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| CORE TIP | We have presented different surveys showing the resistance of *Helicobacter pylori* (*H. pylori*) to furazolidone from Asia and South America. The resi­stance rates varied but were mostly low (< 5%). *H. pylori* mutations occurring in the *oorD* gene, including A041G, A122G, C349A(G), A78G, A112G, A335G, C156T and C165T, and in the *porD* gene, including G353A, A356G, C357T, C347T, C347G and C346A, have been indicated to be possibly related to the observed resistance. Regarding levofloxacin resistance, compound mutations of N87A, A88N and V65I at codon Asn-87 were recently observed in the *gyrA* gene for the first time. |
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LETTERS TO THE EDITOR

Resistance of *Helicobacter pylori* to furazolidone and levofloxacin: A viewpoint

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**Abstract**

In their review, Arslan *et al*[1] did not describe the status of *Helicobacter pylori* (*H. pylori*) treatment with furazolidone and the resistance to this antibiotic. We have presented different surveys showing the resist­ance of *H. pylori* to furazolidone from Asia and South America. The resistance rates varied but were mostly low (< 5%). There are not enough data on its efficacy and resistance in the United States and Europe. *H. pylori* mutations occurring in the *oorD* gene, including A041G, A122G, C349A(G), A78G, A112G, A335G, C156T and C165T, and in the *porD* gene, including G353A, A356G, C357T, C347T, C347G and C346A, have been indicated to be possibly related to the observed resistance. Additionally, to complete Arslan *et al*’s statement regarding levofloxacin resistance, it should be noted that compound mutations of N87A, A88N and V65I at codon Asn-87 were recently observed in the *gyrA* gene for the first time. However, the results on these topics are not sufficient, and more worldwide studies are suggested.

**Key words:** Susceptibility; Furazolidone; *Helicobacter pylori*; Resistance; Levofloxacin; Treatment

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**Core tip:** We have presented different surveys showing the resistance of *Helicobacter pylori* (*H. pylori*) to furazolidone from Asia and South America. The resi­stance rates varied but were mostly low (< 5%). *H. pylori* mutations occurring in the *oorD* gene, including A041G, A122G, C349A(G), A78G, A112G, A335G, C156T and C165T, and in the *porD* gene, including G353A, A356G, C357T, C347T, C347G and C346A, have been indicated to be possibly related to the observed resistance. Regarding levofloxacin resistance, compound mutations of N87A, A88N and V65I at codon Asn-87 were recently observed in the *gyrA* gene for the first time.

**TO THE EDITOR**

We have read with great interest the valuable article by Arslan *et al*[1], titled “Importance of antimicrobial susceptibility testing for the management of eradi­cation in *Helicobacter pylori* infection”. One of the main subjects of the review was the description of the resistance rates of different antibiotics and the potential mechanisms leading to decreased in *Helicobacter pylori* (*H. pylori*) antimicrobial susceptibility. However, the authors should consider clarifying two important issues.

The authors did not allude to the status of *H. pylori* treatment with furazolidone and the resistance to this antibiotic. We have provided existing surveys reporting the resistance of *H. pylori* to furazolidone in Table 1. The resistance rates have been mostly reported to be lower than 5%; however, these rates can vary geographically. Furazolidone is not used widely in the United States and Europe; therefore, there are not enough data on its efficacy and resistance in these regions.

One of the main reasons for the emergence of resistance is related to the extensive use of furazoli­done. In addition, regarding the molecular mechanisms, some genetic mutations have been identified. Muta­tions occurring in the *2-oxoglutarate:acceptor oxidor­eductase* (*oorD*) gene, including *A041G*, *A122G*, *C349A(G)*, *A78G*, *A112G*, *A335G*, *C156T* and *C165T*, and in the *pyruvate oxidoreductase* (*porD*) gene, including *G353A*, *A356G*, *C357T*, *C347T*, *C347G* and *C346A*, are possibly related to the resistance[2,3]. *The oor and por* genes are involved in the generation of acetyl coenzyme A (acetyl-CoA) and succinyl-CoA[4]. Despite these findings, additional molecular methods are proposed to reach a better understanding of the mechanisms that were mentioned.

