



## BÖLÜM 4

# MİDE HASTALIKLARINDA HELİKOBAKTER PİLORİ VE ROLÜ

Aslı KARA<sup>1</sup>

### 1. GİRİŞ

Helikobakter pilori (*H. pilori*), yaklaşık 3.5 mikron uzunluğunda ve 0.5 mikron genişliğinde, spiral şekilli, mikro aerofilik, gram negatif bir bakteridir (1). *H. pilori* insanlarda en sık görülen kronik bakteriyel enfeksiyonlardandır (2,3).

*H. pilori* enfeksiyonuna yakalanma riski, yaşamın erken dönemlerinde sosyo-ekonomik durum ve yaşam koşulları ile ilişkilidir. Aşırı kalabalık, çoklu kardeş sayısı, aynı yatağı paylaşma ve akan su eksikliği gibi faktörlerin tümü, *H. pilori* enfeksiyonunun daha yüksek bulaşma orANIyla ilişkilendirilmiştir (2,3).

*H. pilori* enfeksiyonu tuzlu gıda tüketimi olan hastalarda kalıcı olabilmekte- dir (4,5). Yapılan çalışmalarda *H. pilori* enfeksiyonu pozitif olan hastaların artan tuzlu gıda tüketimi mide kanseri riskini artırdığı saptanmıştır (6,7). *H. pilori* enfeksiyonuna kalitsal yatkınlık kanıtlanmamıştır (8). *H. pilori*, fekal/oral veya oral/oral maruziyet yoluyla kişiden kişiye bulaşmaktadır (9,10). Başarılı anti-bakte- riyal tedavinin ardından *H. pilori* re-enfeksiyonu çok nadirdir. Enfeksiyonun nüksetmesi genellikle yeni bir *H. pilori* suşuna bağlı olarak ortaya çıkmaktadır (11,12).

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## KAYNAKLAR

1. Goodwin CS, Worsley BW. Microbiology of *Helicobacter pilori*. *Gastroenterol Clin North Am* 1993; 22:5.
2. Cave DR. Transmission and epidemiology of *Helicobacter pilori*. *Am J Med* 1996; 100:12S.
3. Pounder RE, Ng D. The prevalence of *Helicobacter pilori* infection in different countries. *Aliment Pharmacol Ther* 1995; 9 Suppl 2:33.
4. Tsugane S, Tei Y, Takahashi T, et al. Salty food intake and risk of *Helicobacter pilori* infection. *Jpn J Cancer Res* 1994; 85:474.
5. Fox JG, Dangler CA, Taylor NS, et al. High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances *Helicobacter pilori* colonization in C57BL/6 mice. *Cancer Res* 1999; 59:4823.
6. Lee SA, Kang D, Shim KN, et al. Effect of diet and *Helicobacter pilori* infection to the risk of early gastric cancer. *J Epidemiol* 2003; 13:162.
7. Machida-Montani A, Sasazuki S, Inoue M, et al. Association of *Helicobacter pilori* infection and environmental factors in non-cardia gastric cancer in Japan. *Gastric Cancer* 2004; 7:46.
8. Graham DY, Malaty HM, Evans DG, et al. Epidemiology of *Helicobacter pilori* in an asymptomatic population in the United States. Effect of age, race, and socioeconomic status. *Gastroenterology* 1991; 100:1495.
9. Perry S, de la Luz Sanchez M, Yang S, et al. Gastroenteritis and transmission of *Helicobacter pilori* infection in households. *Emerg Infect Dis* 2006; 12:1701.
10. Mégraud F. Transmission of *Helicobacter pilori*: faecal-oral versus oral-oral route. *Aliment Pharmacol Ther* 1995; 9 Suppl 2:85.
11. Borody TJ, Andrews P, Mancuso N, et al. *Helicobacter pilori* reinfection rate, in patients with cured duodenal ulcer. *Am J Gastroenterol* 1994; 89:529.
12. Archimandritis A, Balatsos V, Delis V, et al. "Reappearance" of *Helicobacter pilori* after eradication: implications on duodenal ulcer recurrence: a prospective 6 year study. *J Clin Gastroenterol* 1999; 28:345.
13. Suerbaum S, Michetti P. *Helicobacter pilori* infection. *N Engl J Med* 2002; 347:1175.
14. Ernst PB, Peura DA, Crowe SE. The translation of *Helicobacter pilori* basic research to patient care. *Gastroenterology* 2006; 130:188.
15. Hu LT, Mobley HL. Purification and N-terminal analysis of urease from *Helicobacter pilori*. *Infect Immun* 1990; 58:992.
16. Mobley HL. The role of *Helicobacter pilori* urease in the pathogenesis of gastritis and peptic ulceration. *Aliment Pharmacol Ther* 1996; 10 Suppl 1:57.
17. Nilius M, Malfertheiner P. *Helicobacter pilori* enzymes. *Aliment Pharmacol Ther* 1996; 10 Suppl 1:65.
18. Slomiany BL, Kasinathan C, Slomiany A. Lipolytic activity of *Campylobacter pilori*: effect of colloidal bismuth subcitrate (De-Nol). *Am J Gastroenterol* 1989; 84:1273.
19. Hazell SL. Urease and catalase as virulence factors of *Helicobacter pilori*. In: *Helicobacter pilori* 1990, Menge H, Gregor M, Tytgat GN, et al (Eds), Springer Verlag, Berlin 1991
20. Mobley HL. Defining *Helicobacter pilori* as a pathogen: strain heterogeneity and virulence. *Am J Med* 1996; 100:2S.
21. Tombola F, Morbiato L, Del Giudice G, et al. The *Helicobacter pilori* VacA toxin is a urea permease that promotes urea diffusion across epithelia. *J Clin Invest* 2001; 108:929.
22. Fujikawa A, Shirasaka D, Yamamoto S, et al. Mice deficient in protein tyrosine phosphatase receptor type Z are resistant to gastric ulcer induction by VacA of *Helicobacter pilori*. *Nat Genet* 2003; 33:375.
23. Letley DP, Rhead JL, Twells RJ, et al. Determinants of non-toxicity in the gastric pathogen *Helicobacter pilori*. *J Biol Chem* 2003; 278:26734.

