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Original Article

Bacteriology and antibiotic susceptibility of community-acquired intra-abdominal infection in children

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Background and Purpose: Intra-abdominal infection can be a life-threatening condition in children, and aggressive treatment is usually needed. The treatment should include surgical correction and drainage, and administration of antimicrobials that are effective against both aerobic and anaerobic microorganisms. This study investigated the microbiological characteristics of intra-abdominal infection of children in Taiwan.
Methods: Data for bacterial specimens from 113 children (64 males), aged from 9 months to 18 years, who had community-acquired intra-abdominal infections at our hospital during a 10-year period were analyzed.
Results: In total, 113 specimens were collected, including those with only aerobes (62%), and those with mixed aerobic and anaerobic species (35%). A total of 239 aerobes and 86 anaerobes were isolated. Polymicrobial infection was found in 79% of specimens. The predominant aerobe was *Escherichia coli* (42%), and *Bacteroides fragilis* (36%) was the most frequently isolated anaerobic microorganism. Enterococcus was detected in about 14% of Gram-positive aerobic isolates. Review of the results of antibiotic susceptibility testing revealed that the Gram-positive aerobes, apart from staphylococci, had a high susceptibility rate to ampicillin, and 84% of Gram-negative aerobes were susceptible to gentamicin. In addition, *B. fragilis* showed a high resistance rate to clindamycin (52%) but all of these isolates were susceptible to metronidazole.
Conclusion: Triple antibiotic combination therapy including ampicillin, gentamicin and metronidazole remains an alternative empirical antibiotic therapy for pediatric patients with mild to moderate community-acquired intra-abdominal infection.

Key words: Abdominal abscess, bacteriology, community-acquired infection, drug resistance, microbial sensitivity tests

Introduction

Intra-abdominal infections that are the result of secondary peritonitis generally occur due to the entry of enteric microorganisms into the peritoneal cavity through a necrotic defect in the wall of the intestine or other viscus as a result of obstruction or infarction or after rupture of an intra-abdominal visceral abscess [1]. These enteric bacteria are typically synergistic polymicrobial entities, including both aerobes and anaerobes [2]. Characteristically, the greater the number and type of bacteria that can be isolated from an individual, the graver the likely morbidity [3]. The specific pathogens involved in peritonitis are generally those of the normal flora of the gastrointestinal tract [4]. In children, peritonitis is mainly associated with appendicitis, but may occur with intussusception, incarcerated hernia, volvulus, or rupture of a Meckel's diverticulum. Although less common in children than in adults, peritonitis also occurs as a complication of mucosal diseases such as peptic ulcer, ulcerative colitis, Crohn's disease, and pseudomembranous colitis [1,3].

Microbiological investigation of intra-abdominal infections in children has been limited [2,3,5]. Historically, empirical antibiotic therapy with clindamycin or metronidazole, gentamicin, and ampicillin has been used [1,6], but the bacteriology and antibiotic susceptibility

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of specific pathogens involved in peritonitis requires epidemiological monitoring. This retrospective study analyzed the etiology and antimicrobial susceptibility of isolates in pediatric patients with community-acquired intra-abdominal infections over a 10-year period.

Methods

Tri-Service General Hospital is a 1400-bed tertiary medical center located in Taipei, northern Taiwan. Medical charts of hospitalized children (<18 years) presenting with mild to moderate, acute-onset community-acquired peritonitis requiring surgical intervention or percutaneous drainage from May 1995 to April 2005 were retrospectively reviewed. Patients were excluded if they had nosocomially acquired intra-abdominal infections, invasive abdominal procedures in the past 1 month, or no positive-culture reports. Community-acquired infection was defined as a positive result from peritoneal culture performed within 72 h after admission. Data collected from review of medical charts included age, gender, initial presentation, infection sites, microbiological data, and antibiotic susceptibility.

Preparation of samples

The specimens were aspirates of peritoneal fluid or abscess collected with a needle and syringe or swab at the time of surgery. For children managed non-operatively, specimens obtained at the time of percutaneous drainage were also cultured. All specimens were collected using a transporting swab or tube that was suitable for aerobes and anaerobes. Inoculation was performed within 6 h after specimen collection. Duplicate isolates from the same patient were excluded from the analysis.

