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Research Paper

Epidemiology and Treatment of Helicobacter pylori Infection: specific problems in Albania

Medical Science

KEYWORDS : *Helicobacter pylori* infection, prevalence, eradication, resistance, first-line therapy, second-line therapy.

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ABSTRACT

Helicobacter pylori is a gram negative Campilobacter. It's one of the most common causes of ulcerous disease. H.pylori causes chronic inflammation, leading to gastric mucose atrophy, even adenocarcinoma or lymphoma. Its presence in the population is highly related to geographic, demographic or genetic characteristics and socio-economic level.
Even though ulcerous disease treatment is an evident achievement in the Gastro-enterology service, it still remains a problem because of the microbic resistance, attending for new solutions. In some countries, triple therapy with a proton-pump inhibitor, amoxicillin and clarithromycin is still the best option, but eradication results fall short of what would be desired (90-95%) in countries with clarithromycin resistance >20%, bismuth-containing quadruple therapy, or non-bismuth sequential or concomitant therapies may then be the preferred option. Vaccination would be the best option, especially for developing countries, but little progress has been made in designing a vaccine.

Introduction

Last 10-years studies show a reduction in efficiency of the trith-erapies used so far (PPI, amoxicillin, clarithromycin or in case of penicillin allergy: PPI, metronidazole, clarithromycin), due to increased resistance to clarithromycin and metronidazole. Given that, *Helicobacter pylori* culture is realized with difficulty and molecular tests are not widespread, it is recommended a probabilistic effective treatment, which can be: sequential (PPI and amoxicillin for 5 days, PPI and clarithromycin and metronidazole for 5 other days) or with bismuth quadruple therapy (PPI and bismuth and tetracycline and metronidazole for 10 days).

In case of failure of these therapies, the assessment of the sensitivity of antibiotics to *helicobacter pylori* is highly recommended, before a second-line treatment.

Epidemiology in Albania

Helicobacter pylori infection prevalence has highly decreased the last decade. This is significantly related to socioeconomic conditions. A survey carried out in 308 children, aged from 8 to 10 years old, assessing *H.pylori* presence by stool antigen test, had an overall prevalence of 58%. This is a significant drop compared to *H.pylori* prevalence of 91% in 1994 estimated from a survey carried out in 480 children, using the urea breath tests.

Helicobacter pylori prevalence in Albania (1994 vs 2014)[3]

Factors	1994 (n=480)				2014 (n=308)			
	HP neg. (n/%)	HP pos. (n/%)	X2	p value	HP neg. (n/%)	P pos. (n/%)	X2	p value
Gender								
Male	20/9	205/91	0.118	0.4	51/35	95/65	5.51	0.5
Female	25/11	230/89			78/43	84/57		
Total	45/9	435/91			129/42	179/58		
Residence								
Urban	29/11	236/89	38.8	0.001	78/84	28/26	16.5	0.003
Rural	26/9	189/91			100/49	102/51		
Total	55/11	425/89			178/58	130/48		

Helicobacter pylori eradication recommendations

Helicobacter pylori eradication is absolutely indicated in gastric and duodenal ulcers, leading to lesion cicatrization and recidive prevention.

MALT gastric lymphoma is another absolute indication to seek and treat *H.pylori* infection; a tumoral respond is observed in 80% of patients. Despite of a prolonged remission, endoscopic follow up is necessary , because of the high risk to develop gastric cancer. When the t(11,18) translocationis present, however , *H.pylori* eradication is usually ineffective and these patients need adjunctive and alternative treatments.

In non-ulcerous dyspeptic patients, *H.pylori* infection treatment

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used to be questionable. However, the latest meta-analysis show a significant benefit, not that much for symptoms resolution, as for reducing cancer risks.

At a population level, *H.pylori* and GORD (gasto-oesophageal reflux disease) are negatively associated. A review of 26 studies showed a rate of *H.pylori* infection in patients with GORD of 39% compared with50% in controls. Similarly, the sequelae of GORD, such as Barrett's oesophagus and oesophageal adenocarcinoma, are also less common in infected individuals. However, eradication of *H.pylori* in populations of infected patients, on average, neither causes nor exacerbates GORD. In addition, the long-term efficasity of proton pump inhibitor (PPI) maintenance treatment for GORD is not influenced by *H.pylori* status.

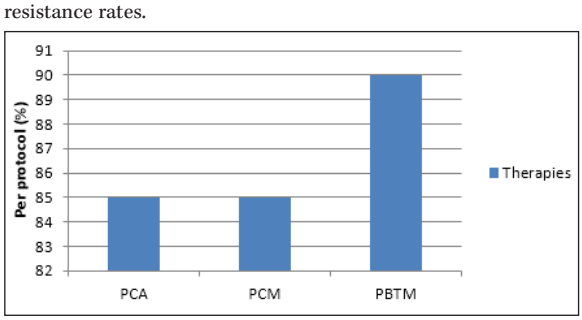
Both *H.pylori* and NSAID use are independent risk factors for the development of peptic ulcer disease and associated bleeding. It has been shown that there is an increased risk when these factors are both present. A meta-analysis showed that eradication seems less effective than treatment with a maintenance PPI for preventing NSAID-associated ulcers.