24. Covacci A, Censini S, Bugnoli M, et al. Molecular characterization of the 128-kDa immunodominant antigen of *Helicobacter pilori* associated with cytotoxicity and duodenal ulcer. *Proc Natl Acad Sci U S A* 1993; 90:5791.
25. Blaser MJ. Role of *vacA* and the *cagA* locus of *Helicobacter pilori* in human disease. *Aliment Pharmacol Ther* 1996; 10 Suppl 1:73.
26. Figura N. *Helicobacter pilori* exotoxins and gastroduodenal diseases associated with cytotoxic strain infection. *Aliment Pharmacol Ther* 1996; 10 Suppl 1:79.
27. Spechler SJ, Fischbach L, Feldman M. Clinical aspects of genetic variability in *Helicobacter pilori*. *JAMA* 2000; 283:1264.
28. Weel JF, van der Hulst RW, Gerrits Y, et al. The interrelationship between cytotoxin-associated gene A, vacuolating cytotoxin, and *Helicobacter pilori*-related diseases. *J Infect Dis* 1996; 173:1171.
29. Huang JQ, Zheng GF, Sumanac K, et al. Meta-analysis of the relationship between *cagA* seropositivity and gastric cancer. *Gastroenterology* 2003; 125:1636.
30. van Doorn LJ, Figueiredo C, Sanna R, et al. Clinical relevance of the *cagA*, *vacA*, and *iceA* status of *Helicobacter pilori*. *Gastroenterology* 1998; 115:58.
31. Atherton JC, Cao P, Peek RM Jr, et al. Mosaicism in vacuolating cytotoxin alleles of *Helicobacter pilori*. Association of specific *vacA* types with cytotoxin production and peptic ulceration. *J Biol Chem* 1995; 270:17771.
32. Atherton JC, Peek RM Jr, Tham KT, et al. Clinical and pathological importance of heterogeneity in *vacA*, the vacuolating cytotoxin gene of *Helicobacter pilori*. *Gastroenterology* 1997; 112:92.
33. Peek RM Jr, Thompson SA, Donahue JP, et al. Adherence to gastric epithelial cells induces expression of a *Helicobacter pilori* gene, *iceA*, that is associated with clinical outcome. *Proc Assoc Am Physicians* 1998; 110:531.
34. Nogueira C, Figueiredo C, Carneiro F, et al. *Helicobacter pilori* genotypes may determine gastric histopathology. *Am J Pathol* 2001; 158:647.
35. Gerhard M, Lehn N, Neumayer N, et al. Clinical relevance of the *Helicobacter pilori* gene for blood-group antigen-binding adhesin. *Proc Natl Acad Sci U S A* 1999; 96:12778.
36. Yamaoka Y, Kikuchi S, el-Zimaity HM, et al. Importance of *Helicobacter pilori* *oipA* in clinical presentation, gastric inflammation, and mucosal interleukin 8 production. *Gastroenterology* 2002; 123:414.
37. Mitchell HM, Hazell SL, Kolesnikow T, et al. Antigen recognition during progression from acute to chronic infection with a *cagA*-positive strain of *Helicobacter pilori*. *Infect Immun* 1996; 64:1166.
38. Kosunen TU. Antibody titres in *Helicobacter pilori* infection: implications in the follow-up of antimicrobial therapy. *Ann Med* 1995; 27:605.
39. Cover TL, Glupczynski Y, Lage AP, et al. Serologic detection of infection with *cagA*+ *Helicobacter pilori* strains. *J Clin Microbiol* 1995; 33:1496.
40. Crabtree JE. Eradication of chronic *Helicobacter pilori* infection by therapeutic vaccination. *Gut* 1998; 43:7.
41. Zeng M, Mao XH, Li JX, et al. Efficacy, safety, and immunogenicity of an oral recombinant *Helicobacter pilori* vaccine in children in China: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2015; 386:1457.
42. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol* 1996; 20:1161.
43. Carpenter HA, Talley NJ. Gastroscopy is incomplete without biopsy: clinical relevance of distinguishing gastropathy from gastritis. *Gastroenterology* 1995; 108:917.
44. Odze RD, Goldblum JR. Inflammatory disorders of the stomach. In: *Surgical Pathology of the GI Tract, Liver, Biliary Tract, and Pancreas*, Lash RH, Lauwers GY, et al (Eds), Saunders, Philadelphia 2009. p.285.