Bacteriological examination

Aerobic culture was performed at 37°C for 2 to 4 days, while anaerobic incubation was performed at 37°C for 5 to 7 days, in an atmosphere of 82% nitrogen, 10% carbon dioxide, and 8% hydrogen. Aerobic and anaerobic species were identified by previously described techniques [7] or with the ATB 32A system (bioMérieux, Marcy l'Etoile, France). Antimicrobial susceptibility was tested by the disk diffusion method in accordance with guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) [8].

Results

The ages of the 113 children included in the study ranged from 9 months to 18 years (mean, 8.7 years). Their presenting conditions included: ruptured appendix in 86; intestinal or other peritoneal viscus perforations or necroses in 20 patients, which involved the cecum in 8, the small intestine in 3, the ascending colon in 3, the transverse colon in 3, the sigmoid colon in 2, and the descending colon in 1. Other clinical conditions included liver abscess in 3, gallbladder empyema in 1, continuous peritoneal dialysis-related peritonitis in 1, rupture of a Meckel's diverticulum in 1, and urachal rupture in 1.

A total of 113 specimens were obtained from 113 children, with only anaerobic bacteria isolated in 3 specimens, only aerobes in 70 specimens, and mixed aerobic and anaerobic isolates in 40 specimens. Thus, 97% of specimens yielded aerobic organisms and 38% anaerobic organisms. In total, 325 bacterial isolates were recovered from the 113 culture-positive specimens (2.9 per specimen; Table 1), including 239 aerobic isolates (2.1 per specimen). The most frequently isolated aerobe was *Escherichia coli* (42%). There were 86 anaerobic bacteria isolated (0.8 per specimen) and the predominant anaerobe was *Bacteroides fragilis* (36%).

The rate of polymicrobial isolation was 79% and the average number of isolates per specimen was 3.4. No consistent pattern of bacterial combination was noted, apart from 1 possible exception of mixed infection with *B. fragilis* and *E. coli* in 24 patients.

As shown in Table 2, the antibiotic susceptibility results revealed that 12% of Gram-positive aerobic cocci were not susceptible to ampicillin (apart from staphylococci, the non-susceptible rate to ampicillin was 8%). As shown in Table 3, 16% of isolates of Gram-negative aerobic bacilli were resistant to gentamicin. Resistance to clindamycin was found in 39% of Gram-negative anaerobic bacilli, although none were resistant to metronidazole. All *Peptostreptococcus* isolates were susceptible to clindamycin, ticarcillin, or metronidazole, except for 1 isolate which was resistant to penicillin G and ampicillin (Table 4).

Discussion

Mixed aerobic and anaerobic flora have previously been recovered from the peritoneal cavity of adults and children with ruptured appendix or intestinal viscus [9, 10]. In this study, aerobic organisms were found in 97% of specimens, anaerobic organisms in 38%, and mixed aerobic and anaerobic flora in 35%. Thus, the presence of mixed aerobic and anaerobic flora in the peritoneal cavity was common following secondary peritonitis in children in this hospital-based study.

Table 1. Microorganisms isolated from children with intra-abdominal infection

Aerobic and facultative isolates	No. of isolates	Anaerobic isolates	No. of isolates
Gram-positive cocci (total)	79	Gram-positive cocci (total)	17
Viridans group streptococci	43	*Peptostreptococcus* spp.	17
Non-A, -B, -D streptococcus	16	Gram-negative bacilli (total)	58
Enterococcus	11	*Bacteroides fragilis* group, other spp.	20
Group D streptococcus	5	*Bacteroides fragilis*	31
Staphylococcus spp.	4	*Fusobacterium* spp.	5
Gram-positive bacilli (Diphtheroids)	2	*Prevotella* spp.	2
Gram-negative bacilli (total)	158	Gram-positive bacilli (total)	11
Escherichia coli	101	*Propionibacterium acnes*	3
Pseudomonas aeruginosa	21	*Eubacterium lentum*	3
Proteus spp.	8	*Clostridium* spp.	2
Klebsiella pneumoniae	8	*Lactobacillus* spp.	3
Morganella morganii	3		
Aeromonas	3		
Acinetobacter lwoffii	3		
Citrobacter spp.	4		
Salmonella spp.	2		
Other aerobic Gram-negative rods	5[a]		
Total number of aerobes and facultatives	239	Total number of anaerobes	86

[a]The other aerobic Gram-negative bacilli included 1 *Pseudomonas pseudoalcaligenes*, 1 *Vibrio* sp., 1 *Klebsiella* subsp. *ozaenae*, 1 *Enterobacter cloacae* and 1 *Acidaminococcus fermentans*.

