Clostridium difficile in general practice and community health

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SUMMARY

The isolation rate for Clostridium difficile in diarrhoeal stools was investigated in patients from general practice and community health centres over a 14-month period. C. difficile or its cytotoxin was detected in specimens from 89 (4.7%) of 1882 patients studied and accounted for 30.3% of all enteropathogenic micro-organisms isolated. Overall C. difficile was second only to Giardia lamblia in frequency. Recovery rates in the different groups of patients surveyed varied from 3.6 to 27.5%. The relationship between stool culture results and stool cytotoxin assay also varied considerably between groups of patients studied. Coincident infections with a variety of enteropathogenic bacteria and intestinal parasites were diagnosed in 14 of the 89 patients. It was concluded that laboratories servicing this type of practice should be aware that C. difficile may be a cause of diarrhoea. An adequate clinical history should facilitate proper processing of the specimen.

INTRODUCTION

The role of Clostridium difficile in antibiotic-associated diarrhoea and pseudomembranous colitis is well established (Bartlett et al. 1978; Larson et al. 1978). Both these conditions have been related to the use of antimicrobial agents (Bartlett et al. 1979), however this is not always the case (Wald, Mendelow & Bartlett, 1980; Howard, Sullivan & Troster, 1980) and the significance of C. difficile in other forms of diarrhoea is still being debated (Falsen et al. 1980; Bolton, Sheriff & Read, 1980; Brettele et al. 1982).

Previous studies on the frequency of isolation of C. difficile in relation to diarrhoeal disease have shown isolation rates of 11.0% in the United States (Gilligan, McCarthy & Genta, 1981), 3% in Sweden (Falsen et al. 1980), 12.3% in Great Britain (Brettele et al. 1982) and 14.5% in Australia (Riley, Bowman & Carroll, 1983). These studies have tended to concentrate on specimens obtained from patients attending large teaching hospitals and may have given the impression that C. difficile-associated diarrhoea was only a problem within large hospitals. The aim of our investigation was to determine the isolation rate for C. difficile in patients with diarrhoea presenting to their general practitioner or community
health centre and not necessarily requiring hospitalization, or patients in small rural hospitals under the care of their general practitioners.

MATERIAL AND METHODS

Patients and specimens

All patients were seen by their general practitioners or at community health centres in either rural centres throughout Western Australia, an area of one million square miles, or the metropolitan area of the capital city, Perth, between May 1983 and July 1984. Stool samples were submitted to the Public Health and Enteric Diseases Unit of the State Health Laboratory Services, in sterile plastic containers, having been transported in a refrigerated state. Specimens were usually cultured within 24 h of collection. However, due to the isolation of some rural centres (up to 1500 miles away) some longer delays were unavoidable. In the majority of cases specimens were accompanied with a request for ‘routine’ microbiological investigation. Unfortunately, in most instances a minimal amount of clinical information was provided, precluding the use of criteria which we had previously found satisfactory for the study of hospital patients (Riley, Bowman & Carroll, 1983; Bowman & Riley, 1984). Therefore, stool samples were cultured if they met only one of those criteria, that being that the stools were loose or watery. On the basis of information on the request form patients were divided into the following four groups: (1) those patients in whom a specific request for culture for C. difficile was made; (2) those patients who were known to have a history of antibiotic therapy; (3) those patients known to be in-patients at small rural hospitals; and (4) those patients remaining.

Because of the difficulty in interpreting the isolation of C. difficile in the very young, children under the age of 1 year were excluded from the study.

Demonstration of C. difficile and other enteric pathogens

The methods employed for the isolation of C. difficile and other enteric pathogens and for the demonstration of C. difficile cytotoxin have been described previously (Riley, Bowman & Carroll, 1983). They include the use of a selective broth for C. difficile containing gentamicin 5 mg/l, cycloserine 250 mg/l and cefoxitin 8 mg/l (GCC broth) (Carroll, Bowman & Riley, 1983). Final identification of C. difficile was made according to the criteria of Holdeman, Cato & Moore (1977). Enteric pathogens other than C. difficile were identified by means of appropriate microscopic, biochemical and serological techniques.