45. Hazell SL, Lee A, Brady L, Hennessy W. *Campylobacter piloris* and gastritis: association with intercellular spaces and adaptation to an environment of mucus as important factors in colonization of the gastric epithelium. *J Infect Dis* 1986; 153:658.
46. Väänänen H, Vauhkonen M, Helske T, et al. Non-endoscopic diagnosis of atrophic gastritis with a blood test. Correlation between gastric histology and serum levels of gastrin-17 and pepsinogen I: a multicentre study. *Eur J Gastroenterol Hepatol* 2003; 15:885.
47. Elitsur Y, Raghuverra A, Sadat T, Vaid P. Is gastric nodularity a sign for gastric inflammation associated with *Helicobacter pilori* infection in children? *J Clin Gastroenterol* 2000; 30:286.
48. Glickman JN, Antonioli DA. Gastritis. *Gastrointest Endosc Clin N Am* 2001; 11:717.
49. Iacobuzio-Donahue CA, Montgomery E, Goldblum JR. Non-neoplastic disorders of the stomach. In: *Gastrointestinal and Liver Pathology*, Bhattacharya B (Ed), Churchill Livingstone Elsevier, Philadelphia 2005. p.72.
50. Yuan W, Li Yumin, Yang Kehu, et al. Iron deficiency anemia in *Helicobacter pilori* infection: meta-analysis of randomized controlled trials. *Scand J Gastroenterol* 2010; 45:665.
51. Tsay FW, Hsu PI. *H. pilori* infection and extra-gastroduodenal diseases. *J Biomed Sci* 2018; 25:65.
52. Mwafy SN, Afana WM. Hematological parameters, serum iron and vitamin B12 levels in hospitalized Palestinian adult patients infected with *Helicobacter pilori*: a case-control study. *Hematol Transfus Cell Ther* 2018; 40:160.
53. Lanas A, Remacha B, Sáinz R, Hirschowitz BI. Study of outcome after targeted intervention for peptic ulcer resistant to acid suppression therapy. *Am J Gastroenterol* 2000; 95:513.
54. Jemal A, Bray F, Center MM, et al. Global cancer statistics. *CA Cancer J Clin* 2011; 61:69.
55. El-Omar EM, Rabkin CS, Gammon MD, et al. Increased risk of noncardia gastric cancer associated with proinflammatory cytokine gene polymorphisms. *Gastroenterology* 2003; 124:1193.
56. Ding SZ, Minohara Y, Fan XJ, et al. *Helicobacter pilori* infection induces oxidative stress and programmed cell death in human gastric epithelial cells. *Infect Immun* 2007; 75:4030.
57. Moss SF, Calam J, Agarwal B, et al. Induction of gastric epithelial apoptosis by *Helicobacter pilori*. *Gut* 1996; 38:498.
58. Jones NL, Shannon PT, Cutz E, et al. Increase in proliferation and apoptosis of gastric epithelial cells early in the natural history of *Helicobacter pilori* infection. *Am J Pathol* 1997; 151:1695.
59. Tsugane S, Tei Y, Takahashi T, et al. Salty food intake and risk of *Helicobacter pilori* infection. *Jpn J Cancer Res* 1994; 85:474.
60. Fox JG, Dangler CA, Taylor NS, et al. High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances *Helicobacter pilori* colonization in C57BL/6 mice. *Cancer Res* 1999; 59:4823.
61. Lee SA, Kang D, Shim KN, et al. Effect of diet and *Helicobacter pilori* infection to the risk of early gastric cancer. *J Epidemiol* 2003; 13:162.
62. Machida-Montani A, Sasazuki S, Inoue M, et al. Association of *Helicobacter pilori* infection and environmental factors in non-cardia gastric cancer in Japan. *Gastric Cancer* 2004; 7:46.
63. You WC, Zhang L, Gail MH, et al. Gastric dysplasia and gastric cancer: *Helicobacter pilori*, serum vitamin C, and other risk factors. *J Natl Cancer Inst* 2000; 92:1607.
64. Block G. Vitamin C and cancer prevention: the epidemiologic evidence. *Am J Clin Nutr* 1991; 53:270S.
65. Feiz HR, Mobarhan S. Does vitamin C intake slow the progression of gastric cancer in *Helicobacter pilori*-infected populations? *Nutr Rev* 2002; 60:34.
66. Cho Y, Lee DH, Oh HS, et al. Higher prevalence of obesity in gastric cardia adenocarcinoma compared to gastric non-cardia adenocarcinoma. *Dig Dis Sci* 2012; 57:2687.
67. Yang P, Zhou Y, Chen B, et al. Overweight, obesity and gastric cancer risk: results from a meta-analysis of cohort studies. *Eur J Cancer* 2009; 45:2867.

