Int J Clin Exp Med 2015;8(2):2939-2943
www.ijcem.com /ISSN:1940-5901/IJCEM0003692

Original Article

Invasive group B streptococcal infection in infants in Shenzhen, China

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Received November 8, 2014; Accepted January 21, 2015; Epub February 15, 2015; Published February 28, 2015

Abstract: Objective: In this study, we aim to investigate the distribution and antibiotic susceptibility of Group B Streptococcus (GBS) in infants younger than 90 days in Shenzhen, China. Methods: A retrospective study was conducted to evaluate GBS infection over an 4-year period. Starting from January 2010, we evaluated the laboratory data, clinical manifestations, treatment and outcomes of patients admitted to our hospital with invasive GBS infection. Furthermore, we analyzed distribution of isolates from infants < 90 days with GBS or non-GBS invasive infection. Results: The registered cases of invasive GBS infection (n = 40, male: 23, female: 17) were classified as sepsis (n = 24), meningitis (n = 2), or both (n = 14). Patients with sepsis recovered completely. Among patients with meningitis, 1 (6.3%) died from ventricular hemorrhage, and 4 (25%) showed sequelae during the follow up of 3 months. Among the 377 isolates (45 from the 40 infants with invasive GBS infection, 332 from infants with non-GBS invasive infections), the detection rate of GBS was 11.9% (45/377), accounted for 11.2% of sepsis and 18.4% of meningitis cases. All 45 isolates were susceptible to penicillin, vancomycin, linezolid, tigecycline, and quinolones. Resistance to erythromycin, clindamycin, and tetracycline was found in 19 (42%), 29 (64%), and 42 (93%) isolates, respectively. Conclusion: GBS is an important pathogen in infants < 90 days in Shenzhen, China, which results in high mortality and neurological sequelae. GBS strains show strong resistance to clindamycin and erythromycin.

Keywords: Group B streptococcus, sepsis, infant

Introduction

Group B streptococcus (GBS), a common bacteria colonized in the genitourinary or gastrointestinal tract, is closely related to serious infection in pregnant women and newborns. Ever since 1970, it has been considered as the major cause of perinatal infection [1-4].

Neonatal GBS infection presents from birth to day 6 (early-onset disease [EOD]) or from day 7 to 89 (late-onset disease [LOD]). For EOD, GBS is the leading cause of sepsis and meningitis with mortality > 50%. For LOD, severe sequelae have been frequently reported, including septic arthritis, osteomyelitis, occult bacteremia, otitis media, accessory nasal sinusitis, conjunctivitis, cellulitis, lymphadenitis, mammary abscess, empyema and impetigo [5-9].

Although GBS is the leading cause of neonatal infections in developed countries, few studies have been carried out in the developing world [10]. The aim of this study was to assess GBS infection in infants < 90 days and the antimicrobial susceptibility pattern of GBS isolates in a single center in China.

Materials and methods

Patients

Our subjects were infants younger than 90 days admitted to Shenzhen Children's Hospital with culture-proven infections from a normally sterile site (eg, blood or cerebrospinal fluid [CSF]).

The study was approved by the Ethic Committee of Shenzhen Children's Hospital. The patient records was anonymized and de-identified prior to analysis.

Methods

377 blood and CSF cultures were obtained from infants (including 40 infants with confirmed invasive GBS infection) with clinical evidence of

Table 1. Distribution of culture-confirmed pathogens

Pathogens	Positive number in blood [n (%)]	Positive number in CSF [n (%)]
Coagulase-negative Staphylococcus (CoNS)	200 (59.0)	13 (34.2)
Group B streptococcus (GBS)	38 (11.2)	7 (18.4)
Escherichia coli (E. coli)	25 (7.4)	9 (23.7)
Staphylococcus aureus	17 (5.0)	1 (2.6)
Klebsiella pneumoniae	17 (5.0)	0
Enterococcus faecalis	16 (4.7)	1 (2.6)
Acinetobacter Baumannii	1 (0.3)	2 (5.3)
Streptococcus pneumoniae	2 (0.6)	4 (10.5)
Meningitis Chryseobacterium	3 (0.9)	1 (2.6)
Other pathogens*	20 (5.9)	0
Total	339 (100)	38 (100)

