SECONDARY BACTERIAL PERITONITIS IN CHILDREN - A BACTERIOLOGICAL APPROACH

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Abstract

Introduction: Despite advances made by medical science, secondary bacterial peritonitis (SBP) still remains a threat for children.

The objectives of this study were to identify aerobic bacteria responsible for SBP in children and to find the proper antibiotic treatment to cure it.

Materials and method: We analyzed medical charts and microbiological data of children suffering from SBP (0-18 years old), admitted to the Pediatric Surgery Department of "Louis Turcanu" Children Emergency Hospital.

Results: Out of 93 children diagnosed with SBP between January 2008-March 2009, 49 had positive peritoneal cultures with aerobic bacteria. E. coli was the dominant bacteria encountered, while Enterococcus isolates were the only Gram-positive bacteria found. Imipenem, Ertapenem, Ticarcillin/Clavulanic acid and Ciprofloxacin seems to be the best choice in the treatment of SBP. Perforated appendix was the common cause of SBP (87.75%), followed by the intestinal perforation (6.13%), necrosis (4.08%), or trauma (2.04%).

Conclusions: An adequate management of SBP assures decreased hospitalization, prevents emergence of antibiotic resistance and it is cost effective too.

Key words: secondary bacterial peritonitis, antibiotic, children

Introduction

Despite advances in diagnosis, surgery, antimicrobial therapy and intensive-care support, severe secondary bacterial peritonitis (SBP) remains a potentially fatal distress. It represents a major cause of morbidity, with a mortality rate of 30%[1]. SBP generally occurs due to the entry of enteric bacteria into the peritoneal cavity. This pathway is due to necrotic defect in the intestinal wall or abdominal organs, caused by infarction, obstruction, or direct trauma[1]. In children, SBP is mainly associated with perforated appendicitis (PA), but may associate with intussusception, incarcerated hernia, volvulus, or rupture of a Meckel's diverticulum. Although less common in children than in adults, SBP can occur as a complication of intestinal mucosal disease, including peptic ulcers, ulcerative colitis, and pseudomembranous enterocolitis[1]. Intra-abdominal infection in the neonatal period is often a complication of necrotizing enterocolitis but may also be associated with meconium ileus or spontaneous rupture of the stomach or intestines or Hirschsprung's disease[1].

The specific bacteria involved in SBP are generally those from the normal gastrointestinal tract flora, at the site of entry to the peritoneal cavity. Some retrospective studies evaluated the microbiology of the peritoneal cavity and post-operative wounds following perforated appendix in children[1,2]. The predominant aerobic bacteria were Escherichia coli, Pseudomonas aeruginosa, while Bacteroides fragilis and Peptostreptococcus spp. were dominant in the anaerobic group. In addition, bacteria responsible for SBP differed in newborns than in older children. Klebsiella, Enterobacter, Streptococcus spp, and Clostridium difficile were the main isolated from peritoneal fluid in newborns that had peritonitis associated with necrotizing enterocolitis[1].

The dynamics and changes in the microbial flora from the gastrointestinal tract influence the nature and severity of infections that follow perforation. The alkaline environment of the lower intestines, the billiary effect and the decrease in oxygen tension in the lower intestine explains the increase in the number of bacteria found at the distal portions of the gastrointestinal tract.

The necessity of obtaining cultures from the peritoneal cavity of pediatric patients with SBP is believed to be an absolute necessity by many surgeons. It is axiomatic to identify the bacteria present and their antibiotic sensitivities, as they are vital to the care of the child after the surgery. Examining the results of intra-operative cultures, evaluating the bacterial sensitivity and resistance, as well as making appropriate adjustments of antibiotic coverage are necessary for good childcare.

Objectives

The aim of our study was to identify aerobic bacteria responsible for acute SBP in children. In addition, their antibiotic susceptibility was tested.

