HELICOBACTOR PYLORI INFECTION IN CHILDREN

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INTRODUCTION

Helicobacter Pylori (Hp), discovered by warren and Marshall in 1983 has opened a new are of discovery and understanding of gastroduodenal pathology. Since then inflammatory mucosal lesions of the upper gastrointestinal tract, namely esophagitis, chronic gastritis, duodenitis, peptic ulcer and doudenal ulcers have been suggested to be caused by H. pylori[1].

EPIDEMIOLOGY

H. Pylori is distributed world wide[2]. The prevalence of infection varies with age, ethnic background, socioeconomic status and living conditions[3]. In developed countries the children of families at the lowest socioeconomic level are infected while children from privileged classes show lower prevalence of infection (4). In developing countries the infection seems to occur during childhood[5]. In India study of Gill (1994) showed present or past infection in 22% and 48% of children respectively[5]. In other studies from our country it has been noted that over 80% of subjects in the second decade had exposure to H. Pylori[6,7].

ORGANISM

H. Pylori is a spiral, gram negative organism with bluntly rounded ends. It has multiple, sheathed unipolar flagella on the human gastric mucosa. It is a curved or spiral bacterium. The abundant production of urease is a distinct characterstic of H.Pylori. Campylobacter and Helicobacter species resemble each other in many aspects including growth requirements and morphology. Hence H.Pylori has initially known as campylobacter pyloridis. It was reclassified as H. Pylori as its unique fatty acid composition, 16s ribosomal RNA sequence and ultrastructural characteristics, helped in differentiting it from campylobacter species[8].

PATHOGENESIS

H. Pylori has a predilection for gastric mucosa and found abundantly in the gastric antrum. It is highly motile in mucus, after penetrating the mucus protective layer it resides in the intracellular space where urea and hemin are present. Urease acts as a virulence factor, producing ammonium from urea, thereby increasing local gastric pH and protecting the acid labile organism. H.Pylori attracts and activates the neutrophils. H. Pylori also elaborates a protease capable of degrading gastric mucin and may also have unknown cytotoxic effects. The gastric mucosa is destroyed and inflammation results, possibly predisposing the patient to ulcer formation because the damaged cells are more prone to acid damage. H. Pylori may also damage doudenal epithelium. Colonization of gastro duodenal mucosa by H. pylori appears to be the primary event in the pathogenesis of

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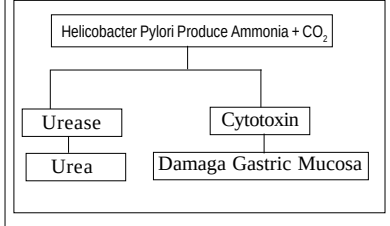
infection. Interaction between H.Pylori and gastric epithelial cells leads to local release of cytokines such as interleukin-resulting in recruitment and activation of inflammatory cells. H.Pylori suppresses the inhibitory peptide somatostatin in gastric mucosa and increases the release of the acid stimulating hormone gastrin. These changes lead to excessive acid secretion which may result into gastritis, gastric or doudenal ulcers. The current understanding is that DNA sequences in Hp genome are different in patients with peptic ulcer as compared to simple gastritis. Although no definite etiological role can be ascribed to Hp in causing recurrent abdominal pain in children. H.Pylori infection can be considered as an infection of children, Given the rising rates of prevalence of infection with age it can be assumed that in most of these children the infection lasts throughout their life.



CLINICAL MANIFESTATION

The clinical manifestation of Hp infection are not very clearly defined in children. Recurrent abdominal or periumbilical pain, retrosternal chest pain, nausea, vomiting, abdominal distention and hematemesis are the main symptoms of infection H.Pylori. H.pylori cause peptic ulcer in children as it does in adults. Increasing age has consistently been shown to be a major risk factor for Hp infection. Recent data has shown that over crowding, sharing a bed, low socioeconomic group with low parental education, low family income, general living conditions and consumption of contaminated water are major risk factors for Hp infection. Spiral organism have been seen in the stomach of humans and animals since 1893. But their significance was first pointed out by Barry Marshall & Robin Warren in 1983[9]. They associated these bacilli with chronic gastritis in adults, their report gave a significant impetus to the study of gastric bacteriology. It is not known whether H. Pylori gastritis causes symptoms in children, although the typical presentation of children with chronic gastritis is recurrent abdominal pain (RAP) and vomiting. A recently published study has demonstrated association of H. Pylori with RAP[10]. Peptic ulcer disease is uncommon in children and especially gastric ulcers are very rare. When they occur they are probably secondary in nature. However there is a strong correlation between doudenal ulceration and H. pylori infection in children[11].

Kilgridge et. al (1988), found antral gastritis in 40% of symptomatic children and of these 55% were associated with H. pylori infeciton[11]. Glsssman et. al (1989), found H. pylori positive gastrits in 44%[12] of symptomatic children. An increasing prevalence of H. pylori infection with increasing age has been observed among asymptomatic population[13]. Macarther et al have carried out a meta analysis of studies published in English literature from 1983 to 1994 and have been concluded that there is a strong evidence for an association between H. pylori infection and antral gastritis & duodenal ulcer disease in children. Czinn et. al (1998) have reported positive correlation between the severity of histopathological gastritis with severity of symptoms such as epigastric pain, burping and nausea in patient with H. pylori. Heldenberg and associates report on 54% children with RAP having the H. pylori gastritis by histopathology and CLO test on endoscopy[14].