*Other pathogens include Candida albicans in 4, Candida Parapsilosis in 3, Enterobacter cloacae in 2, Salmonella D group in 2, Ochrobactrum anthropi in 2, Neisseria meningitides in 2, Serratia marcescens in 1, Pseudomonas aeruginosa in 1, Candida glabrata in 1, Citrobacter freundii in 1, Listeria monocytogenes in 1.

infection. All samples were collected before antimicrobial therapy and were cultured in standard aerobic and anaerobic BacT/Alert (BioMerieux Corp., Cambridge, MA, USA). The identification of the microorganisms was carried out using a VITEK 2 Compact cassette (BioMerieux Corp., Cambridge, MA, USA). The results were interpreted according to the standards issued by national committee for clinical laboratory standards (NCCLS).

Medical records of all 40 infants with confirmed invasive GBS infection were reviewed, including maternal age, labor event, clinical manifestation, treatment, length of hospital stay, complication and outcome.

Sepsis was defined as the growth of single potentially pathogenic organism from blood culture with clinical and laboratory findings consistent with infection.

Meningitis was defined as presence of clinical symptoms associated with: (1) a positive result on CSF culture; or (2) a positive result on blood culture and CSF pleocytosis (defined as the presence of > 30 white blood cells/mm^3 and < 45000 red blood cells/mm^3).

Results

The proportion of GBS

Table 1 shows the overall distribution of culture-confirmed pathogens in the study population presenting with sepsis or meningitis. Of the 377 isolates, coagulase-negative staphylococcus was the most common pathogen (213/377, 56.5%), while GBS was the second one (45/377, 11.9%). GBS accounted for 11.2% of sepsis and 18.4% of meningitis cases.

Clinical characteristics

Of the 40 infants with invasive GBS infection, 39 (97.5%) were term, and 1 (2.5%) was preterm. 28 (70.0%) were delivered vaginally, and 12 (30.0%) were delivered by cesarean section. 3 (7.5%) were born from mothers with history of premature rupture of amniotic membrane and bloody amniotic fluid. 5 (12.5%) were classified as EOD and 35 (87.5%) were classified as LOD. 24 were diagnosed as sepsis, 2 as meningitis, and 14 as both. Of 16 infants with meningitis, 2 (12.5%) were EOD. Colonization with GBS at maternal rectovaginal site was unclear. Intrapartum antibiotic use was also unclear.

On admission, all 40 infants had fever, 1 had scrotal swelling, 1 had cough.

18 (45.0%) infants had leukocytosis (white blood cell count > 11.000/mm^3), 12 (30.0%) had leukopenia (white-cell count, < 4000/mm^3), 27 (67.5%) had elevation of C-reactive protein (CRP) (> 10 mg/L). Procalcitonin (PCT) test was carried out in 19 patients, 16 (84.2%) were elevated (3.68-363.4 ng/L; normal range: 0-0.50 ng/L).

Among 16 infants with meningitis, 2 had convulsion. Poor response and paroxysmal cyanosis are generally noticed. Of the Computed tomography (CT) or magnetic resonance imaging (MRI) scan results, 4 (25%) were normal, and 12 (75%) suggested purulent meningitis. CSF parameters are as follows: pleocytosis (20-24030 × 10^6/L) and increased protein concentration (861-9058 mg/L) are found in 16 (100%) infants, while increased mononuclear cells and decreased glucose concentration

Table 2. Antimicrobial susceptibility patterns of GBS strains isolated (N = 45*)

Antibiotic	Sensitive (%)	Intermediate (%)	Resistant (%)
Penicillin	45 (100)	0 (0)	0 (0)
Ampicillin	43 (98)	0 (0)	1 (2)
Vancomycin	45 (100)	0 (0)	0 (0)
Linezolid	45 (100)	0 (0)	0 (0)
Tigecycline	45 (100)	0 (0)	0 (0)
Erythromycin	20 (44)	6 (13)	19 (42)
Tetracycline	3 (7)	0 (0)	42 (93)
Clindamycin	16 (36)	0 (0)	29 (64)
Levofloxacin	45 (100)	0 (0)	0 (0)
Ciprofloxacin	45 (100)	0 (0)	0 (0)
Moxifloxacin	45 (100)	0 (0)	0 (0)

*38 strains come from blood, 7 strains come from cerebrospinal fluid.

