World Journal of Gastroenterology

Submit a Manuscript: http://www.f6publishing.com

World J Gastroenterol 2017 October 7; 23(37): 6920-6922

DOI: 10.3748/wjg.v23.i37.6920

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LETTERS TO THE EDITOR

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

Mohammad Zamani, Arash Rahbar, Javad Shokri-Shirvani

Mohammad Zamani, Student Research Committee, Babol University of Medical Sciences, Babol 47176-47745, Iran

Mohammad Zamani, Cancer Research Center, Health Research Institute, Babol University of Medical Sciences, Babol 47176-47745, Iran

Arash Rahbar, Student Research Committee, Babol University of Medical Sciences, Babol 47176-47745, Iran

Javad Shokri-Shirvani, Department of Internal Medicine, Babol University of Medical Sciences, Babol 47176-47745, Iran

ORCID number: Mohammad Zamani (0000-0003-1916-3873); Arash Rahbar (0000-0002-1935-2247); Javad Shokri-Shirvani (0000-0002-2090-2234).

Author contributions: Zamani M and Shokri-Shirvani J contributed in study design; Zamani M and Rahbar A drafted the manuscript; Shokri-Shirvani J revised the manuscript for important intellectual content; All authors have read the manuscript and approved its final version.

Conflict-of-interest statement: The authors declared no conflict of interest.

Manuscript source: Unsolicited manuscript

Correspondence to: Javad Shokri-Shirvani, MD, Department of Internal Medicine, Babol University of Medical Sciences, Ganjafrooz Street, Babol 47176-47745, Mazandaran, Iran. j.shokri@mubabol.ac.ir
Telephone: +98-11-32199592
Fax: +98-11-32190971

Received: June 29, 2017
Peer-review started: June 30, 2017
First decision: July 13, 2017
Revised: July 30, 2017
Accepted: August 15, 2017
Article in press: August 15, 2017
Published online: October 7, 2017

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

Core tip: We have presented different surveys showing the resistance of *Helicobacter pylori* (*H. pylori*) to furazolidone from Asia and South America. The resi-

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]

stance 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.

Zamani M, Rahbar A, Shokri-Shirvani J. Resistance of *Helicobacter pylori* to furazolidone and levofloxacin: A viewpoint. *World J Gastroenterol* 2017; 23(37): 6920-6922 Available from: URL: http://www.wjgnet.com/1007-9327/full/v23/i37/6920.htm DOI: http://dx.doi.org/10.3748/wjg.v23.i37.6920

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]

P- Reviewer: Ananthakrishnan N, Bao ZJ, Jamali R **S- Editor**: Ma YJ
L- Editor: A **E- Editor**: Huang Y

Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

ISSN 1007-9327