Pediatrics and Neonatology (2012) 53, 228–234

Available online at www.sciencedirect.com

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journal homepage: http://www.pediatr-neonatol.com

ORIGINAL ARTICLE

Prevalence and Pathogen Distribution of Neonatal Sepsis Among Very-Low-Birth-Weight Infants

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Received Mar 23, 2011; received in revised form Nov 2, 2011; accepted Dec 1, 2011

Key Words
neonatal intensive care unit;
sepsis;
very-low-birth-weight infants

Background: Neonatal sepsis contributes to great mortality and morbidity among very-low-birth-weight (VLBW) infants. Prevalence and pathogen distribution of sepsis in the neonatal intensive care units (NICUs) vary with time and geographic location. Such information serves as a guide for selection of empirical antibiotics coverage.
Methods: This is a case series study performed by retrospective chart review of VLBW infants (birth body weight, BBW, <1500 g) in a medical center during a 5-year period from January 2005 to December 2009. Episodes of positive blood cultures, pathogen distribution and related clinical manifestations were described.
Results: A total of 158 episodes of sepsis were identified from 1042 VLBW infants. Sepsis rate was 152 per 1000 live births. The vast majority of infections (60.7%) were caused by Gram-positive organisms [G(+)], and overall *Coagulase-negative staphylococci* (*CoNS*) (52.5%) were the most common pathogen identified. Prevalence for early-onset sepsis (EOS) was 1% and for late-onset sepsis (LOS) was 14.2%. Infants with EOS had a much higher case fatality rate than LOS (40% vs. 4.7%). *Escherichia coli* (40%) were the leading pathogen of EOS while *CoNS* (54.7%) was the leading pathogens of LOS. Overall, apnea and/or bradycardia and/or cyanosis (65.8%), poor activity (48.7%), and increased respiratory effort (43.0%) were the most common presenting features of sepsis.

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http://dx.doi.org/10.1016/j.pedneo.2012.06.003

Conclusion: Unlike term infants, Gram-negative organism and *E coli* were the leading pathogen of EOS among VLBW infants. Judicious and timely use of antibiotic therapy is crucial in the care of VLBW infants.

1. Introduction

Recent advances in neonatal care have successfully improved survival rate and reduced complications in premature infants. However, sepsis remains a significant and frequent cause of mortality and morbidity in very-low-birth-weight (VLBW) infants.[1,2] Early recognition of clinical signs implying significant infection and an appropriate choice of empirical antibiotics are vital for successful management of sepsis. Rationale on choices of empirical antibiotics should be based on epidemiologic knowledge of frequent pathogens and their drug sensitivity. While risk factors for sepsis in VLBW infants may differ from those found in term infants, also true is the fact that causative pathogens for neonatal sepsis vary with time and geographic distribution.

Current available studies have all been focused on sepsis in all neonatal intensive care unit (NICU) patients, or only on early onset sepsis (EOS) or late onset sepsis (LOS) of VLBW infants.[1,2] The aim of this study was to describe current epidemiologic, microbiologic, and clinical characteristics of both EOS and LOS among VLBW infants in a medical center in northern Taiwan.

2. Methods

This is a retrospective case study conducted in the NICUs of Chang Gung Memorial Hospital (CGMH), Lin Kou, by analyzing the NICU database and reviewing medical records. All preterm infants admitted to these NICUs between January 2005 to December 2009 with birth body weight, (BBW) $<$ 1500 g, who also had a diagnosis of neonatal sepsis were enrolled in this study. Their medical records were reviewed and relevant clinical features including presenting symptoms, laboratory findings such as culture results, use of antibiotics, possible risk factors, especially use of indwelling catheters, ventilators, and parenteral nutrition were recorded and analyzed.

Sepsis was defined by a positive blood culture and clinical symptoms. EOS was defined as sepsis within the first 3 days of life while LOS was defined as any episodes occurring after 3 days of life.[2] Blood cultures positive for organisms generally considered as contaminants, including corynebacterium, propionibacterium, penicillium, and diphtheroids, were excluded.[1] For patients with multiple episodes of sepsis, only those with the same pathogen identified after a 10-day course of appropriate antibiotic therapy or a different organism identified from an *in vitro* susceptible culture were considered as different episodes.[1] For *Coagulase-negative staphylococci* (*CoNS*), those with two positive cultures of blood specimens drawn within 2 days or one positive culture and a serum C-reactive protein (CRP) level greater than 1 mg/dL within 2 days were considered as definite cases; those with one positive culture and treated with an antistaphylococcal drug to which the organism was susceptible for at least 5 days were considered as possible cases.[1] Contamination was defined as one positive culture without an elevated CRP or antibiotic therapy. Definite and possible cases were included in this study.

Central venous catheter (CVC) and endotracheal tube placed before the onset of sepsis and in place at the time of positive blood culture were defined as CVC at sepsis and ventilator at sepsis, respectively. Total parenteral nutrition (TPN) used before and during the time of positive blood culture was defined as TPN at sepsis. For clinical symptoms, apnea, and/or bradycardia, and/or cyanosis were included when the episodes were new in onset, more frequent, or more severe than previously observed. Fever and hypothermia were defined as a core body temperature of $\geq$38°C or $\leq$36.5°C, respectively. Hyperglycemia was defined as blood glucose of $\geq$140 mg/dL.[2] New onset of hypotension with use and increasing dose of inotropes were defined as hypotension during sepsis. Thrombocytopenia was defined as a platelet count of $<$150,000/mm^3. Increased respiratory effort was defined as increased fraction of inspired oxygen (FiO_2), positive inspiratory pressure, or end expiratory pressure at onset of sepsis.

Statistical analysis was performed using the SPSS software version 15.0 (SPSS Inc.,Chicago, IL, USA).

Categorical data were analyzed with the standard chi square test. Continuous data were analyzed with independent *t* test and analysis of variance (ANOVA) was applied for intergroup comparisons. Statistical significance was defined as $p \leq 0.05$.

3. Results

3.1. Prevalence

Between January 2005 and December 2009, there were a total of 1042 preterm infants with BBW of less than 1500 g admitted to our NICUs. A total of 134 infants had one or more episodes of blood culture-proven sepsis. After excluding eight infants with 10 episodes of blood culture positive for an organism considered as a contaminant, 126 (12.9%) infants with 158 episodes of sepsis were included in our study. The sepsis rate was 15.2%. Among these infants, 99 infants had a single episode of sepsis (78.6%), 20 infants (20.9%) had two episodes, and seven infants (5.6%) had three episodes of sepsis.