In this study, *E. coli* was the most frequently encountered aerobe (31% of all isolates) and *B. fragilis* (10% of all isolates) was the most frequently recovered anaerobe. These findings are similar to previous reports of patients with gangrenous or perforated appendicitis [3, 11,12]. A similar study in adults found that *E. coli* was the most commonly isolated pathogen (47% of all isolates) and *Bacteroides* spp. were the most commonly isolated anaerobes (6% of all isolates) [13]. Such difference in etiology and proportion rates may be due to differences in the condition of patients. The majority of children in this study (76%) had complicated appendicitis, but 38% of atients in the study of adults had complicated appendicitis and 23% had perforation of the stomach and duodenum [13]. In general, Gram-negative aerobic organisms colonize the upper gastrointestinal tract but the colonic contents are predominantly anaerobes [1].

Bennion et al found that in studies of gangrenous and perforated appendicitis before 1988, the mean number of the aerobic and anaerobic isolates per specimen was 1.2 and 0.9, respectively [11]. This number was rather small in comparison to their report, that documented a much greater number of bacterial isolates (mean number of aerobes, 2.7; mean number of anaerobes, 7.4) per specimen from individuals suffering similar diseases [11]. In this study, the number of aerobic and anaerobic isolates per specimen was 2.1 and 0.8, respectively.

The comparatively small number of anaerobic isolates in this study may have been due to the practice of administering, almost routinely, metronidazole prior to surgery in children with suspected acute intra-abdominal infection [12]. Moreover, swabs probably do not provide a reliable specimen-conveying technique

Table 2. Resistance rates of aerobic Gram-positive cocci isolates to various antimicrobial agents

Aerobic Gram-positive cocci isolates	No. of isolates (n = 79) [%]	No. of resistant isolates/ no. of isolates tested for susceptibility (%)			
		Penicillin G	Ampicillin	Cephalothin	Gentamicin
Viridans group streptococci	43 (54)	4/40 (10)	4/42 (10)	1/24 (4)	0/27 (0)
Non-A, -B, -D streptococcus	16 (20)	0/16 (0)	1/16 (6)	0/8 (0)	0/4 (0)
Enterococcus	11 (14)	1/10 (10)	1/10 (10)	4/6 (67)	2/7 (29)
Group D streptococcus	5 (6)	0/5 (0)	0/5 (0)	0/2 (0)	0/2 (0)
Staphylococcus spp.	4 (5)	4/4 (100)	3/3 (100)	-	1/4 (25)
Total	79 (100)	9/75 (12)	9/76 (12)	5/40 (13)	3/44 (7)

Table 3. Resistance rate of aerobic Gram-negative bacilli (GNB) isolates

Aerobic GNB isolates	No. of isolates (n = 158) [%]	Ampicillin	Cephalothin	Gentamicin	Amikacin
Escherichia coli	101 (64)	76/98 (78)	46/99 (46)	22/99 (22)	0/99 (0)
Klebsiella pneumoniae	8 (5)	8/8 (100)	0/8 (0)	0/8 (0)	0/8 (0)
Proteus spp.	8 (5)	4/8 (50)	3/8 (38)	0/8 (0)	0/8 (0)
Pseudomonas aeruginosa	21 (13)	-	-	1/21 (5)	0/21 (0)
Acinetobacter lwoffii	3 (2)	2/3 (67)	1/3 (33)	0/2 (0)	0/2 (0)
Citrobacter spp.	4 (3)	4/4 (100)	1/3 (33)	1/3 (33)	0/4 (0)
Aeromonas	3 (2)	3/3 (100)	2/3 (67)	0/3 (0)	0/3 (0)
Morganella morganii	3 (2)	3/3 (100)	1/3 (33)	0/3 (0)	0/3 (0)
Salmonella spp.	2 (1)	0/2 (0)	0/1 (0)	-	0/1 (0)
Total[a]	153 (97)	100/129 (78)	12/128 (95)	24/147 (16)	0/149 (0)