Method and materials

Our study took place at the Pediatric Surgery Department of "Louis Ţurcanu" Children Emergency Hospital, between January 2008 and March 2009. All children (aged 0-18 years) admitted in hospital for SBP were included in the study group. Exclusion criteria consisted in the presence of intra-abdominal or visceral abscess**,** invasive abdominal procedures in the last month, or no previous positive peritoneal-culture. SBP is to be defined as a positive result when obtained from peritoneal fluid culture, which is performed within 72 hours after admission, in a child with abdominal pain, fever, vomiting, or anorexia.

The following data were obtained after reviewing medical charts: age, gender, infection sites, initial presentation defined according to the criteria of ASA (American Society of Anesthesiologists) score, severity of the underlying disease, total hospital stay and mortality rate. Microbiological data and antibiotic susceptibility were noted.

One or more peritoneal fluid specimen(s) were collected during surgery. Inoculation of these samples was on aerobic medium and then incubated at 37ºC for 5-7 days. Antibiotic susceptibilities of bacterial isolates were determined using the disk-diffusion method, according to the actual recommendations. The susceptibilities of aerobic bacteria were determined for antibiotics (Ciprofloxacin, Levofloxacin, Ampicilin, Trimethoprim/Sulfamethoxazole, Gentamicin, Amikacin, Ticarcillin/Clavulanic acid, Cefotaxime, Ceftazidime, Ceftriaxone, Meropenem, Imipenem, Ertapenem, Colistin, Rifampicin, Clindamicyn, Vancomycin and Linezolid).

Results

During the study period, 93 children were admitted to the hospital having SBP. Out of these, 49 children (74.46% boys and 25.53% girls) had SBP with aerobic bacteria. Their age ranged between 10 days and 18 years, with a mean of 10.29 years. Among these, perforated appendix was the common cause of SBP (87.75%), followed by the intestinal perforation (6.13%), necrosis (4.08%), or trauma (2.04%) (Figure 1). Severe underlying disease included sepsis with multiple organ failure, tetraparesis, and neurofibromatosis.

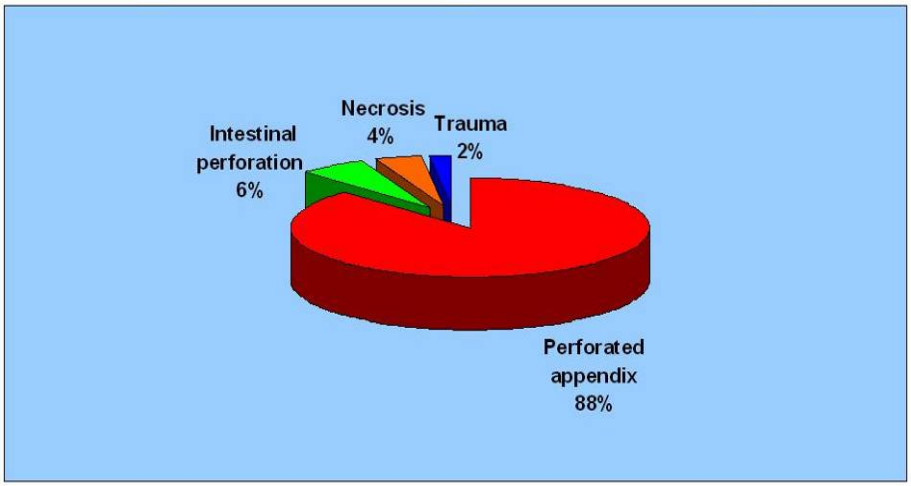

Figure 1 Common causes of SBP encountered.

Upon admission to the Pediatric Surgery Department, four children presented severe conditions having an ASA score of 4, 7 children had an ASA score of 3 and the rest were with ASA 2. The median length of stay at the hospital was 10 days (range 3-40 days). In all patients, surgical treatment consisted of evacuation of pus and peritoneal lavage. The types of surgeries carried out were as follows: appendectomy (n = 43), small bowel suture (n =1), small bowel resection with anastomosis (n = 4), and colonic resection (n =1). Mortality rate was 4.08%, in two newborns. One of them was small for gestational age, with neonatal peritonitis due to a cecal volvulus complicated with intestinal ischemia. The other was a preterm baby with Gram-negative sepsis having multiple organ failure associated with necrotizing enterocolitis accompanied by severe acid-base and electrolyte disorders.