Arslan *et al*[1] accurately documented the mech­anism of levofloxacin resistance; *i.e.*, point mutations in the *gyrA* (DNA *gyrase*) gene were stated to be potentially linked to the resistance. However, to complete their statement, it should be noted that compound mutations of N87A, A88N and V65I at codon Asn-87 were recently observed in the *gyrA* gene for the first time. L45F, A55S, A97V, D91N, R130K and G60S are other possible mutations that need to be assessed in studies with broader sample bases[5].

**REFERENCES**

1 **Arslan N**, Yılmaz Ö, Demiray-Gürbüz E. Importance of antimicrobial susceptibility testing for the management of eradication in Helicobacter pylori infection. *World J Gastroenterol* 2017; **23**: 2854-2869 [PMID: 28522904 DOI: 10.3748/wjg.v23.i16.2854]

2 **Su Z**, Xu H, Zhang C, Shao S, Li L, Wang H, Wang H, Qiu G. Mutations in Helicobacter pylori porD and oorD genes may contribute to furazolidone resistance. *Croat Med J* 2006; **47**: 410-415 [PMID: 16758519]

3 **Dong F**, Ji D, Huang R, Zhang F, Huang Y, Xiang P, Kong M, Nan L, Zeng X, Wu Y, Bao Z. Multiple Genetic Analysis System-Based Antibiotic Susceptibility Testing in Helicobacter pylori and High Eradication Rate With Phenotypic Resistance-Guided Quadruple Therapy. *Medicine* (Baltimore) 2015; **94**: e2056 [PMID: 26632710 DOI: 10.1097/MD.0000000000002056]

4 **Hughes NJ**, Clayton CL, Chalk PA, Kelly DJ. Helicobacter pylori porCDAB and oorDABC genes encode distinct pyruvate:flavodoxin and 2-oxoglutarate:acceptor oxidoreductases which mediate electron transport to NADP. *J Bacteriol* 1998; **180**: 1119-1128 [PMID: 9495749]

5 **Phan TN**, Santona A, Tran VH, Tran TN, Le VA, Cappuccinelli P, Rubino S, Paglietti B. High rate of levofloxacin resistance in a background of clarithromycin- and metronidazole-resistant Helicobacter pylori in Vietnam. *Int J Antimicrob Agents* 2015; **45**: 244-248 [PMID: 25499186 DOI: 10.1016/j.ijantimicag.2014.10.019]

6 **Sun QJ**, Liang X, Zheng Q, Gu WQ, Liu WZ, Xiao SD, Lu H. Resistance of Helicobacter pylori to antibiotics from 2000 to 2009 in Shanghai. *World J Gastroenterol* 2010; **16**: 5118-5121 [PMID: 20976850 DOI: 10.3748/wjg.v16.i40.5118]

7 **Su P**, Li Y, Li H, Zhang J, Lin L, Wang Q, Guo F, Ji Z, Mao J, Tang W, Shi Z, Shao W, Mao J, Zhu X, Zhang X, Tong Y, Tu H, Jiang M, Wang Z, Jin F, Yang N, Zhang J. Antibiotic resistance of Helicobacter pylori isolated in the Southeast Coastal Region of China. *Helicobacter* 2013; **18**: 274-279 [PMID: 23418857 DOI: 10.1111/hel.12046]

8 **Ji Z**, Han F, Meng F, Tu M, Yang N, Zhang J. The Association of Age and Antibiotic Resistance of Helicobacter Pylori: A Study in Jiaxing City, Zhejiang Province, China. *Medicine* (Baltimore) 2016; **95**: e2831 [PMID: 26937912 DOI: 10.1097/MD.0000000000002831]

9 **Gehlot V**, Mahant S, Mukhopadhyay AK, Das K, De R, Kar P, Das R. Antimicrobial susceptibility profiles of Helicobacter pylori isolated from patients in North India. *J Glob Antimicrob Resist* 2016; **5**: 51-56 [PMID: 27436467 DOI: 10.1016/j.jgar.2015.09.009]