RESULTS

During the period of the study, stool samples from 14,877 patients were received by the Public Health and Enteric Diseases Unit of the State Health Laboratory Service. Of these, specimens from 1882 patients (12.6%) were examined for C. difficile. From the 1882 patients, recognized enteric pathogens were recovered in 444 (23.4%). Two hundred and ninety-four patients (15.6%) yielded enteropathogenic bacteria; intestinal parasites were found in 217 (11.5%). Table 1 shows the incidence and types of enteric pathogens found in the study population. C. difficile
C. difficile in diarrhoeal stools

Table 1. Incidence of enteric pathogens in 1882 patients from either general practice or community health centres

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. positive</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Giardia lamblia</em></td>
<td>131</td>
<td>(7-0)</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>89</td>
<td>(4-7)</td>
</tr>
<tr>
<td><em>Shigella</em> spp.</td>
<td>60</td>
<td>(3-2)</td>
</tr>
<tr>
<td><em>Campylobacter jejuni</em></td>
<td>60</td>
<td>(3-2)</td>
</tr>
<tr>
<td><em>Salmonella</em> spp.</td>
<td>54</td>
<td>(2-9)</td>
</tr>
<tr>
<td><em>Hymenolepis nana</em></td>
<td>47</td>
<td>(2-5)</td>
</tr>
<tr>
<td><em>Aeromonas hydrophila</em></td>
<td>30</td>
<td>(1-6)</td>
</tr>
<tr>
<td><em>Ancylostoma duodenale</em></td>
<td>20</td>
<td>(1-1)</td>
</tr>
<tr>
<td><em>Strongyloides stercoralis</em></td>
<td>14</td>
<td>(0-7)</td>
</tr>
<tr>
<td><em>Enterobius vermicularis</em></td>
<td>3</td>
<td>(0-2)</td>
</tr>
<tr>
<td>Vibri spp.</td>
<td>1</td>
<td>(&lt; 0-1)</td>
</tr>
<tr>
<td><em>Entamoeba histolytica</em></td>
<td>1</td>
<td>(&lt; 0-1)</td>
</tr>
<tr>
<td><em>Trichuris trichiura</em></td>
<td>1</td>
<td>(&lt; 0-1)</td>
</tr>
</tbody>
</table>

Table 2. Results of stool cultures for *C. difficile* and stool cytotoxin assays

<table>
<thead>
<tr>
<th>Patient group</th>
<th>No. of patients studied</th>
<th>Stool culture no. positive (%)</th>
<th>Cytotoxin assay no. positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Requests for <em>C. difficile</em></td>
<td>40</td>
<td>11 (27-5)</td>
<td>9 (22-5)</td>
</tr>
<tr>
<td>(2) History of antibiotic therapy</td>
<td>88</td>
<td>14 (15-9)</td>
<td>10 (11-4)</td>
</tr>
<tr>
<td>(3) Small hospital in-patient</td>
<td>446</td>
<td>16 (3-6)</td>
<td>6 (1-3)</td>
</tr>
<tr>
<td>(4) Loose or watery stools</td>
<td>1308</td>
<td>48 (3-7)</td>
<td>11 (0-8)</td>
</tr>
<tr>
<td>Total</td>
<td>1882</td>
<td>89 (4-7)</td>
<td>36 (1-9)</td>
</tr>
</tbody>
</table>

or its cytotoxin was found in 89 patients, and accounted for 30-3% of all enteropathogenic bacteria isolated.

Recovery rates for *C. difficile* in the different groups of patients surveyed are summarized in Table 2. There was no difference in isolation rate between in-patients in small rural hospitals and the remaining patients with loose or watery stools. However, there were significant differences between these two groups of patients and those with either a history of antibiotic therapy or a request for *C. difficile* culture.

An interesting trend is apparent in the relationship between stool culture results and stool cytotoxin assay. Only 23% of the 48 patients in group 4 had demonstrable cytotoxin in their stools, compared to 37% of the 16 in group 3, 71% of the 14 in group 2 and 82% of the 11 in group 1.