Fifty-four specimens were collected from 49 children, including 51 Gram-negative isolates. Escherichia coli (72.22%) were by far the most frequently encountered bacteria in our study, followed by Pseudomonas aeruginosa (12.96%), Enterobacter (3.70%), Chromobacterium violaceum (3.70%) and Klebsiella ascorbata (1.85%). Three isolates of Enterococcus faecium were the only Gram-positive strains found in our lot. Five children had polymicrobial infections (E. coli + Pseudomonas aeruginosa or E. coli + Enterococcus faecium).

Gram-negative bacteria were highly sensible to Carbapenems, Ticarcillin/Clavulanic acid and Ciprofloxacin as presented in figure 2. E. coli, the dominant bacteria encountered, was 100% susceptible to Ticarcillin/Clavulanic acid. High rate of sensibility was found to Carbapenems, Quinolones, 3rd and 4th generation Cephalosporin and Aminoglycosides. Pseudomonas aeruginosa was susceptible to the same antibiotics as E. coli, but was 100% susceptible to Colistin. Both Klebsiella ascorbata and Enterobacter isolates were sensible to penicillin plus a beta lactamase inhibitor, Carbapenems and Cephalosporins. In addition, Enterobacter isolates were susceptible to Colistin and Quinolones. All Enterococcus faecium isolates were 100% susceptible to Vancomycin, Linezolid, Teicoplanin and Rifampicin (Figure 2). Only three isolates of extended beta lactamases (ESBL) producing strains were present as multiple drug resistant bacteria. We recovered no Vancomycin resistant Enterococcus.

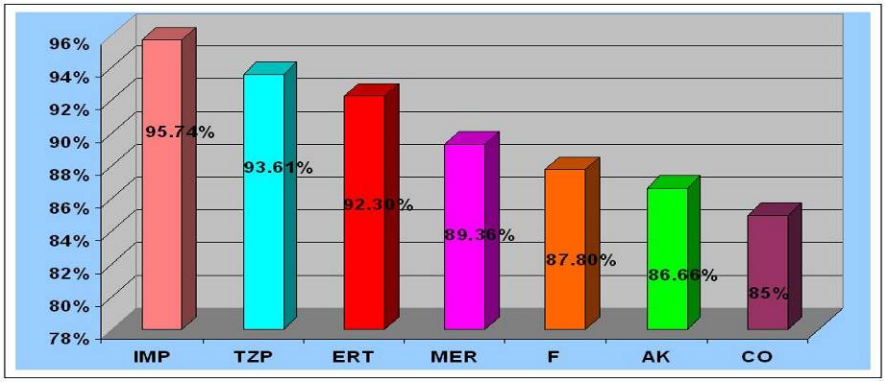

Figure 2 Antibiotics susceptibly of Gram-negative isolates in SBP. (IMP-Imipenem, TZP-Ticarcillin/Clavulanic acid, ERT-Ertapenem, MER-Meropenem, F-Ceftazidime, AK-Amikacin, CO-Colistin)

Conclusions

In our study, E. coli was the most frequently encountered bacteria, similar with previous reports of children with gangrenous and perforated appendicitis[4,1]. Enterococcus spp. recovered in peritoneal cultures significantly increased morbidity but not the mortality rate[1]. The treatment of other bacteria, such as E. coli or anaerobic bacteria stops the development of Enterococcus, a fact that suggests its pro inflammatory role[1].

Perforated appendicitis was responsible for the majority of SBP found in our study. Alexander noticed that between one third and three quarters of children present with PA at the time of diagnosis depending on age[1]. The high rates of perforation mainly encountered are due to delays in seeking care at a hospital rather than errors in diagnosis or hospital delays[1].

