Drug Resistance in Helicobacter Pylori

Pages with reference to book, From 1 To 2

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Helicobacter pylon is associated in different pathophysiological conditions of gastritis, peptic ulcer and gastric carcinoma. Eradication of H. pylori from gastric mucosa may be an important goal of therapy since ii markedly reduces the frequency of duodenal ulcer repapse[1-3]. Numerous studies with different antimicrobial agents have been performed to determine the optimal drug to eradicate H. pylon from gastric mucosa[1]. Among the agents. more frequently used, are bismuth salts, amoxicillin, metronidazole and other 5-ni-troimidazoles[4,5].

Amoxicillin and nitroimidazole have been considered antibiotics of choice, but resistance to both these drugs is now seen worldwide[6-9] Metronidazole resistance in European countries varies from 5-50% with the highest reported from Finland[6]. In Eastern Zaire, 84% patients were infected with metromdazole resistant strains[9]. In this study most patients received metromdazole before investigation as self-medication or for the treatment of giardiasis or amoebiasis. Varied resistance rates were reported from different geographical locations, e.g., North America (30%)[6], Brussels (27%)[9], Spain (12.5%)[10] and Australia (17%)[6]. European study group on antibiotic susceptibility of H. pylori[11] has reported 27.5% resistance to metronidazole in their recent multicentre study. Problem of metromdazole resistance also exists in South America where 64.7% Brazilian[12] and 30% of the Peruvian strains are resistant[6].

Metronidazole resistance was more common in patients above 20 years of age[9] and occasionally higher in women than in men[13]. The differences in the resistance levels between genders were restricted to certain age groups[11]. The high frequency of resistance to metmnidazole among women aged 20-3 9 years varied from 50-72% and among men 22-40%[11,13]

The fact that metronidazole is secreted in gastric mucus and achieves high levels in gastric juices after parentemi administration[14], is an important property for using this compound for H. pylon. However, primary resistance to metronidazole is associated with a higher rate of treatment failure. The means of acquiring metronidazole resistance is not clear. It is possible that after coming in contact with metronidazole, H. pylon strains undergo a genetic modification which could lead to metronidazole resistance. However, it is proposed that drug resistance in H. pylon is either due to decreased ability of resistant strains to achieve a sufficiently low redox potential under microaerophilic conditions for reduction of intro group of metronidazole[15] or decreased uptake of drug by bacterial cell wall[16] It is also hypothesized that resistant mutants may pre-exist and the use of second active agent for treatment will lower the inoculum size of infecting organisms and in turn reduce the chances of emerging resistant mutants. This was observed with tinidazole/bismuth therapy[17] and was also true if the bismuth is replaced with amoxidilin or tetracycline.

Resistance to quinolone group of antibiotics was also observed in H. pylon strains. This was first reported in 1987 when 13 patients treated with ofloxacin developed resistance during treatment[18]. Other quinolones (ciprofloxacin and norfioxacin) have proved unsuccessful in eradication of H. pyiori from gastric mucosa and in instances rapid development of resistance to quinolones occurred in 70-100% of the strains[8]. Indus in of resistance to one quinolone has led to cross resistance to other quinolones but not to other groups of antibiotics. Since this induction is common, it is likely that this type of resistance will increase in future due to worldwide use of quinolones for other infections. Resistance to this class of antibiotics may be exhibited by two different mechanisms: a) it may involve

the modification of the bacterial DNA gyrase, which is a target enzyme for quinolones or, b) it may be due to modification L the bacterial outer membrane proteins which is restricting the drug to enter inside the bacteria[16].

H. pylon strains have also shown resistance to clindamycin. Although resistance to this drug is <1% in Europe and Australia and 27% in West Virginia, clindamycin resistance does not seem to be induced by exposure to antibiotic. In one clinical trial no resistance developed to cindamycin although treatment failure was seen among patients[6]. The specific mechanisms of resistance to clindamycin is not known. Apart from three types of drug resistance mentioned above, there are also reports of resistance to other antibiotics, e.g., azythromycin[8] tetracycline (0.4%), penicillin (Ø•9%)[6]. The genetic detenninants responsible for resistance to macrolides inH. pylori have not beenelucidated. The stability of resistance and its persistence for long time inthe same strain of H. pylori is likely to be chromosomally mediated ratherthan plasmid mediated. Although plasmids were seen in about 50% of the isolates[19], so far no evidence that any of these plasmid confer antibiotic resistance has been reported. In order to decrease the risk of future development of drug resistance, it is recommended that atleast two antimicrobial agents be used simultaneously because monotherapy increases the risk of developing resistance and carries a low therapeutic yield[6]. The trends in drug resistance of H. pylon should be monitored by accurately comparing the data from different investigators worldwide.

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