 2023;11(2):351. doi: 10.3390/microorganisms11020351.
 89. von Arnim U, Peitz U, Vinson B, et al. STW 5, a phytopharmakon for patients with functional dyspepsia: results of a multicenter, placebo-controlled double-blind study. *American Journal of Gastroenterology*. 2007;102:1268-1275. doi: 10.1111/j.1572-0241.2006.01183.x.
 90. Rich G, Shah A, Koloski N, et al. A randomized placebo-controlled trial on the effects of Menthacarin, a proprietary pepper mint- and caraway-oil preparation, on symptoms and quality of life in patients with functional dyspepsia. *Neurogastroenterology and Motility*. 2017;29(11). doi: 10.1111/nmo.13132.
 91. Rodrigues DM, Motomura DI, Tripp DA, et al. Are psychological interventions effective in treating functional dyspepsia? A systematic review and meta-analysis. *Journal of gastroenterology and hepatology*. 2021;36(8):2047-57. doi: 10.1111/jgh.15566.
 92. Mikocka-Walus A, Evans S, Linardon J, et al. Psychotherapy appears to improve symptoms of functional dyspepsia and anxiety: systematic review with meta-analysis. *Psychology, health & medicine* 2023;28(5):1309-1335. doi: 10.1080/13548506.2022.2141278.