Leading Article

Helicobacter pylori infection in children

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Helicobacter pylori (H. pylori) infection is one of the common gastrointestinal infections in humans. It is now clear that *H. pylori* infection is acquired during childhood. The prevalence of *H. pylori* infection in children in developed countries ranges from 4.8% to 12.2%[1,2]. In developing countries the prevalence rates are much higher and vary from 15% in Gambian children aged less than 20 months[3] to 69.7% in preschoolers in Brazil[4]. An age related increase of prevalence, irrespective of the economic status of the country, has been observed by several independent studies across the world[2,3].

H. pylori was first reported in Sri Lanka in 1992 in 67% of adult patients with duodenitis and 8% of adults with non-ulcer dyspepsia[5]. Six years later, *H. Pylori* was isolated from an 80 year old man with an antral gastric ulcer and atropic gastritis[6]. A subsequent study has shown *H. pylori* infection in 2.9% of adult patients with functional dyspepsia[7]. Two studies done among Sri Lankan school children have reported prevalence of 6.5%[8] and 5%[9] by using a stool antigen test and 27.7% by detection of salivary (IgG) antibodies[8]. The reason for this relatively lower prevalence of *H. pylori* in Sri Lanka, compared to other developing countries, is multifactorial. Easily accessible free health care system, reasonably good housing and sanitary facilities and availability of safe drinking water are possible reasons. Furthermore, almost all studies done in developing countries have used serological tests to find the prevalence of *H. pylori* infection. Serological positivity does not necessarily indicate active infection, and can sometimes be a marker of a past infection. Only children having acute infection will shed antigen in their stools. Therefore, the prevalence rate using a stool antigen test may be lower compared to seroprevalence.

The main predisposing factor for *H. pylori* infection in children seems to be low socioeconomic status. However, McCallion et al. suggest that with regard to acquisition of infection, social class was acting as a proxy measure for conditions and practices within the household that increase the transmission of organism from infected to uninfected individuals[10].

The human stomach is the primary natural reservoir of *H. pylori*. Person-to-person spread appears to be the most likely mode of transmission. The possible routes are faeco-oral, oral-oral and gastro-oral. Several investigators have isolated viable *H. pylori* from human faeces suggesting the potential for faeco-oral transmission[11]. Oral-oral transmission was suggested after isolation of *H. pylori* from dental plaques and saliva[12]. The possibility of gastro-oral transmission was postulated after the organism was cultured from the vomitus of an infected child[13]. However, further research in this area is needed as the current knowledge on exact modes of transmission is far from conclusive.

Diagnosis is based on invasive and non invasive tests. A variety of invasive tests are used in the diagnosis of *H. pylori*. They include histological examination of gastric tissue, bacterial culture, rapid urease test, and polymerase chain reaction (PCR). Invasive tests need upper gastrointestinal endoscopy (UGIE) and gastric biopsy. Endoscopy and biopsy cannot be justified in children unless one wishes to isolate the organism for antibiotic sensitivity testing or there is a clear clinical indication for UGIE.

Histology demonstrates inflammation (gastritis) and *H. pylori* itself, if plentiful. Cultures are only performed in research settings and suspected drug resistance. The ability of the organism to split urea by the enzyme urease is used to identify *H. pylori* in biopsy specimens using the rapid urease test. The accuracy of this test is dependent on the number of tissue specimens tested, the location from which the biopsy was obtained, bacterial load, previous use of antibiotics and proton pump inhibitors, as well as the prevalence of infection in the community[14].

Non-invasive tests for *H. pylori* include measurement of Helicobacter antibodies, urea breath test and stool antigen test. *H. pylori* infection exerts an immunological response in the body. The presence of *H. pylori* antibodies does not always denote active infection. IgG antibodies can be

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measured in serum and saliva. Currently serological tests are not recommended for the diagnosis of *H. pylori* infection in children owing to their varying sensitivities and specificities in the paediatric age group[15]. The ^{13}C urea breath test is a safe method for diagnosing *H. pylori* infection in children. The sensitivity, specificity, positive predictive value and negative predictive values of the ^{13}C urea breath test are approximately 100%, 97%, 98% and 100% in children[16]. *H. pylori* stool antigen test is another safe diagnostic test. The sensitivity, specificity, positive predictive value and negative predictive value of this test in children are approximately 96%, 95%, 95% and 97%, and this has become the recommended test for diagnosis of *H. pylori* infection in paediatric patients[16].

It is important to keep in mind that testing children for *H. pylori* infection is only recommended in conditions that have a definite association with *H. pylori*. Definitive associations are gastritis, peptic ulcer disease, gastric adenocarcinoma, gastric non-Hodgkin lymphoma and gastric MALToma while the doubtful associations are gastro-oesophageal reflux disease, iron deficiency anaemia, growth faltering, recurrent abdominal pain and functional dyspepsia[17]. The tests used should have the ability to diagnose active infection. These include demonstration of the organism by histology or culture from endoscopic biopsy, urea breath test or stool antigen test[15].

Conditions that require treatment for *H. pylori* infection include endoscopically proven gastric or duodenal ulcer, histological evidence of gastric MALToma and pathologically proven gastric metaplasia in atrophic gastritis[15]. Treatment is not recommended in children with recurrent abdominal pain, and functional dyspepsia. It is also important to note that there is no evidence that treatment is beneficial in children with unexplained short stature, or in those that are at risk of infection (e.g. asymptomatic children who have a family member with either peptic ulcer or gastric cancer)[15].

Treatment is intended to eradicate *H. pylori* from the gastro-duodenal mucosa. It is vital to accomplish complete eradication as even a small residual colony will lead to re-colonization and re-infection. Under treatment also leads to drug resistance[15]. It is imperative that treatment is reserved for those patients who will benefit from eradication, and when offered, complete courses are given, and appropriate protocols that account for common local resistance patterns are followed. Evidence based data regarding anti-*H. pylori* treatment in children is not widely available. Most are open-labelled, case series and uncontrolled, anecdotal observations that do not meet the minimum criteria for determining efficacy[15]. Current treatment strategies have been developed primarily by using data from adults. Most of the treatment options have not been formally tested on children in developing countries, where the prevalence is high. The standard "triple therapy" used in children includes 2 weeks treatment with amoxicillin, clarithromycin and a proton pump inhibitor (omeprazole or lansoprazole) or clarithromycin, metronidazole and a proton pump inhibitor. As a second a line option, a combination of bismuth subsalicylate, amoxicillin and metronidazole for 2 weeks has been used successfully[18]. "Quadruple therapy", sequential therapy and salvage regimes with other antibiotics (rifabutin, levofloxacin and furozolidone) have not been tested in children up to now. It is also important that eradication is confirmed with a urea breath test or faecal antigen test 8 weeks after treatment. Failure to eradicate is an indication to use second line drugs. Repeated treatment failure is a clear indication to perform culture and antibiotic sensitivity of the organism[19].

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