CAMPYLOBACTER ENTERITIS IN CHILDREN:
CLINICAL AND LABORATORY FINDINGS IN 137 CASES

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ABSTRACT

One hundred and thirty-seven children with Campylobacter diarrhoea were reviewed. The predominant species was C. jejuni. Ninety-five percent of the children were below 5 years of age with 61% of these being 2-12 months old. A slight male preponderance was noted. About half the cases presented with fever and bloody diarrhoea; vomiting was seen in 25% and abdominal colic in only 8%. Moderate to severe diarrhoea was present in 48% of the children. Thirty-seven percent had a history of recent or concurrent illness. Other bacterial enteropathogens together with Campylobacter were isolated in 15% of the children. Erythromycin, the most useful drug, when indicated for Campylobacter infections, had an MIC90 of 2 mg/l with 96.2% of the strains being sensitive.

Keywords: Campylobacter, enteritis, children, antimicrobial susceptibility, clinical features

INTRODUCTION

Campylobacter jejuni and Campylobacter coli are well established human enteric pathogens that cause diarrhoea and enteritis in patients in both developing and developed countries. Both species make up the most common bacterial cause for acute diarrhoeal illness in developed countries(1) and there appeared to be a bimodal age distribution of Campylobacter infection with the highest incidence in infants and in young adults between 15-27 years(2). In developing countries, the prevalence in children is particularly high and Campylobacters ranked as the third most common cause of acute diarrhoeal disease after rotavirus and enterotoxigenic Escherichia coli(2).

The few published reports from Singapore and Malaysia(3,4) give a low isolation rate of Campylobacters but the true incidence may be 5-10 times greater than that of the industrialised countries. However, the ratio of illness to infection is probably lower and symptomless excreters are common in developing countries(5). There is still controversy over the exact pathogenic mechanism(s) by which Campylobacters induce diarrhoea but there is no doubt that these organisms are aetiological agents implicated in human diarrhoeal disease.

In this paper, we describe the bacteriological, demographic and some clinical characteristics of Campylobacter diarrhoeal cases seen in children at the University Hospital, Kuala Lumpur.

PATIENTS AND METHODS

From June 1982 to May 1988, 7,221 specimens of stool and rectal swabs from paediatric patients less than 12 years of age, were processed for enteropathogens by standard bacteriological techniques. For the isolation of Campylobacters, only bloody and watery stool specimens were inoculated on Skirrow's medium (Oxoid, UK) and incubated at 42°C for 48 hours under microaerophilic conditions using an anaerobic gas generating kit (Oxoid, UK) without the catalyst. Organisms showing typical comma, S or spiral forms in Gram-stained smears, actively motile, oxidase and catalase positive, and sensitive to nalidixic acid but resistant to cephalothin were provisionally identified as Campylobacter jejuni/coli. The hippurate hydrolysis test was used to distinguish the two species.

The in-vitro susceptibility of 52 strains of Campylobacters to 12 antimicrobial agents was determined by an agar dilution method. Antibiotic powders with known potencies used were erythromycin, cotrimoxazole (trimethoprim: sulphamethoxazole 1:19), chloramphenicol, tetracycline, nalidixic acid, ampicillin and kanamycin (Sigma Chemicals, USA), cefotaxime and gentamicin (Roussel Uclaf Laboratories, France), cefoxoperazone (Pfizer, USA), norfloxacin (Astra, Sweden) and pefloxacin (Rhone-Poulenc, France). Minimum inhibitory concentrations (MIC) were determined using doubling dilutions of antibiotics prepared in Mueller-Hinton agar (Difco, USA) supplemented with 7% laked horse blood (Oxoid, UK) except for cotrimoxazole where supplemented isosensitst agar (Oxoid, UK) was used. The inoculum was prepared from 48-hour plate cultures diluted in Mueller-Hinton broth to give a final inoculum size of approximately 10^8 organisms per spot when delivered by a Denley multipoint inoculator. Inoculated plates were incubated for 48 hours at 37°C under microaerophilic conditions as described earlier. Controls used in each plate were Oxford Staphylococcus aureus NCTC 6571 and Escherichia coli NCTC 10418. The MIC was defined as the lowest concentration of antimicrobial agent at which there was complete inhibition of growth or the presence of a barely visible haze. For cotrimoxazole, the concentration which inhibited at least 80% of growth

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Patients' records were reviewed for demographic data such as age, sex, ethnic group and the following clinical data: (i) presenting signs and symptoms such as fever, vomiting, abdominal colic, severity of diarrhoea, and bloody stool; (ii) previous or concurrent illness such as measles, upper respiratory tract infections, otitis media, bronchopneumonia and others; (iii) oral or intravenous rehydration; and (iv) antibiotic therapy.