68. Lee YC, Chiang TH, Chou CK, et al. Association Between Helicobacter pilori Eradication and Gastric Cancer Incidence: A Systematic Review and Meta-analysis. *Gastroenterology* 2016; 150:1113.
69. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer* 1972; 29:252.
70. Clark EA, Ledbetter JA. How B and T cells talk to each other. *Nature* 1994; 367:425.
71. Eck M, Schmausser B, Haas R, et al. MALT-type lymphoma of the stomach is associated with *Helicobacter pilori* strains expressing the CagA protein. *Gastroenterology* 1997; 112:1482.
72. Wotherspoon AC, Doglioni C, Diss TC, et al. Regression of primary low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of *Helicobacter pilori*. *Lancet* 1993; 342:575.
73. Laine L, Lewin D, Naritoku W, et al. Prospective comparison of commercially available rapid urease tests for the diagnosis of *Helicobacter pilori*. *Gastrointest Endosc* 1996; 44:523.
74. Gatta L, Vakil N, Ricci C, et al. Effect of proton pump inhibitors and antacid therapy on <sup>13</sup>C urea breath tests and stool test for *Helicobacter pilori* infection. *Am J Gastroenterol* 2004; 99:823.
75. Weston AP, Campbell DR, Hassanein RS, et al. Prospective, multivariate evaluation of CLO-test performance. *Am J Gastroenterol* 1997; 92:1310.
76. Wright CL, Kelly JK. The use of routine special stains for upper gastrointestinal biopsies. *Am J Surg Pathol* 2006; 30:357.
77. Leide-Svegborn S, Stenström K, Olofsson M, et al. Biokinetics and radiation doses for carbon-14 urea in adults and children undergoing the *Helicobacter pilori* breath test. *Eur J Nucl Med* 1999; 26:573.
78. Howden CW, Hunt RH. Guidelines for the management of *Helicobacter pilori* infection. Ad Hoc Committee on Practice Parameters of the American College of Gastroenterology. *Am J Gastroenterol* 1998; 93:2330.
79. Laine L, Estrada R, Trujillo M, et al. Effect of proton-pump inhibitor therapy on diagnostic testing for *Helicobacter pilori*. *Ann Intern Med* 1998; 129:547.
80. Vakil N, Rhew D, Soll A, Ofman JJ. The cost-effectiveness of diagnostic testing strategies for *Helicobacter pilori*. *Am J Gastroenterol* 2000; 95:1691.
81. Trevisani L, Sartori S, Galvani F, et al. Evaluation of a new enzyme immunoassay for detecting *Helicobacter pilori* in feces: a prospective pilot study. *Am J Gastroenterol* 1999; 94:1830.
82. Lin HJ, Lo WC, Perng CL, et al. *Helicobacter pilori* stool antigen test in patients with bleeding peptic ulcers. *Helicobacter* 2004; 9:663.
83. Gisbert JP, Trapero M, Calvet X, et al. Evaluation of three different tests for the detection of stool antigens to diagnose *Helicobacter pilori* infection in patients with upper gastrointestinal bleeding. *Aliment Pharmacol Ther* 2004; 19:923.
84. Chey WD, Wong BC, Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of *Helicobacter pilori* infection. *Am J Gastroenterol* 2007; 102:1808.
85. Cutler AF, Toskes P. Comparison of [<sup>13</sup>C]urea blood test to [<sup>13</sup>C]urea breath test for the diagnosis of *Helicobacter pilori*. *Am J Gastroenterol* 1999; 94:959.
86. Ahmed F, Murthy UK, Chey WD, et al. Evaluation of the Ez-HBT *Helicobacter* blood test to establish *Helicobacter pilori* eradication. *Aliment Pharmacol Ther* 2005; 22:875.
87. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pilori* infection--the Maastricht IV/ Florence Consensus Report. *Gut* 2012; 61:646.
88. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of *Helicobacter pilori* Infection. *Am J Gastroenterol* 2017; 112:212.
89. Cutler AF, Prasad VM, Santogade P. Four-year trends in *Helicobacter pilori* IgG serology following successful eradication. *Am J Med* 1998; 105:18.

