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ORIGINAL ARTICLE

Treating Children with *Helicobacter Pylori* Gastritis in East London: is it time for New Guidelines?

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ABSTRACT

AIM: The joint guidelines for the management of *Helicobacter pylori* (*H. pylori*) in children and adolescents by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) were last updated in 2016

More recent guidelines from the National Institute for Health and Care Excellence (NICE) updated in 2019 only focus on adult patients. Our study aimed to benchmark practices at a tertiary paediatric gastroenterology unit against national and international guidelines.

MATERIALS AND METHODS: Retrospective data from children diagnosed with *H. pylori* gastritis between 2015 and 2017 were collected and analysed by two independent reviewers. Baseline characteristics (age at time of diagnosis, gender, co-morbidities) and details related to *H. pylori* gastritis (*H. pylori* faecal antigen result, symptoms at diagnosis, endoscopic and histological findings, treatments and follow-up) were recorded in an anonymised Excel spreadsheet and evaluated.

RESULTS: 638 (18.5%) of 3451 children investigated in East London during the study period had a positive stool antigen test. During the same time period, 40 children were referred to our tertiary centre for an upper GI endoscopy that confirmed *H. pylori* gastritis. Only 26 children (65%) were re-tested to confirm eradication, which was achieved in 18. Only 30% of family members were tested in the community and treated if positive.

CONCLUSION: Further integration between general practice and specialist paediatric care and guideline updates are needed to ensure efficacy of eradication and to tackle the risk of a re-infection within the patient's household.

Key words: Paediatric Gastroenterology; *Helicobacter pylori*; Antibiotic Resistance; Eradication; Integrated Practice

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Authorship credits

All Authors listed (JM, JD, VB, JL, SN, AK, PD, NC, MG) have contributed to: (1) conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of

the version to be published. More specifically, JM and JD contributed equally to this paper. MG and JD conceived the study design and were responsible for data collection. PD, SN and AK participated in the study set up at the time of its conception. MG, JD and JM were responsible for data analysis and interpretation. JM drafted the initial manuscript, reviewed and revised it. MG critically reviewed the manuscript and revised it. JL, VB and NC gave important input for revising and improving the quality of the manuscript. All co-authors approved the final manuscript.

List of abbreviations

ESPGHAN: European Society of Paediatric Gastroenterology, Hepatology and Nutrition;

GI: gastro-intestinal;

GP: general practitioner;

H. Pylori: Helicobacter Pylori;

NASPGHAN: North American Society for Paediatric Gastroenterology, Hepatology and Nutrition;

NHS: National Health System;

NICE: National Institute for Health and Care Excellence;

PPI: proton pump inhibitor;

SD: standard deviation.

INTRODUCTION

The joint guidelines for the management of *Helicobacter pylori* (*H. pylori*) in children and adolescents by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) were last updated in 2016 in view of increasing challenges with eradication therapy due to rising prevalence of antibiotic-resistant strains^[1]. Key recommendations include avoiding a “test and treat” strategy for *H. pylori* infection in children, monitoring success of therapy by non-invasive testing after 4-8 weeks, and evaluating the effectiveness of first line therapy in national/regional centres.

More recent guidelines from the National Institute for Health and Care Excellence (NICE) only focus on adult patients^[2]. These guidelines recognise the overall increase in treatment use and potentially significant costs to the National Health Service (NHS) associated with the management of dyspepsia, as well as the increase in drug resistance. In contrast to the paediatric guidelines, a “test and treat” approach is recommended. Suggested first-line antibiotic regimes are the same but recommended duration is limited to 7 days compared to 14 days in children.

Whilst the mechanisms whereby *H. pylori* is spread are still not fully understood, intra-familial transmission is thought to play an important role^[3]. East London has an ethnically diverse population and high prevalence of *H. pylori* infections. The area includes some of the most socioeconomically deprived boroughs in England with a high proportion living in overcrowded households^[4].