(0.61-3.03 mmol/L) are found in 13 (81.25%). After treatment, repeated lumbar puncture were performed and CSF examinations showed improvement in 14 infants.

Antimicrobial susceptibility

Table 2 shows the antimicrobial susceptibility of 45 isolated GBS strains. All isolates were susceptible to penicillin, vancomycin, linezolid, tigecycline, and quinolones. Resistance to erythromycin, clindamycin, and tetracycline was found in 19 (42%), 29 (64%), and 42 (93%) isolates, respectively.

Treatment and outcomes

All the patients received antibiotics. 12 patients were treated with penicillin, 18 with cephalosporin (ceftazidime, ceftriaxone and cefuroxime), and 10 with meropenem. For infants with meningitis, 13 received multiple antibiotics, 11 received linezolid, 2 received vancomycin.

All infants with sepsis (n = 24) recovered completely. Of infants with meningitis (n = 16), 1 (6.3%) died from ventricular hemorrhage, 4 (25%) had sequelae during the follow up of 3 months: hypermyotonia (n = 1), epilepsia (n = 1), subdural effusion (n = 1) and oculomotor paralysis (n = 1).

Discussion

The epidemiology of GBS in the developed world has been well studied [11-13]. To date, no surveillance of GBS infection has been carried out in China and its effect on neonatal infection is still unclear. To our knowledge, this is the largest report of invasive GBS infection in infants in China.

GBS remains the leading cause of neonatal sepsis and meningitis in developed countries [14, 15]. China is a large country with vast population. While there are few studies of GBS infection in the past two decades in China, the number of reports is growing [16-21], which may be associated with the increasing attention and the improvement of detection techniques. In our study, GBS was the second most common pathogen (11.9%) in invasive infection. The proportion of GBS may be higher if the possibly contaminated cultures of coagulase negative Staphylococcus were taken into account. In our study, 6.3% of patients with meningitis died and 25% had neurological sequelae, which suggested that GBS is an important pathogen in infants < 90 days in China with high mortality.

EOD is the result of vertical transmission (at delivery or shortly before) from a mother colonized with GBS in the anorectal and vaginal sites. Therefore, different exposure to GBS, with different maternal GBS carriage, may explain the various incidence of GBS infection. Recently, a large-scale study showed that 6.9%-7.1% of pregnant women carry GBS in vaginal-rectal tract [22, 23]. Compare to other developing countries with a rate of 14%-22% [24-26], this is lower and may partially explain the lower incidence of GBS infection in China.

In developed countries, vertical transmission, in the absence of intrapartum antibiotic prophylaxis (IAP), is the primary mode of GBS neonatal infection and EOD predominates [27, 28]. In this study, LOD predominated (87.5%), though IAP have not been introduced in China. The difference may be associated with the lower maternal GBS carriage rate and poor identification of EOD in China. Community-acquired LOD may be associated with poor sanitary conditions.

All GBS isolates were sensitive to penicillin, cephalosporin and vancomycin, consistent with previous reports all over world. Clindamycin was recommended to patients allergic to peni-

cillin. However, 64% of the isolates were resistant to clindamycin and 42% were resistant to erythromycin, higher than those in developed countries [29-31]. Fluoroquinolone is an important alternative. Our study showed all isolates were sensitive to quinolones, whereas two recent studies in China indicated resistance to levofloxacin (37.7% and 29.4%, respectively) [20, 32]. In our report, it is of concern that nearly 50% of patients received meropenem, linezolid, or vancomycin despite the results of antimicrobial susceptibility. The overtreatment is due to the poor identification of GBS.

Our study has several limitations. First, there was no comparison between infants with invasive GBS infection and infants with non-GBS infection since maternal GBS carriage rate was unclear. Second, intrapartum antibiotic use was unkonwn, which may underestimate the mortality of GBS infection.

Since IAP have been widely adopted in developed countries, incidence of neonatal EOD has dramatically declined [33]. This study emphasize that GBS is an important cause of severe infection in infants <90 days and incidence of GBS infection may be underestimated in China. Further prospective, population-based GBS surveillance is needed before implementation of GBS screening program and introduction of IAP in China.

Acknowledgements

The authors sincerely thank all members who took part in this study.

Disclosure of conflict of interest

None.

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