"Triple" antibiotic therapy (Ampicilin, an Aminoglycoside and Metronidazole or Clindamicyn)[1] has been the gold standard in treating SBP and PA in pediatric patients. According to our study, implementation of this triple regimen is not possible because of the antibiotic resistance encountered; Ampicillin had high resistance (72.5%). Aminoglycosides were significantly more nephrotoxic than 3rd generation Cephalosporins, and are inefficient in the low pH level of the infected peritoneal environment[1]. In addition, these antibiotic regimens require multiple doses of various antibiotics, a fact that makes it inappropriate for child administration.

According to the Surgical Infection Society, monotherapy with broad-spectrum agents in SBP and PA is equally effective, possibly even more cost-effective; children are treated in the same manner as adults[1]. In addition, a retrospective study demonstrated that single broad-spectrum antibiotic in the treatment of PA used with increasing frequency might offer improvements in terms of length of stay, pharmacy charges and hospital charges[12].

Medical studies illustrated that single-agent therapy with Carbapenems (Imipenem, Ertapenem) or penicillin plus a beta lactamase inhibitor (Ticarcillin-Clavulanic acid) were at least as effective as combination therapies[1,2,3]. These drugs have single or double daily dose administration schedule and are generally better tolerated by children. Cephalosporins are efficient as single-agent therapy in the management of peritonitis following trauma[1]. The advantages of single-agent therapy consist in elimination of Aminoglycosides side effects, as well as reduction of associated costs.

Sganga[1] recommended the use of antibiotics in the treatment of SBP according to the severity of infections. Mild and moderate infections need a short-term therapy with a single active drug against anaerobes bacteria. Severe infections require a more aggressive therapy specifically, an association between antibiotics that cover anaerobic, Gram-positive and Gram-negative bacteria.

According to our results, the treatment of mild-to-moderate SBP (ASA score 2) consists in the use of antibiotics with narrower spectrum of activity e.g. Ticarcillin/Clavulanic acid or Ertapenem, similar with medical literature[1]. Pediatric patients with more severe infections, as defined by ASA score 3 or 4, might benefit from regimens with a broad spectrum of activity against facultative and aerobic Gram-negative organisms. Our recommendations consist in monotherapy with Imipenem or Meropenem[1].

Despite common beliefs that Ciprofloxacin association with Metronidazole is very efficient against Gram-negative bacteria responsible for SBP, its activity against anaerobic bacteria is only moderate[1]. For the same reason, 3rd or 4th generation Cephalosporins are suitable for the treatment of SBP just in association with Metronidazole[1].

Switch therapy from injection to oral antibiotic in SBP is associated with good evolution. The proper time of the switch is when the body temperature has dropped to 37.5 ºC and blood, as well as clinical findings has demonstrated the tendency to improve by the 4th day[1].

SBP still represents the "bread and butter" for pediatric surgeons. SBP controlled effectively and with low associated morbidity by removal or repair of the infected focus, antibiotic treatment according to antibiograms sensibility, infection severity and restoration of anatomy if resection is performed for definitive source control. Proper management of SBP in children is cost effective, decreases

hospitalization, and can prevent the emergence of antibiotic resistance.