90. Crowe SE. *Helicobacter pilori Infection*. N Engl J Med 2019; 380:1158.
91. Qasim A, Sebastian S, Thornton O, et al. Rifabutin- and furazolidone-based *Helicobacter pilori* eradication therapies after failure of standard first- and second-line eradication attempts in dyspepsia patients. *Aliment Pharmacol Ther* 2005; 21:91.
92. Fischbach LA, van Zanten S, Dickason J. Meta-analysis: the efficacy, adverse events, and adherence related to first-line anti-*Helicobacter pilori* quadruple therapies. *Aliment Pharmacol Ther* 2004; 20:1071.
93. Gatta L, Zullo A, Perna F, et al. A 10-day levofloxacin-based triple therapy in patients who have failed two eradication courses. *Aliment Pharmacol Ther* 2005; 22:45.
94. Gisbert JP, Gonzalez L, Calvet X. Systematic review and meta-analysis: proton pump inhibitor vs. ranitidine bismuth citrate plus two antibiotics in *Helicobacter pilori* eradication. *Helicobacter* 2005; 10:157.
95. Graham DY, Hammoud F, El-Zimaity HM, et al. Meta-analysis: proton pump inhibitor or H2-receptor antagonist for *Helicobacter pilori* eradication. *Aliment Pharmacol Ther* 2003; 17:1229.
96. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of *Helicobacter pilori* Infection. *Am J Gastroenterol* 2017; 112:212.
97. Fallone CA, Chiba N, van Zanten SV, et al. The Toronto Consensus for the Treatment of *Helicobacter pilori* Infection in Adults. *Gastroenterology* 2016; 151:51.
98. Chey WD, Wong BC, Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of *Helicobacter pilori* infection. *Am J Gastroenterol* 2007; 102:1808.
99. Shah SC, Iyer PG, Moss SF. AGA Clinical Practice Update on the Management of Refractory *Helicobacter pilori* Infection: Expert Review. *Gastroenterology* 2021; 160:1831.
100. van der Hulst RW, Keller JJ, Rauws EA, Tytgat GN. Treatment of *Helicobacter pilori* infection: a review of the world literature. *Helicobacter* 1996; 1:6.
101. De Francesco V, Margiotta M, Zullo A, et al. Clarithromycin-resistant genotypes and eradication of *Helicobacter pilori*. *Ann Intern Med* 2006; 144:94.
102. McMahon BJ, Hennessy TW, Bensler JM, et al. The relationship among previous antimicrobial use, antimicrobial resistance, and treatment outcomes for *Helicobacter pilori* infections. *Ann Intern Med* 2003; 139:463.
103. Shah SC, Iyer PG, Moss SF. AGA Clinical Practice Update on the Management of Refractory *Helicobacter pilori* Infection: Expert Review. *Gastroenterology* 2021; 160:1831.
104. Mahadevan U, Kane S. American gastroenterological association institute technical review on the use of gastrointestinal medications in pregnancy. *Gastroenterology* 2006; 131:283.