RESULTS

One hundred and thirty-seven separate cases of Campylobacter diarrhoeas were recorded during the study period. The total number of paediatric stool processed during the period was 7,221 giving a crude isolation rate of 2%. Seventy-six (55%) of the children were seen as in-patients and 61 (45%) were seen on an out-patient basis. Although 137 isolates had been identified as C. jejuni/coli, only 83 of these were available for the hippurate hydrolysis test which distinguished 62 (75%) as C. jejuni and 21 (25%) as C. coli. There were 85 boys and 52 girls, giving a male to female ratio of 1.6:1. About half the patients (41%) were Chinese, 32% Malays, 25% Indians and 2% were classified as others. The distribution amongst the various ethnic groups is in keeping with the racial composition of the population served by the hospital. The age distribution of these cases is shown in Fig 1; the youngest was a 2-day-old baby and the oldest was 10 years. The largest group (61%) was from the 2-12 month age group, 19% from the 2-5 year group and 14% from neonates.

The results of the in-vitro susceptibility studies are shown in Table I. All strains tested were susceptible to chloramphenicol and gentamicin with 96.2% of the strains being sensitive to erythromycin, the traditional drug recommended for invasive Campylobacter jejuni disease. The minimum concentration of erythromycin inhibiting the growth of 50% of the strains (MIC<sub>50</sub>) and 90% of strains (MIC<sub>90</sub>) was 2 mg/l. Tetracycline had poor in-vitro activity with a MIC<sub>50</sub> of 4 mg/l and a MIC<sub>90</sub> of 128 mg/l. 94.2% of the strains tested were susceptible to nalidixic acid while the newer quinolones norfloxacin and pefloxacin had excellent in-vitro activity with a MIC<sub>90</sub> of 1.0 mg/l for both drugs. Ampicillin at a breakpoint susceptibility of <32 mg/l was active against 90.2% of the strains and amongst the third-generation cephalosporins tested, good activity was seen with cefotaxime (MIC<sub>90</sub> 32 mg/l) but no activity was observed with cefoperazone (MIC<sub>90</sub> >128 mg/l).

A little more than half of the children, 74 (54%), presented with fever. The passage of bloody stool was recorded in 70 (51%) of the cases although moderate to severe diarrhoea was recorded only in 66 (48%) children. Other features were vomiting in 38 (28%) cases and abdominal colic was recorded in only 10 (8%) of the children.

Fifty-one children (37%) had a history of recent or concurrent illness such as upper respiratory tract infections in 14, bronchopneumonia 6, post-measles 5, haematological malignancies 4, febrile fits 4, otitis media 3, and surprisingly 9 cases were recorded in children who had been admitted for milk challenge. Other miscellaneous factors such as intussusception, Reye's syndrome and congenital duodenal atresia were recorded in 6 children.

Other bacterial enteropathogens were isolated together with Campylobacters in 15% of the children. These were: Salmonella species in 11, Aeromonas species 3, Plesiomonas shigelloides 3, Shigella species 2 and enteropathogenic E. coli in 2.
Antibiotic therapy for enteritis was administered to 36 (26%) children, these being cotrimoxazole for 10 children, neomycin 9, erythromycin 9, ampicillin 7 and amoxycillin for one.

Rehydration therapy was recorded in 50 (37%) children; of these, 12 required intravenous infusion and 39 were given oral fluids (glysolte).

DISCUSSION

Most microbiology laboratories are well equipped to isolate and identify Campylobacters. Nevertheless, our crude isolation rate of 2% is low compared to published reports from the West. One of the reasons may be that Campylobacter diarrhoea is a self limiting disease and only the moderate to severe infections are seen in the hospital. This is supported by the fact that only 55% of our cases needed in-patient treatment, and of these, only 12 required intravenous fluids. Another reason may be that not all stool samples were processed for Campylobacters and the true incidence may be higher.