Of the 89 patients from whom *C. difficile* was isolated 14 had coincident infections with other enteric pathogens. There were 11 coincident infections in group 4 patients. These comprised seven different infecting agents; *Campylobacter jejuni* (5), *Salmonella* sp. (1), *Shigella* sp. (1), *Aeromonas hydrophila* (1), *Giardia lamblia* (1), *Ancylostoma duodenale* (1) and *Strongyloides stercoralis* (1). There were three coincident infections in those patients from small rural hospitals comprising

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A. hydrophila (1), G. lamblia (1) and A. duodenale (1). There were no coincident infections recorded in either of the other two groups of patients.

DISCUSSION

We have previously reported the isolation rate for C. difficile from patients with diarrhoeal disease to be 14.5% (Riley, Bowman & Carroll, 1983). Since these results were derived from a study of patients attending a large general hospital we decided to conduct a further survey of patients from general practice and community health. The present study has demonstrated that the isolation of C. difficile from diarrhoeal stools does not occur only in large hospitals. C. difficile was the most common microbial isolate in association with diarrhoeal stools in 1882 patients from general practice and community health centres. The isolation rate was 4.7% and C. difficile was second only to G. lamblia in frequency of detection.

While the overall isolation of 4.7% was considerably lower than our previous report (14.5%), it is of interest to compare isolation rates from the different groups of patients studied. The isolation rates of 3.6 and 3.7% in groups 3 and 4 respectively were only slightly higher than the figure of 3% quoted as the carriage rate in normal population studies (George, Sutter & Finegold, 1978). However, in a previous study we found a much lower isolation rate of 0.8% in patients with an appropriate history, which suggested that the carriage rate of C. difficile may have been less than 3% (Bowman & Riley, 1984). The isolation rates from patients in groups 1 and 2 of 27.5 and 15.9% respectively are more in keeping with our previous findings (Riley, Bowman & Carroll, 1983; Bowman & Riley, 1984). Prior exposure to antibiotic agents (group 2) is the major predisposing factor for C. difficile-associated diarrhoea, and it may be assumed that specific requests to look for C. difficile probably originated when diarrhoea occurred after antibiotics. It is difficult to gauge antibiotic usage in general practice, however some inappropriate use of antibiotics must occur. In particular, clindamycin is apparently commonly used for the treatment of infections with Staphylococcus aureus. This is one of the main antibiotics incriminated in C. difficile-associated diarrhoea (Bartlett et al. 1979).

The relationship between stool culture results and stool cytotoxin assay for the different groups of patients was interesting. Bartlett et al. (1979) have reported a relationship between the concentration of C. difficile cytotoxin and the number of organisms present in the stool specimen. Although the clinical histories obtained in many cases were less than ideal, the apparent trend in this study indicates a relationship between the presence of cytotoxin and severity of disease. However, there appears to be no relationship between cytotoxin titre and severity of disease (Burdon et al. 1981).

Falsen et al. (1980) studied C. difficile in relation to other enteric bacterial pathogens and found shigella, campylobacter and yersinia in 36% of their 56 patients from whom C. difficile was isolated, while Gilligan, McCarthy & Genta (1981) found no co-infections in 161 patients studied. We found other enteric pathogens in 16% of our 89 patients. To our knowledge this is the first report of C. difficile being isolated from patients in whom various intestinal parasites had been detected such as G. lamblia, A. duodenale and S. stercoralis. In addition C. difficile was isolated coincidentally with A. hydrophila, a significant cause of
C. difficile in diarrhoeal stools

Gastrointestinal disease in local studies (Gracey et al. 1982). These findings are in keeping with the suggestion made by Falsen et al. (1980) that any change in normal bacterial faecal flora due to other enteric infections increases the possibility of isolating C. difficile.

The most difficult aspect of this investigation involved trying to obtain an adequate clinical history from the requesting physician. In a previous study, carried out in hospital environment, to determine whether routine culturing for C. difficile was warranted, compliance of clinical staff enabled several criteria to be defined (Bowman & Riley, 1984). Unfortunately when dealing with general practitioners and community health workers up to 1500 miles away, obtaining an adequate history was sometimes impossible, precluding the use of our previously tested criteria.

In conclusion, this study has demonstrated that the isolation of C. difficile and detection of its cytotoxin is common in general and rural practice. Accordingly, microbiology laboratories servicing this type of practice should be aware of this fact and be able to provide the relevant diagnostic procedures.

REFERENCES