H.pylori eradication has the potential to prevent gastric cancers. A study on the effect of *H.pylori* eradication on patients with premalignant lesions showed that eradication may prevent their progression. It is thought that a so-called 'point of no return' may exist in the histological cascade from chronic gastritis to adenocarcinomaafter which eradication is unlikely to prevent gastric cancer.

There is evidence linking *H.pylori* to the aetiology of otherwise unexplained iron-deficiency anaemia, idiopathic thrombocytopenic purpura (ITP) and vitamin B12 deficiency. In these disorders, *H.pylori* should be sought and eradicated.

Treatment of *Helicobacter pylori* infection

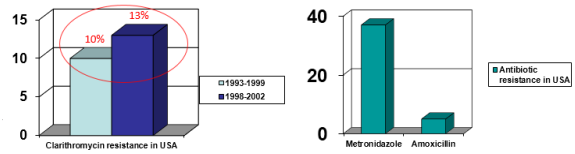
A considerable amount of work has been conducted over the last year assessing many issues around Helicobacter pylori eradication therapy. These focused primarly on assessing the efficacy of current standard triple therapy and exploring new first-line treatments. There was also progress in investigating antibiotic resistance rates.



First-line treatment

Numerous studies have assessed the efficacy of standard triple therapy with amoxicillin , clarithromycin and a proton-pump inhibitor or amoxicillin, metronidazole and a proton-pump inhibitor for the eradication of *H.pylori*, which have perceived to be in decline in recent years.

One search in Albania, involving 70 patients suffering ulcerous disease, which aimed to assess the efficasity of standard therapy with clarithromycin and amoxicillin or clarithromycin and metronidazole for ten days use and a proton-pump inhibitor, found out that after four week treatment the ulcerous disease heeled in 95% of patients. However, respectively, 40% and 60% of patients of each group, were *H.pylori* positive, assessed by biopsy. What's more, 60% of patients still had epigastric pain.



A meta-analysis[1] including 24 randomized controlled trials and randomized comparative trials including 2,102 patients, concluded that 97-98% of patients with gastric and duodenal ulcerous disease without *H.pylori* infection achieved a 12-month remission, where as, only 61-65% of patients with persistent *H.pylori* infection gained a 12-month remission.

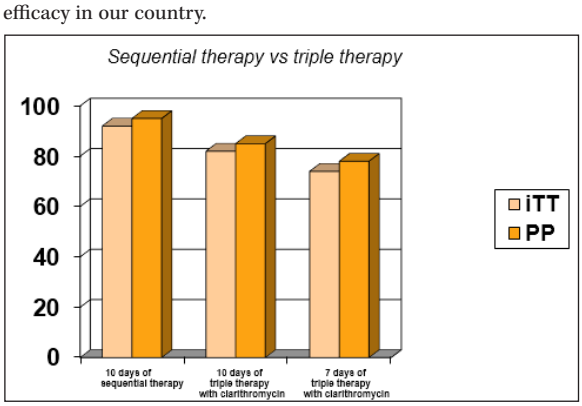
In areas of high clarithromycin resistance, because of its great efficacy, over 90% and compliance, sequential therapy is highly recommended. That consists on using a proton-pump inhibitor and amoxicillin for five days, and, a proton-pump inhibitor, clarithromycin and metronidazole for the other five days. Several studies in Italy have shown consistently impressive eradication rates for the regimen with one study showing eradication rates of 95% by per-protocol analysis, vs 85% for standard triple therapy in a treatment-naïve population.

A large multicenter trial[2] evaluated the efficacy of sequential therapy versus clarithromycin triple therapy in clarithromycin resistant patients and showed eradication rates of 82% vs 44% for clarithromycin triple therapy.

Second-line treatment

Quadruple therapy with bismuth salts, tetracycline, metronidazole and a proton-pump inhibitor shows eradication rates of 60% versus 87% of triple therapy with levofloxacin, amoxicillin and a proton-pump inhibitor.

According to third-line treatment with rifabutin, amoxicillin and a proton-pump inhibitor, or furazolidone, amoxicillin and a proton-pump inhibitor, further studies are needed to evalue its efficacy in our country.



Conclusion

The literature published recently appears to show that the rate of eradication achieved with standard triple therapy has stabilized but is inadequate. This is because of clarithromycin high resistance rates. As to metronidazole, its resistance can be bypassed by using high antibiotic doses.

The guidelines published by the European Helicobacter Study Group provide an excellent framework for clinicians to address all issues around *H.pylori* infection and recommend regimens and follow-up protocols that can insure near full eradication. The evidence base for sequential therapy has shown eradication rates over 90%, adopting the sequential therapy as the new preferred first-line regime in Albania.

Even though, quadruple therapy with bismuth, is widely used now days, as a second-line therapy, because of its high cost, it is used as an alternative therapy in Albania, for patients resistant to sequential therapy.

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