[a]Not including other aerobic Gram-negative rods in Table 1.

for detecting anaerobic bacteria, particularly when the biological specimen is not transported to the microbiology laboratory in an anaerobic transport system, or when the specimen is not inoculated in an appropriate culture medium as soon as possible [14,15]. Differences in the culture techniques rather than regional differences in the bowel flora have been mentioned as a possible explanation for the wide variation of isolation rates among studies [11,12,14].

Prophylactic antibiotic therapy appears to reduce the frequency of wound infection and intra-abdominal abscess formation in patients undergoing appendectomy for suspected appendicitis [12]. Therefore, the use of antimicrobials which are effective against both aerobic and anaerobic bacteria has become the cornerstone of current clinical practice in dealing with such infections [16,17]. Empirical therapy for such disease should include agents effective against *E. coli* and *B. fragilis*. However, it is important to be aware that *Pseudomonas aeruginosa* has been recovered from approximately 20% of healthy children hospitalized for acute appendicitis [6]. In this study, the second most frequently isolated Gram-negative bacilli was *P. aeruginosa;* this organism accounted for 13% of all Gram-negative bacilli isolates, 5% of which were resistant to gentamicin.

The traditional antibiotic regimen for treating Gram-negative bacilli and anaerobes in such infections is gentamicin and either metronidazole or clindamycin, although there has been a significant increase in the rate of resistance to clindamycin among isolates of *B. fragilis* group organisms in Taiwan and many other countries [5,14,18]. In Taiwan, Teng et al reported that the rate of resistance to clindamycin for isolates of *B. fragilis* group organisms was high (33%-70%). They also reported a high resistance rate of *B. fragilis* to clindamycin of 33%, although the age distribution of patients was not mentioned [18]. In this study, the overall activity of clindamycin against *B. fragilis* group organisms was poor; the resistance rate of *B. fragilis* to clindamycin was 52%, which was higher than that of other *B. fragilis* group spp. (26%). In a study from South Korea reported in 1994, Lee et al demonstrated that the rate of resistance to clindamycin among isolates of *B. fragilis* group organisms from children was higher than that of similar isolates from adult patients (53.3% versus 40.5%) [5]. A study from Japan found the resistance rate of *B. fragilis*

Table 4. Resistance rate of anaerobic isolates to various antimicrobial agents

Anaerobic isolates	No. of isolates (n = 77) [%]	No. of resistant isolates/no. of isolates tested for susceptibility (%)				
		Metronidazole	Penicillin G	Clindamycin	Ampicillin	Ticarcillin
Bacteroides fragilis	31 (40)	0/18 (0)	30/30 (100)	16/31 (52)	30/30 (100)	1/27 (4)
Bacteroides fragilis group, other species	20 (26)	0/12 (0)	16/20 (80)	5/19 (26)	16/20 (80)	1/19 (5)
Fusobacterium spp.	5 (6)	0/3 (0)	1/5 (20)	1/5 (20)	1/5 (20)	0/3 (0)
Prevotella spp.	2 (3)	0/2 (0)	2/2 (100)	0/1 (0)	1/2 (50)	0/2 (0)
Gram-negative bacilli (total)	58 (75)	0/36 (0)	50/58 (86)	22/57 (39)	49/58 (84)	2/52 (4)
Peptostreptococcus spp.	17 (22)	0/11 (0)	1/12 (8)	0/10 (0)	1/12 (8)	0/9 (0)
Clostridium spp.	2 (3)	-	1/1 (100)	1/1 (100)	-	0/1 (0)