References

1. Campbell JR, Bradley JS. Peritonitis and intra-abdominal abscess. In: Long SS, Pickering LK, Prober CG, editors. Principles and practice of pediatric infectious diseases, 2nd ed. Philadelphia: Churchill Livingstone;2003:702-9.
2. Grosfeld JL, Molinari F, Chaet M, Engum SA, West KW, Rescorla FJ, Scherer LR 3rd. Gastrointestinal perforation, and peritonitis in infants and children: experience with 179 cases over ten years. Surgery 1996;120 (4):650-5.
3. Asabe K, Oka Y, Kai H, Shirakusa T. Neonatal gastrointestinal perforation. Turk J Pediatr 2009; 51(3):264-70.
4. Brook I. Microbiology and management of abdominal infections. Dig Dis Sci 2008;53(10): 2585-91.
5. Brook I. Intra-abdominal, retroperitoneal, and visceral abscesses in children. Eur J Pediatr Surg 2004;14(4): 265-73.
6. Brook I. Microbiology and management of neonatal necrotizing enterocolitis. Am J Perinatol 2008;25(2) :111-8.
7. Newman N, Wattad E, Greenberg D, Peled N, Cohen Z, Leibovitz E. Community-acquired complicated intra-abdominal infections in children hospitalized during 1995-2004 at a pediatric surgery department. Scand J Infect Dis 2009; 13:1-7.
8. Gauzit R, Péan Y, Barth X, Mistretta F, Lalaude O, et al. Epidemiology, management, and prognosis of secondary non-postoperative peritonitis: a French prospective observational multicenter study. Surg Infect 2009;10(2):119-27.
9. Montravers P, Andremont L, Massias L, et al. Investigation of the potential role of Enterococcus faecalis in the pathophysiology of experimental peritonitis. J Infect Dis 1994; 169:821–30.
10. Alexander F, Magnuson D, DiFiore J,et al. Specialty versus generalist care of children with appendicitis: an outcome comparison. J Pediatr Surg 2001;36:1510-13.
11. Pittman-Waller VA, Myers JG, Stewart RM, et al. Appendicitis: why so complicated? Analysis of 5755 consecutive appendectomies. Am Surg 2000;66:548-4.
12. Goldin AB, Sawin RS, Garrison MM, Zerr DM, Christakis DA. Aminoglycoside-based triple-antibiotic therapy versus monotherapy for children with ruptured appendicitis. Pediatrics 2007;119(5):905-11.
13. Simmen HP, Battaglia H, Kossmann T, Blaser J. Effect of pH in peritoneal fluid on outcome of aminoglycoside treatment in intraabdominal infections. World J Surg 1993: 17:393-397.
14. Nadler EP, Gaines BA, et al. The Surgical Infection Society guidelines on antimicrobial therapy for children with appendicitis. Surg Infect 2008;9(1):75-83.
15. Dougherty SH, Sirinek KR, Schauer PR, et al. Ticarcillin/clavulanate compared with clindamycin/gentamicin (with or without ampicillin) for the treatment of intra-abdominal infections in pediatric and adult patients. Am Surg 1995;61(4): 297-303.
16. Yellin AE, Johnson J, Higareda I, Congeni BL, Arrieta AC, Fernsler D, West J, Gesser R. Ertapenem or ticarcillin/clavulanate for the treatment of intra-abdominal infections or acute pelvic infections in pediatric patients. Am J Surg 2007;194(3):367-74.
17. Uhari M, Seppänen J, Heikkinen E. Imipenem-cilastatin vs. tobramycin and metronidazole for appendicitis-related infections. Pediatr Infect Dis J 1992;11(6):445-50.
18. Bozorgzadeh A, Pizzi WF, Barie PS, Khaneja SC, LaMaute HR, Mandava N, Richards N, Noorollah H. The duration of antibiotic administration in penetrating abdominal trauma. Am J Surg. 1999;177(2):125-31.
19. Sganga G. Antibiotic treatment of intra-abdominal and post-surgical infections. Infez Med 2005;Suppl:18-24.
20. Falagas ME, Peppas G, Makris GC, Karageorgopoulos DE, Matthaiou DK Meta-analysis: ertapenem for complicated intra-abdominal infections. Aliment Pharmacol Ther 2008;27(10):919-31.
21. SJ Geroulanos et al.Meropenem versus imipenem/cilastatin in intra-abdominal infections requiring surgery. J Antimicrob Chemother 1995;36:191-205
22. Whiting JL, Cheng N, Chow AW. Interactions of ciprofloxacin with clindamycin, metronidazole, cefoxitin, cefotaxime, and mezlocillin against gram-positive and gram-negative anaerobic bacteria. Antimicrob Agents Chemother 1987;31(9):1379-82.
23. Nichols RL, Smith JW. Use of third-generation cephalosporins. Anaerobes. Hosp Pract 1991;26 Suppl 4:11-7; discussion 48.
24. Mikamo H, Tamaya T, Ito K, Izumi K, Tanaka K, Watanabe K. Effectiveness of switch therapy for peritonitis. Jpn J Antibiot 2007; 60(4):200-5.

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