We performed an internal audit at our tertiary level Gastroenterology unit in East London to benchmark our practices against the standards described in the joint ESPGHAN/NASPGHAN and NICE guidelines and to identify how these recommendations would apply to our *H. pylori* high-prevalence catchment area.

METHODS

The Cerner Millennium electronic patient record system at Bart’s Health NHS Trust was interrogated to identify the number of children (i.e. age < 18 years at the time of testing) who were investigated

for *H. pylori* faecal antigen between January 2015 and December 2017. Retrospective data from 40 children diagnosed with *H. pylori* gastritis based on histological examination of gastric biopsies during the same time period were collected by 2 independent reviewers using information from the electronic patient records. Baseline characteristics (age at time of diagnosis, gender, co-morbidities) and details related to *H. pylori* gastritis (*H. pylori* faecal antigen result, symptoms at diagnosis, endoscopic and histological findings, treatments and follow-up) were recorded in an anonymised Excel spreadsheet and evaluated.

RESULTS

Within the study period, *H. pylori* antigen test was undertaken on faecal samples from 3451 children in our catchment area, of which 638 (18.5%) were positive.

Due to clinical concerns, during the study period 40 children (24 males, mean age 11.7 years, median 13 +/- SD 3.94, range 3-16) were referred to our tertiary level centre for a diagnostic confirmation based on histological examination of gastric biopsies. In terms of co-morbidities, 14 children had none, 6 children had Crohn’s disease, 2 had irritable bowel syndrome, 2 had severe constipation, 2 had rumination syndrome, and 14 had other illnesses. All these co-morbidities were known about when the children were investigated with an upper GI endoscopy.

The most common symptom at referral was abdominal pain in 30 (75%) patients, with a specific epigastric location in 19 (47.5%). Eighteen (45%) patients presented with nausea, reflux or vomiting, 5 (12.5%) with haematemesis, 4 (10%) with chest pain and 5 (12.5%) with anaemia. Four patients with anaemia required pre-endoscopy transfusion (Table 1).

All 40 children had histological confirmation of *H. pylori* gastritis i.e. presence of gastritis and *H. pylori* visible on gastric biopsies. Gastritis was severe in 8 patients (21%), moderate in 14 patients (37%), mild in 16 patients (42%) and non-specific in 2 patients (5%). Three patients had gastric ulcers and five had duodenal ulcers on upper gastrointestinal endoscopy (Table 1).

Twelve (30%) had faecal antigen tested before/at diagnosis, all of these tested positive. Rapid urease test (CLO) was positive in 24/32 of the patients tested (75%). The total number of patients diagnosed according to the ESPGHAN/NASPGHAN guidelines (*H. pylori* gastritis on histopathology and one other positive test i.e. CLO or faecal antigen) was 26 (Table 1).

All patients received *H. pylori* eradication therapy; the majority of patients (69%) responded to 1st (amoxicillin, clarithromycin, PPI) or 2nd line (clarithromycin, metronidazole, PPI) treatments. 4/40 patients (10%) required 3rd line antibiotics (tetracycline, metronidazole, bismuth) with input from Microbiology. Two treatment-refractory patients also had antibiotic sensitivity on culture from gastric biopsies tested (Table 2).

Twenty-six (65%) patients were re-tested with *H. pylori* faecal antigen and/or endoscopy to confirm eradication. In this group, successful eradication was achieved in 18 (69%) patients.

From the records available to us only 30% of the time were family members tested in the community and successfully treated if positive (Table 2). In the cases where the family members weren’t tested, there was no evidence in the records that this had been requested of the GP (Table 2).

DISCUSSION

To our knowledge, this is one of the most comprehensive studies

to examine practices around *H. pylori* care in children in England. According to our findings, there is a very high prevalence of *H. pylori* in children in East London. We believe this reflects the level of socioeconomic deprivation of the patients we see and the high proportion of them living in overcrowded households, and that these results do not necessarily apply to other areas of England or abroad where the epidemiology may be different.

