Journal of Microbiology, Immunology and Infection (2016) 49, 430—435

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Risk factors of late-onset neonatal sepsis in Taiwan: A matched case-control study

Yin-Hsiang Kung [a,f], Yi-Fan Hsieh [a,f], Yi-Hao Weng [b], Rey-In Lien [b], Jian Luo [c], Yuan Wang [c], Yhu-Chering Huang [a,d], Chyi-Liang Chen [e], Chih-Jung Chen [a,d,*]

[a] *College of Medicine, Chang Gung University, Taoyuan, Taiwan*
[b] *Division of Neonatology, Department of Pediatrics, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[c] *Division of Neonatology, Department of Pediatrics, Xiamen Chang Gung Hospital, Xiamen, People's Republic of China*
[d] *Division of Pediatric Infectious Diseases, Department of Pediatrics, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[e] *Molecular Infectious Diseases Medical Research Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan*

Received 14 March 2013; received in revised form 11 July 2013; accepted 5 August 2013
Available online 22 November 2013

KEYWORDS
Bloodstream infections;
Neonates;
Parenteral nutrition;
Risk factors

Background: Infants in a neonatal intensive care unit (NICU) have a higher incidence of bloodstream infections (BSIs) than any other pediatric or adult population. The predisposing factors have not been comprehensively evaluated in this population in Taiwan.
Methods: A retrospective matched case-control study was conducted in the NICUs of a teaching hospital in Taiwan. The case patients were identified from a staff-maintained electronic database containing the records of BSIs from July 2003 to June 2006. The case patients and the control patients (who did not develop BSI during their NICU stay) were 1:1 matched by birth weight, gestational age, gender, Apgar score, and date of birth.
Results: A total of 164 infants with culture-proven BSI were identified. Of these, 74 (45.1%) infants were female. The mean gestational age and birth weight were 30.7 ± 0.7 weeks and 1512 ± 804 g, respectively. The common etiologic pathogens included coagulase-negative staphylococci (28.7%), *Staphylococcus aureus* (16.5%), and *Klebsiella pneumoniae* (14.6%). Candida *spp.* accounted for 11 (6.7%) episodes. Two independent factors associated with BSIs in the neonates, as identified by multivariate analysis using conditional logistic regression,

* Corresponding author. Division of Pediatric Infectious Diseases, Department of Pediatrics, Chang Gung Children's Hospital, Number 5, Fu-Shin Street, Kweishan 333, Taoyuan, Taiwan.
E-mail address: chinjung@adm.cgmh.org.tw (C.-J. Chen).
[f] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.jmii.2013.10.001

were the use of parenteral nutrition (matched odds ratio [mOR], 6.07; 95% confidence interval [CI], 1.14—32.32; $p = 0.034$) and intraventricular hemorrhage (mOR, 2.68; 95% CI, 1.20—5.99; $p = 0.017$).
Conclusion: Parenteral nutrition was a significant and independent risk of late-onset neonatal sepsis. This risk should be considered when implementing early parenteral nutrition in NICUs.

Introduction

Neonatal bloodstream infections (BSIs) are an important complication among premature infants in neonatal intensive care units (NICU) all over the world.[1] The invasive infections can lead to severe morbidities and mortality, prolong the length of hospitalization, and increase the cost of medical care. Managing neonatal BSIs is a challenge for physicians. In the past few decades, the mortality rate of late-onset sepsis has remained at a high level (5—15%) in most neonatal care facilities, despite with a declining trend.[2—6] The incidence of late-onset BSI on admission differs in infants at certain gestational ages, birth weights, gender, and conditions, and it is associated with various invasive procedures performed during intensive care.[3,7,8] To lessen the disease burden, it is essential to identify potential risk factors, followed by effective preventive or infection control measures.

In Taiwan, the incidence of neonatal late-onset BSIs ranged from 4% to 11.4% with a mortality rate of 7.2—20%.[7,9—11] The risk factors preceding BSIs were not comprehensively evaluated in this population. To identify the risk factors, we conducted a retrospective case-control study in the NICUs of a teaching hospital.

Materials and methods

Ethics statement

The study was approved by the institute review boards from Chang Gung Memorial Hospital (Taoyuan, Taiwan), which allowed the retrieval of patient lists from the electronic database and a retrospective review of the medical information. A waiver of consent was granted because of the retrospective nature of the project and the anonymous analysis of the data.

Study design

A retrospective matched case-control study was performed in the NICUs of Chang Gung Children's Hospital (CGCH) from July 1, 2003 to June 30, 2006. The CGCH is a 532-bed teaching hospital in northern Taiwan that provides primary to tertiary care for children younger than 18 years old. This hospital has three NICUs with a total of 98 beds. Since 1 July 2003, an electronic database was established to routinely collect the demographic data and information of several predefined major events that occurred in each neonate patient during her/his stay in the NICUs. The predefined major events included BSIs; any surgery; intraventricular hemorrhage; bronchopulmonary dysplasia; retinopathy of prematurity; necrotizing enterocolitis; and all positive culture results (i.e., blood culture, urine culture, sputum culture), irrespective of their clinical relevance. All discharge diagnoses were also collected. A well-trained nurse was responsible for gathering these data on the day of patient discharge by comprehensively reviewing the written and electronic medical records. During the study period, a list was retrieved from this database of the neonatal patients who fulfilled the criteria of late-onset culture-proven BSIs (discussed later). At a case-control ratio of 1:1, the case infants were matched to control infants (who never developed BSI during their stay in NICU) by birth weight (±250 g), gestational age (±2 weeks), gender, and date of birth (±1 month). The medical records of the case infants and the control infants were retrospectively reviewed. A standardized data collection form was used to collect the clinical information needed in this study. The data were digitized and cleaned before we proceeded with statistical analysis.

Definition of late-onset culture-proven BSIs in the neonates

The definition of late-onset neonatal BSI was adapted and modified from the 2008 criteria of the National Nosocomial Infection Surveillance System.[12] Neonatal late-onset culture-proven BSI was defined when a recognized pathogen was cultured from the blood of a patient older than 7 days and was unrelated to an infection at another body site (e.g., pneumonia with bacteremia). The BSIs of common skin contaminants (e.g., diphtheroids, *Bacillus*, *Propionibacterium*, coagulase-negative staphylococci, or micrococci) were identified if the organism was cultured from two or more blood cultures drawn on separate occasions or from at least one blood culture from a patient with an intravascular line and appropriate physician-instituted antimicrobial therapy, and if the patient had at least one of the following manifestations: fever (greater than 38°C), hypothermia (less than 37°C), apnea, or bradycardia. In our institute, the body temperature was measured by placing the thermometer under the back of the infants.

Assessment of risk factors

We assessed the exposure to potential risk factors for BSI. To avoid the influence of known general risks on the occurrence of BSI, univariate and multivariate analyses