

Campylobacter pylori gastritis: long term results of treatment with amoxycillin

G ODERDA,* D DELL'OLIO,* I MORRA,† AND N ANSALDI*

*Gastroenterology Service, Department of Paediatrics, University of Turin, and †Pathology Department, Children's Hospital Regina Margherita, Turin, Italy

SUMMARY To evaluate the efficacy of amoxycillin in eradicating *Campylobacter pylori*, endoscopic biopsy specimens were taken from the antral mucosa of 40 children with gastritis before, immediately after, and (in 30 patients) three months after treatment. Immediately after treatment 34 patients (85%) no longer had the organism in the mucosa, and the gastritis had healed in 23 (58%). Three months later the infection had recurred in 22 of 30 patients (73%), and the gastritis had relapsed in all of them. Significantly more children in whom *C pylori* recurred had family histories of peptic ulcer disease. The results suggest that amoxycillin alone is ineffective in the long term treatment of *C pylori* gastritis.

Since the description by Warren and Marshall of S shaped spiral Gram negative bacteria in the antral mucosa of adult patients with gastritis or peptic ulcer,¹ the association between *Campylobacter pylori* and gastritis has also been described in children,^{2,3} and the incidence among children undergoing endoscopy for upper gastrointestinal symptoms varies between 20 and 24%.^{4,5} Though the relationship has not been proved to be causal, preliminary studies have shown that elimination of the organism results in improvement or healing of the gastritis,⁶ thereby providing indirect evidence of its pathogenic role. Eradication has been achieved in adults with courses of amoxycillin,⁶ or tripotassium dicitratobismuthate,⁷ or a combination of the two, but relapse is common.

The aim of this study was to evaluate the efficacy of amoxycillin in the eradication of *C pylori* and the resolution of the peptic mucosal lesions in children with gastritis both immediately after the course of treatment, and three months later.

Patients and methods

Forty two children who had had *C pylori* isolated from the gastric mucosa were entered into the study between March 1987 and February 1988 (table 1). Fifteen of the children had undergone upper gastrointestinal endoscopy for recurrent abdominal pain (with or without vomiting) of six months to five years' duration; the remainder had the examination as part of their follow up after treatment for peptic

ulcer or reflux oesophagitis. Those with peptic ulcers had all been treated with ranitidine, and all but one were free of symptoms: those with reflux oesophagitis had been treated with antacids and all were free of symptoms.

Endoscopy was carried out with a paediatric gastroscope (Olympus GIF P3 or GIF XP20) after an overnight fast. Patients were sedated with oral diazepam and their throats were anaesthetised with amethocaine. Three biopsy specimens were taken from the antral mucosa within 1 cm from the pylorus. One was inserted into a rapid urease test (CLO-test, Delta West),⁸ one was put into chocolate agar medium for microaerobic culture, and the third

Table 1 Clinical details of 42 patients at presentation. Figures given are number of patients except for age

Age (years):	
Mean (SD)	12.2 (2.6)
Range	8-18
Sex (male:female)	26:16
Symptoms:	
Recurrent abdominal pain	16
Vomiting	7
Nausea	2
Anorexia	1
Haematemesis	1
Indication for endoscopy:	
Recurrent abdominal pain	15
History of peptic disease	18
Healing ulcer	17
Exacerbation of symptoms	1
History of oesophagitis	9

was cut into sections and stained with haematoxylin and eosin for histological examination, and Giemsa stain for identification of *C pylori*. Antral gastritis was defined according to the criteria of Whitehead *et al*⁹: a diffuse chronic inflammatory cell infiltration of the lamina propria was considered to be quiescent chronic superficial gastritis, and if neutrophils were present within the superficial or glandular epithelium, or both, it was considered to be active chronic superficial gastritis. Atrophic changes in the glandular epithelium were not found.

Treatment with amoxycillin 25 mg/kg twice daily was started as soon as colonisation by *C pylori* had been confirmed either by the CLO-test or on the Giemsa stained biopsy specimen, and continued for four weeks. In addition the nine patients who had had reflux oesophagitis continued postural treatment, and six children who had had relapses of their symptoms of peptic ulceration continued to take maintenance doses of ranitidine (2.5 mg/kg at bedtime). Patients were also allowed to take antacids if necessary.

The morning after the course of amoxycillin had finished the children were endoscoped again, and if *C pylori* had been eradicated no further treatment was given and they were asked to return three months later for further endoscopy. If *C pylori* was still present treatment with other drugs was started. At each endoscopy the presence of *C pylori* was assessed both by CLO-test and by Giemsa staining of an antral biopsy specimen.

To see if there were any differences between children in whom *C pylori* recurred and those in whom it did not, details of history, age, sex, family

history of peptic ulcer disease, duration of symptoms, activity of the gastritis, and the pattern of the antrum at endoscopy were recorded.

Unpaired data were compared by the χ^2 test with Yates's correction and paired data by McNemar's test; ordinal data were compared by Student's *t* test. A *p* value of <0.05 was accepted as significant. There is no ethical committee in our hospital, but it is our practice to inform parents and children fully about every procedure and to obtain consent even for the most routine measures.

Results

C pylori was identified by Giemsa staining of antral biopsy specimens in all 42 children. The CLO-test was positive in 38 (90%), and *C pylori* was grown on culture in 34 (81%). Endoscopic and histological findings are summarised in table 2.