10 **Pandya HB**, Agravat HH, Patel JS, Sodagar NR. Emerging antimicrobial resistance pattern of Helicobacter pylori in central Gujarat. *Indian J Med Microbiol* 2014; **32**: 408-413 [PMID: 25297026 DOI: 10.4103/0255-0857.142256]

11 **Maleknejad S**, Mojtahedi A, Safaei-Asl A, Taghavi Z, Kazemnejad E. Primary Antibiotic Resistance to Helicobacter pylori Strains Isolated From Children in Northern Iran: A Single Center Study. *Iran J Pediatr* 2015; **25**: e2661 [PMID: 26635938 DOI: 10.5812/ijp.2661]

12 **Kohanteb J**, Bazargani A, Saberi-Firoozi M, Mobasser A. Antimicrobial susceptibility testing of Helicobacter pylori to selected agents by agar dilution method in Shiraz-Iran. *Indian J Med Microbiol* 2007; **25**: 374-377 [PMID: 18087088]

13 **Abadi AT**, Taghvaei T, Mobarez AM, Carpenter BM, Merrell DS. Frequency of antibiotic resistance in Helicobacter pylori strains isolated from the northern population of Iran. *J Microbiol* 2011; **49**: 987-993 [PMID: 22203563 DOI: 10.1007/s12275-011-1170-6]

14 **Siavoshi F**, Safari F, Doratotaj D, Khatami GR, Fallahi GH, Mirnaseri MM. Antimicrobial resistance of Helicobacter pylori isolates from Iranian adults and children. *Arch Iran Med* 2006; **9**: 308-314 [PMID: 17061600]

15 **Fallahi GH**, Maleknejad S. Helicobacter pylori culture and antimicrobial resistance in Iran. *Indian J Pediatr* 2007; **74**: 127-130 [PMID: 17337822]

16 **Siavoshi F**, Saniee P, Latifi-Navid S, Massarrat S, Sheykholeslami A. Increase in resistance rates of H. pylori isolates to metronidazole and tetracycline--comparison of three 3-year studies. *Arch Iran Med* 2010; **13**: 177-187 [PMID: 20433221]

17 **Sirous M,** Mehrabadi JF, Daryani N, Eshraghi S, Hajikhani S, Shirazi M. Prevalence of antimicrobial resistance in Helicobacter pylori isolates from Iran. *Afr J Biotechnol* 2010; **9**: 5962–5965

18 **Rafeey M**, Ghotaslou R, Nikvash S, Hafez AA. Primary resistance in Helicobacter pylori isolated in children from Iran. *J Infect Chemother* 2007; **13**: 291-295 [PMID: 17982716 DOI: 10.1007/s10156-007-0543-6]

19 **Kim JJ**, Kim JG, Kwon DH. Mixed-infection of antibiotic susceptible and resistant Helicobacter pylori isolates in a single patient and underestimation of antimicrobial susceptibility testing. *Helicobacter* 2003; **8**: 202-206 [PMID: 12752732]

20 **Goh KL**, Navaratnam P. High Helicobacter pylori resistance to metronidazole but zero or low resistance to clarithromycin, levofloxacin, and other antibiotics in Malaysia. *Helicobacter* 2011; **16**: 241-245 [PMID: 21585611 DOI: 10.1111/j.1523-5378.2011.00841.x]

21 **Siddiqui TR**, Ahmed W, Arif A, Bibi S, Khan A. Emerging trends of antimicrobial resistance in Helicobacter pylori isolates obtained from Pakistani patients: The need for consideration of amoxicillin and clarithromycin. *J Pak Med Assoc* 2016; **66**: 710-716 [PMID: 27339574]

22 **Mendonça S**, Ecclissato C, Sartori MS, Godoy AP, Guerzoni RA, Degger M, Pedrazzoli J Jr. Prevalence of Helicobacter pylori resistance to metronidazole, clarithromycin, amoxicillin, tetracycline, and furazolidone in Brazil. *Helicobacter* 2000; **5**: 79-83 [PMID: 10849055]