No. of resistant isolates/No. of isolates tested for susceptibility (%)					
Aztreonam	Cefuroxime	Ceftazidime	Ceftrixone	Imipenem	Cefepime
0/61 (0)	0/44 (0)	0/63 (0)	0/61 (0)	0/61 (0)	0/39 (0)
0/6 (0)	0/5 (0)	0/7 (0)	0/6 (0)	0/7 (0)	0/4 (0)
0/4 (0)	2/4 (50)	0/4 (0)	0/4 (0)	0/4 (0)	0/4 (0)
0/10 (0)	-	8/11 (73)	8/11 (73)	0/12 (0)	0/6 (0)
1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/2 (0)	0/1 (0)
0/2 (0)	0/2 (0)	0/1 (0)	0/1 (0)	0/2 (0)	0/1 (0)
0/3 (0)	1/3 (33)	0/2 (0)	0/2 (0)	0/3 (0)	0/3 (0)
0/2 (0)	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
0/1 (0)	0/1 (0)	0/2 (0)	0/1 (0)	0/1 (0)	0/1 (0)
1/90 (1)	5/62 (8)	8/62 (13)	8/89 (9)	0/94 (0)	0/61 (0)

to clindamycin was 26.5% [19]. Results from our study suggest a high prevalence of clindamycin-resistant *B. fragilis* group organisms in our country (especially for children), as well as Japan [19] and South Korea [5], in contrast to that in Indonesia, Europe, and the United States [10]. Further, our data indicate that metronidazole remains the most active agent against *B. fragilis* group organisms. No resistance to this drug was found in this series, although metronidazole-resistant *B. fragilis* group organisms have occasionally been recovered in Taiwan and other countries [18-20].

According to NCCLS guidelines, *Peptostreptococcus* spp. have been considered to be fully susceptible to several beta (β)-lactam drugs, including penicillin G. In Korea, Lee et al reported the emergence of *Peptostreptococcus* spp. isolates resistant to β-lactam drugs, including 7.4% to penicillin G and metronidazole, respectively, and 25.9% to clindamycin [5]. In Taiwan, Teng et al reported that isolates of *Peptostreptococcus* spp. had a 16% resistance rate to penicillin, 55% to clindamycin and 32% to metronidazole [18]. In this study, we did not find any *Peptostreptococcus* spp. resistant to metronidazole or clindamycin, and the resistance rate to penicillin G and ampicillin was 8%.

Triple-agent therapy, including clindamycin or metronidazole, gentamicin, and ampicillin has been advocated for the treatment of intra-abdominal infections or acute appendicitis in children in several previous studies [1,6,16,17,21]. However, in the United States, a high proportion of *E. coli* isolates from community-acquired infections appear to be no longer susceptible to ampicillin [6], and the significance of enterococci in polymicrobial, intra-abdominal infections has been questioned [22]. Thus, the use of ampicillin in combination with other antimicrobial agents for the treatment of intra-abdominal infections has often been debated [6,15,22], although mortality rates appeared to be greater when enterococcus was involved in intra-abdominal infections [22]. In this study, enterococcus was found in 14% of Gram-positive aerobes, and apart from staphylococci, isolated Gram-positive aerobes revealed a high susceptibility to ampicillin (92%).

The results of this study suggest that a combination antibiotic regimen including ampicillin, gentamicin and metronidazole is an alternative empirical antibiotic regimen for the treatment of pediatric patients with mild to moderate community-acquired intra-abdominal infections. However, such regimens typically require multiple doses of the various agents daily, and it has been recommended that aminoglycoside levels be monitored when the anticipated duration of therapy is longer than 3 days [6]. Several recent studies have reported that some of the newer antibiotics, such as imipenem, meropenem, ticarcillin/clavulanate and piperacillin/tazobactam can provide the necessary breadth of antibacterial spectrum with a single agent [12]. The application of such single-agent therapy might be appropriate in order to avoid the use of aminoglycosides for patients with renal disease or hearing loss [6]. Further studies regarding the treatment of children with intra-abdominal infections are needed in this hospital and elsewhere to evaluate the relative efficacy and safety of these new single agents as compared to combination regimens.

In conclusion, this study found a rather high prevalence of clindamycin-resistant *B. fragilis* group isolates in children with community-acquired intra-abdominal infections, none of which was resistant to metronidazole. This finding suggests that initial antibiotic therapy should include metronidazole instead of clindamycin. We conclude that triple antibiotic combination therapy including ampicillin, gentamicin and metronidazole remains an alternative empirical antibiotic choice for the treatment of pediatric patients with mild to moderate community-acquired intra-abdominal infection.

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