The majority of our isolates (75%) were C. jejuni and this confirms published reports of C. jejuni being the most common species giving rise to human infection(9). Campylobacters exist as commensals in the intestinal tracts of a wide variety of wild and domestic animals and commercially raised poultry are known to be one of the most common sources of infection(9). In Malaysia, Campylobacters have been isolated from chickens, puppies as well as from poultry for sale(10).

It is not surprising that 75% of the children in our study were less than one year of age. In Thailand, Varavithya et al(11) found Salmonella and C. jejuni as the common cause of diarrhoea in children less than 6 months of age. Campylobacter is a foodborne infection and strict food hygiene is necessary for its prevention, especially in infants and young children. Since the disease is mainly confined to young children in developing countries, repeated exposure probably results in immunity early in life(11). In our study there were 3 babies less than 3 days old with Campylobacter infection, but we were unable to obtain any antepartum history of diarrhoea from the mothers. Perinatal transmission maybe due to exposure in utero, during passage through the birth canal or during the first days of life(11).

Symptoms and signs of Campylobacter infections are not so distinctive to differentiate it from illness caused by other enteropathogens. Published reports indicate that about 50% of patients present with fever which agrees with our figure of 54%. Abdominal colic is said to be a characteristic feature of Campylobacter diarrhoea but in our study only 8% had abdominal colic. This low figure is probably a reflection of the age group of our patients as most were less than 1 year-old and hence would have been unable to complain of abdominal pain or discomfort. Vomiting was seen in 26% of children although this is said to be rare in Campylobacter infection.

Inflammatory changes accompanied by haemorrhagic lesions have been reported in the jejunum and ileum of patients with Campylobacter enteritis(12). But the frequent finding of bloody stools suggests mucosal damage of the large intestine is also involved(12).

Bloody stool seen macroscopically was recorded only in 51% of our patients. The type of diarrhoea ie either watery or with blood is probably due to the type of exotoxin produced by the infecting strain whether it is a cytotoxic enterotoxin(13) or a cytotoxin(14). It is a well known fact that recent debilitating illness can predispose children to infectious diarrhoea. Fifty-one of the 137 (37%) children gave a history of recent or concurrent illness, the commonest being upper respiratory tract infection, bronchopneumonia and measles.

Isolation of more than one enteropathogen is not infrequent in developing countries and 15% in our study is not too high. But these children with mixed pathogens did not have a more severe infection. Normal carriage of some enteropathogens is possible but very rare in Campylobacter being less than 1%. (15).

The role of antimicrobial agents in the therapy of diarrhoea is somewhat controversial. Chemotherapy for most intestinal infections is often considered ineffective and even disadvantageous.

Antimicrobial therapy of invasive disease with C. jejuni coli has traditionally been with erythromycin. However, varying geographical differences have been noted in the in-vitro susceptibility of C. jejuni to this macrolide (16). In our setting, erythromycin with MIC90 of 2 mg/l remains a useful drug in the empirical management of invasive disease. Resistance to erythromycin and cotrimoxazole was lower amongst our strains (3.8% and 15.4% respectively) as compared to 12.6% and 30.1% respectively in the study carried out by Michel et al on C. jejuni strains isolated in Israel (16). However, resistance to ampicillin and tetracycline was higher in our study. Gentamicin and chloramphenicol with MIC90 of 0.5 mg/l and 8.0 mg/l respectively were active against all the strains tested at our centre but the in-vivo response to these agents is not well documented. The fluoroquinolones, norfloxacin and pefloxacin had high degrees of in-vitro activity (MIC90 of 1 mg/l for both) and while both drugs may be useful in the management of severe cases of enteritis, pefloxacin with good serum and tissue levels is an alternative to erythromycin for invasive disease. However, the safety of using quinolones in children is an unresolved issue. The newer macrolide azithromycin, with greater intrinsic activity and improved pharmacokinetic properties needs to be investigated as an alternative therapy.

REFERENCES