Significant faecal antigen testing appears to be happening in the

Table 1 Patients with histologically confirmed *H. pylori* gastritis (n=40), Characteristics at diagnosis.

Baseline Characteristics	
Age of diagnosis (Years)	Average: 11.7 +/- SD 3.94; median: 13; range: 3-16
Co-morbidities (number affected)	None: 14
	Crohn's disease: 6
	Irritable bowel syndrome: 2
	Severe constipation: 2
	Rumination syndrome: 2
	Others: 14
Gender	Male: 24; Female: 16
Characteristics at Diagnosis	
Symptoms (number affected)	Abdominal pain: epigastric 19, generalised 17, both 6
	Nausea, reflux, vomiting: 18
	Chest pain: 4
	Anaemia: 5
	Haematemesis: 5
	Need for blood transfusion: 4
Haemoglobin (g/L)	Average 118 +/- SD 24.58; median 122; range 50-163
Haematocrit (%)	Average 36.4 +/- SD 4.84; median 37; range 24-46
Histology of gastric biopsies	Confirmatory of <i>H. Pylori</i> gastritis: 40
	Mild gastritis: 16
	Moderate gastritis: 14
	Severe gastritis: 8
	Non-specified: 2
Ulcers on upper GI endoscopy (number affected)	Gastric ulcers: 3
	Duodenal ulcers: 5
H. Pylori faecal antigen test (number tested)	Positive: 12
	Negative: 0
	Not tested: 28
Rapid Urease Test on upper GI endoscopy (CLO)	Positive: 24
	Negative: 7
	Not performed: 9

Table 2 Patients with histologically confirmed *H. pylori* gastritis (n=40) - Treatment and follow-up.

Treatment and follow-up	
1st line only (amoxicillin, clarithromycin, PPI) (number treated)	28
2nd line (clarithromycin, metronidazole, PPI) (number treated)	8
3rd line (tetracycline, metronidazole, bismuth) (number treated)	3
Antibiotic sensitivity on culture from gastric biopsies (number tested)	2
Post-treatment testing to confirm effective eradication (number tested)	Tested: 26 (23 <i>H. Pylori</i> faecal antigen, 2 upper GI endoscopies, 1 both)
	Not tested: 14
Efficacy of eradication treatment in those re-tested	Successful eradication (negative test result): 18
	Failed eradication (positive test result): 8
Testing of family members (number tested)	Tested and treated if positive: 12
	Requested to GP but outcome unknown: 5
	Not tested: 23

community without patients being referred to tertiary services for endoscopy. Given that general practitioners (GPs) may be more familiar with the “test and treat” strategy used for adults as per NICE guidelines, it may be possible that this approach is also being employed in children and that they are being over-diagnosed/treated if compared with NASPGHAN/ESPGHAN guidelines. Clearer guidance on faecal antigen testing in children and what to do with positive results is desirable.

Of note, our current practice differs from ESPGHAN/NASPGHAN guidelines in that all of our patients with confirmed *H. pylori* received treatment. However, treatment was rarely based on antibiotic sensitivities, which may explain why some children needed 2nd and 3rd line eradication therapy and this could be contributing to resistance patterns. Very few children who tested positive for *H. pylori* and received treatment showed evidence of peptic ulcer disease.

A significant proportion of our cohort was not assessed for eradication, and it was difficult to tell if testing of family members had occurred and actioned upon. Neither the joint ESPGHAN/NASPGHAN guidelines nor the NICE guidelines give clear guidance regarding testing and treating household members, and we suggest that this should be a future emphasis for guidelines updates. It also highlights the ongoing requirement for more integrated and joined up care for paediatric services especially between general practice and specialist paediatric care.

Further integration between general practice and specialist paediatric care is needed to ensure efficacy of the eradication treatment implemented and to tackle the risk of a re-infection within the patient's household.

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