Forty of the 42 children had the endoscopy repeated immediately after the course of amoxycillin (two refused). Giemsa staining of antral biopsy specimens showed that in 34 children *C pylori* had been eradicated (85%, *p*<0.001); the CLO-test was negative in all of them. Two children complained of recurrent abdominal pain, although it was less severe, but in the remainder it had resolved in a mean (SD) of 15 (9) days. No other symptoms were reported. In six children Giemsa staining of the antral biopsy specimens showed that *C pylori* was still present, and the CLO-test was positive in four of these. In one of these the recurrent abdominal pain was worse, but the others were free of symptoms.

Thirty of the 34 children in whom *C pylori* had

Table 2 Endoscopic and histological findings

	Before treatment started	Immediately after treatment stopped		Three months after treatment stopped	
		<i>C pylori</i> not present	<i>C pylori</i> present	<i>C pylori</i> not present	<i>C pylori</i> present
No of children	42	34	6	8	22
Endoscopic findings:					
Normal antrum	—	18	—	4	8
Nodular antritis	23	7	2	1	9
Pyloric hyperaemia	19	9	4	3	5
Oesophagitis	8	7	—	2	3
Duodenitis	6	2	—	—	1
Duodenal ulcer	1	—	—	—	2
Histological findings:					
Normal antrum	—	23	—	8	—
Chronic superficial gastritis:					
Quiescent	26	9	4	—	9
Active	16	2	2	—	13
Oesophagitis	11	4	—	1	—
Duodenitis	6	1	—	1	2

been eradicated immediately after the course of treatment had further endoscopies three months later. In 22 of these Giemsa staining of antral biopsy specimens showed that *C pylori* had recurred (73%, $p < 0.001$); the CLO-test was positive in 19. Two of the children developed recurrent abdominal pain about two months after the course of amoxicillin, but the pain was less severe than it had been at presentation and there were no associated symptoms. In eight children the *C pylori* did not recur and the CLO-test was negative in all eight. One of these developed mild recurrent abdominal pain about a month after treatment had been stopped.

There were no significant differences between the 22 children in whom *C pylori* recurred and the eight in whom it did not except in the incidence of a family history of peptic ulcer disease; all the children who had a recurrence had a family history of peptic ulcer compared with two of the eight who did not ($p < 0.001$).

Discussion

The prevalence of *C pylori* infection in children is lower than in adults, and increases with age.¹⁰ In children with gastritis, however, it is similar to that in adults with peptic ulcer disease and varies from 70¹¹ to 80%.¹²

The endoscopic picture of the gastric antrum in children with gastritis associated with *C pylori* has been described as nodular¹³; in a retrospective study of 31 children with nodular antral gastritis we found *C pylori* in 90%,¹⁴ but this is not the only picture found in gastritis associated with *C pylori*. In the present series nodular antral gastritis was found in only 23 (55%) of children before treatment. In the rest there was only mild hyperaemia of the pylorus, a nearly normal picture. If the antrum is nodular, therefore, *C pylori* should be sought, but other findings do not exclude its presence. Macroscopically normal mucosa may be histologically abnormal both in children and adults, but a nodular antrum is not predictive of a higher recurrence rate. There was a good correlation between the presence of *C pylori* and gastritis, but signs of active gastritis were not predictive of recurrent infection.

C pylori can also be associated with oesophagitis,¹⁵ and in the present series histological changes typical of peptic oesophagitis (lengthening of the papillae, inflammatory infiltration of the epithelium, and thickening of the basal layer) were more common than macroscopic oesophagitis at endoscopy. We treated these children even if they had no symptoms, because traditional treatment had failed to heal the histological damage of the mucosa that looked normal at endoscopy: our results suggest

that eradication of *C pylori* is associated with the healing of oesophagitis.

Seventeen of the 18 children who had histories of peptic ulcer disease were free of symptoms, but we elected to treat them because we hoped to do them good by eradicating *C pylori*. In a long term follow up study of children with peptic ulcers¹⁶ we found that 89% of those with relapsing peptic ulcer disease were carriers of *C pylori*, compared with 29% of those in whom it did not relapse. In the present series one child had a duodenal ulcer that healed after the course of amoxicillin, and in two others ulcers relapsed when the *C pylori* infection recurred three months later. Longer periods of follow up and larger series of patients are needed to confirm these data.

Though symptoms that were present before treatment disappeared within a fortnight in most cases, the response to amoxicillin was not predictive of recurrence of *C pylori*. Mild abdominal pain recurred in three children in whom *C pylori* had recurred (13%) and in one in whom it had not (12%).

From these data it seems that upper gastrointestinal endoscopy is the only way of proving that *C pylori* is present in the stomach, but to do the endoscopy immediately after treatment is useless as it will not show whether long term eradication of the organism has been achieved.

Amoxicillin alone does not seem to be effective in the long term eradication of *C pylori*; we had planned to enrol more patients in the study but because of the unacceptably high recurrence rate (73%) we did not feel justified in doing so. It seems likely that treatment with combinations of drugs—for example, amoxicillin with tripotassium dicitratobismuthate or metronidazole, or both¹⁷—may be necessary to eradicate the organism entirely. The six children from whose stomachs *C pylori* was isolated at the first follow up, and the 22 in whom it had recurred at three months, were treated with combinations of drugs.

Whether recurrence of *C pylori* infection is caused by relapse, or reinfection by exogenous strains, is not certain but the significantly higher incidence of recurrence among those children with family histories of peptic ulcer disease suggests that reinfection from contacts in the families may be the cause. Long term eradication may be better effected by treatment of all infected family members.

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Correspondence to Dr G Oderda, Gastroenterology Service, University of Turin, Piazza Polonia 94, 10126 Torino, Italy.

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