Most of the children acquire the infection in childhood, usually before 5 years. The prevalence of H. pylori infection is about equal to age in years and is highly dependent on

childhood living conditions. There is a strong correlation between prevalence of H. pylori infection and markers of social deprivation in childhood. Infection is more likely in homes in which children share beds and where there is an outside toilet and no running Water. Transmission occurs via oro-faecal route, including contamination of water supplier. Recently infected infants may be particularly infectious.

H. pylori causes peptic ulcers in children as it does in adults. Increasing age has consistenly been shown to be a major risk factor for H. pylori infection. H. pyori has been classified as a group I carcinogen by the World Health Organization. Infection of gastric mucosa in childhood may be a particular risk factor for the development of gastric carcinoma in adult.

DIAGNOSIS

1. **Endoscopy :** GI endoscopy and biopsy of gastric mucosa is the investigation of choice. Nodularity of antral mucosa has been described in majority of children with H. pylori gastritis. These nodules give the antrum a cobblestone appearance. This appearance is not usually seen in adults with H. pylori gastritis. Biopsy specimen obtained by endoscopy can be assessed for H. pylori infection by culture on Columbia blood agar which is a gold standard for histological examinations and urease test as H. pylori produces high levels of enzyme urease this property is used to screen for the presence of bacteria in biopsy specimen. The warthin starry silver stain is 100% sensitive and specific and urease testing.
2. **Serology:** The H. pylori specific serum lgG has specificity of 99% and sensitivity of 96%, in detecting children with H. pylori infection. This sensitivity and specificity varies considerably, depending on the assay employed. Measurement of H. pylori specific serum lgG and lgA antibodies in children are not a sensitive indicator of gastric colonization[13].
3. **Urea Breath Test :** It is a non-invasive test for diagnosis of H. pylori infection. It is based on the fact that H. pylori produces large amount of urease. When labelled urea is given to a patient who is infected with H. pylori the urease enzyme splits urea into ammonia and labelled co_2 can be measured in the expired breath. This test has been shown to be safe and 100% sensitive and 97.6% specific for diagnosis of H. Pylori infection in children. The urea breath test is also 100% sensitive and specific in children following treatment for H. Pylori infection and can easily replace the need for follow up endoscopy in these children.

TREATMENT

Helicobacter pylori has been associated with several diseases including peptic ulcer disease and gastric cancer. Eradication of H. pylori not only result in healing but reduced recurrences. Eradication of H. pylori can be difficult. The most common drugs used to treat this infection include amoxycilin, clarithromycin, bismuth, omeprazole or lansoprazole. Triple therapy using at least two antibiotics and either bismuth or a proton pump inhibitor gives satisfactory eradication rates of 90%. However these regimens are complicated and have significant side effects. Problems of compliance have led to various regimen being used in eradication.

In children standard therapy has consisted of bismuth containing preparation combined with one antibiotic for a period of 2 to 6 weeks. Compliance is a very important factor in achieving high eradication rates in children. The long duration of treatment and the strong taste of ammonia associated with liquid bismuth may reduce compliance. A one week treatment regimen of colloidal bismuth substrate - 480 mg/ 1.73 m^3/day (max/120 mg Q.I.D.) + Clarithromycin 7.5 mg/kg/day (max. 250 mg B.D.) + Metronidazole 20 mg/kg/day (max. 200 mg TDS) eradicates H. Pylori infection in 95.5% cases. Only 10% children had significant side effects (vomiting and diarrhea) with its regime. Another suggested regimen is colloidal bismuth substrate (240 mg. B.D. in children > 10 yrs and 120 mg B.D. in children < 10 yr) + Amoxycillin (50 mg/kg/day 8 hrly) + Metronidazole (30 mg/kg/d 8 hrly) for two weeks.

Metronidazole resistance is an increasing problem in adults but is less common in children. Proton pump inhibitors are widely used in treatment regimens in adults but as yet, there is no information on their usefulness in children. In children long term remission of duodenal ulcer disease can be achieved with regimens which eradicate H. Pylori. The necessity of treating H. pylori infection in absence of duodenal ulcer disease in children is controversial.[15, 16, 17, 18].

CONCLUSION

H Pylori is an infection which is acquired in childhood with the major risk factor being poor socio-economic condition. H. Pylori gastritis alone is not a cause of symptoms in children. Duodenal ulcer disease in children is nearly always associated with H. pylori infection and long term healing of doudenal ulcer can be achieved by eradication of organisms. A strong association of H. Pylori infection acquired in childhood and development of gastric carcinoma in adult life exists. However, there are no guidelines at present in relation to the need of treating H. pylori infection in children. There is paucity of data on endoscopic, histologic and microbiological evaluation of children with upper abdominal pain, particularly from our country.

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