23 **Godoy AP**, Ribeiro ML, Benvengo YH, Vitiello L, Miranda Mde C, Mendonça S, Pedrazzoli J Jr. Analysis of antimicrobial susceptibility and virulence factors in Helicobacter pylori clinical isolates. *BMC Gastroenterol* 2003; **3**: 20 [PMID: 12911839 DOI: 10.1186/1471-230X-3-20]

24 **Eisig JN**, Silva FM, Barbuti RC, Navarro-Rodriguez T, Moraes-Filho JP, Pedrazzoli Jr J. Helicobacter pylori antibiotic resistance in Brazil: clarithromycin is still a good option. *Arq Gastroenterol* 2011; **48**: 261-264 [PMID: 22147131]

25 **Ogata SK**, Gales AC, Kawakami E. Antimicrobial susceptibility testing for Helicobacter pylori isolates from Brazilian children and adolescents: comparing agar dilution, E-test, and disk diffusion. *Braz J Microbiol* 2015; **45**: 1439-1448 [PMID: 25763052]

26 **Ogata SK**, Godoy AP, da Silva Patricio FR, Kawakami E. High Helicobacter pylori resistance to metronidazole and clarithromycin in Brazilian children and adolescents. *J Pediatr Gastroenterol Nutr* 2013; **56**: 645-648 [PMID: 23403439 DOI: 10.1097/MPG.0b013e31828b3669]

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**Table 1 Studies evaluating the *Helicobacter pylori* resistance to furazolidone**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Continent | Country | Study year | Strains (*n*) | Method | Resistance (%) | Author |
| Asia | China (Shanghai) | 2000-2009 | 293 | Agar dilution | 0 | Sun *et al*[6] |
| China (Zhejiang) | 2010-2012 | 21 | Agar dilution | 0.1 | Su *et al*[7] |
| China (Zhejiang) | 2009-2014 | 9687 | Agar dilution | < 0.01 | Ji *et al*[8] |
| India (Ghaziabad and New Delhi) | NA | 68 | Agar dilution | 22.1 | Gehlot *et al*[9] |
| India (Gujarat) | 2008-2011 | 80 | Disk diffusion | 13.8 | Pandya *et al*[10] |
| Iran (Rasht) | 2012-2014 | 169 | Disk diffusion | 61.9 | Maleknejad *et al*[11] |
| Iran (Shiraz) | 2004-2005 | 106 | Agar dilution | 9.4 | Kohanteb *et al*[12] |
| Iran (Sari) | 2009 | 197 | Disk diffusion | 61.4 | Abadi *et al*[13] |
| Iran (Tehran) | 2001-2004 | 135 | Disk diffusion | 0 | Siavoshi *et al*[14] |
| Iran (Tehran) | 2002-2003 | 24 | Disk diffusion | 0 | Fallahi *et al*[15] |
| Iran (Tehran) | 2005-2008 | 110 | Disk diffusion | 4.5 | Siavoshi *et al*[16] |
| Iran (Tehran) | 2007-2008 | 104 | Disk diffusion | 0 | Sirous *et al*[17] |
| Iran | 2003-2005 | 100 | Disk diffusion | 9 | Rafeey *et al*[18] |
| South Korea | 1994-1999 | 220 | Agar dilution | 1.4 | Kim *et al*[19] |
| Malaysia (Malacca) | 2009 | 90 | Epsilometer test | 0 | Goh *et al*[20] |
| Pakistan (Karachi) | 2008-2013 | 93 | disk diffusion | 4.3 | Siddiqui *et al*[21] |
| South America | Brazil (Bragança Paulista) | NA | 90 | Agar dilution | 4 | Mendonça *et al*[22] |
| Brazil (Bragança Paulista) | NA | 138 | Agar dilution | 13 | Godoy *et al*[23] |
| Brazil (Sao Paulo) | NA | 39 | Agar dilution | 0 | Eisig *et al*[24] |
| Brazil (Sao Paulo) | 2008-2009 | 77 | Agar dilution and disk diffusion | 0 | Ogata *et al*[25] |
| Brazil (Sao Paulo) | 2008-2009 | 77 | Agar dilution | 0 | Ogata *et al*[26] |