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Major Article

Efficacy of periodic surveillance culture in a neonatal intensive care unit in the presumption of causative pathogens of late-onset bacterial infection

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Background: Surveillance cultures have been recommended for infection control of resistant bacteria in neonatal intensive care units (NICUs). However, the utility of surveillance cultures in the presumption of causative bacteria in late-onset bacterial infection has been controversial. The aim of the present study was to investigate the relationship between the causative pathogens of late-onset bacterial infection and the results of periodic surveillance cultures in a NICU.

Methods: A retrospective study was performed on 600 patients hospitalized in the NICU of a large metropolitan hospital from 2010-2013. The correspondence of the results of surveillance cultures with causative pathogens was analyzed in patients who developed late-onset bacterial infection.

Results: *Staphylococcus* species and enterobacterium were the most prevalent in the samples obtained from the oropharynx and rectum, respectively, during the investigation period. Twenty patients (3.3%) developed late-onset bacterial infection. The causative pathogens in 15 patients (75%) were also detected from the final surveillance cultures; these patients tended to be older than the other 5 patients ($P = .003$).

Conclusions: Surveillance cultures might be useful for the presumption of causative pathogens of late-onset bacterial infection in patients with risk factors for the development of nosocomial bacterial infection.

Sepsis remains a major cause of death and long-term complications among premature infants. Unlike early-onset sepsis mainly caused by vertical transmission, the origin of late-onset sepsis is believed to be horizontal transmission from nosocomial sources or the result of persistent colonization.[1] The trends in the epidemiology of early-onset sepsis have shown a decreasing incidence of group B *Streptococcus* disease because of the implementation of a prenatal screening and treatment protocol.[2] In contrast, the incidence of late-onset sepsis has not changed. The morbidity of late-onset sepsis is 15%-30% in very-low-birth-weight infants,[3-5] and the mortality rate in these infants remains 15%, even in developed countries.[6,7] Furthermore, very-low-birth-weight infants who developed sepsis are prone to developing neurodevelopmental impairment at age 5 years.[8] It is important to rapidly identify the causative pathogen of late-onset sepsis and start an appropriate antimicrobial treatment.

Surveillance cultures have been recommended for infection control of resistant bacteria in neonatal intensive care units (NICUs).[9] Colonization of bacteria may lead to the development of invasive bacterial infection in patients hospitalized in NICUs. Prematurity, neonatal asphyxia, long-term application of medical devices such as an endotracheal tube and central venous catheter, introduction of intravenous hyperalimentation, and surgical procedure were risk factors for the development of late-onset bacterial infection in patients hospitalized in a NICU for a long time.[1,10-12] Previous studies have suggested that surveillance cultures might be useful for predicting invasive late-onset infection due to specific bacteria.[13,14] However, the usefulness of surveillance cultures to determine the causative bacteria in late-onset invasive bacterial infections remains controversial.

In the present study, to investigate the utility of surveillance cultures in the presumption of causative bacteria in late-onset invasive bacterial infection, we analyzed the relationship between the causative pathogens of late-onset bacterial infection and the results of periodic surveillance cultures in a NICU.

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MATERIALS AND METHODS

Study populations and sample collection

We performed a retrospective cohort study on 600 patients who were admitted to the NICU at a large metropolitan hospital January 1, 2010-May 31, 2013. The medical records of all neonates admitted to the NICU and their mothers were reviewed. Surveillance cultures were routinely performed using oropharynx and rectum swabs obtained from the patients once a week until discharge. In addition to these samples, blood, urine, and bronchoalveolar lavage fluid (BALF) (if possible) samples were also obtained from patients showing symptoms of infection.

Microbiologic studies

Gram staining, bacteria culture, and identification and antimicrobial susceptibility testing of isolated bacterial pathogens were routinely performed in the bacteriology laboratory of the hospital. Antimicrobial susceptibility testing of bacterial isolates was performed by the dilution method, and the minimal inhibitory concentrations were recorded. The breakpoint of the susceptibility of bacteria to antimicrobial agents was set according to the standards created by the Clinical and Laboratory Standards Institute.

Correlation between causative pathogens and the results of surveillance cultures

Late-onset bacterial infection was defined by both the detection of a pathogen from a sterile sample or a nonsterile sample obtained from the lesion specified in a radiologic imaging study and the presence of clinical and laboratory signs of infection beyond 72 hours of life. Urinary tract infection was defined as the isolation of a single bacterium in a concentration >10^5 CFU/mL urine. BALF was obtained for the diagnosis of bacterial pneumonia. When phagocytized bacterial cells were seen on the Gram stain smear of the BALF sample and the corresponding bacterium was isolated later, a bacterial infection was considered to be present.[15] Preexisting mucosal colonization was defined as the presence of bacteria on mucosal surfaces 2-7 days before the development of a bacterial infection. The detection of the same bacteria with the same results of antimicrobial susceptibility testing from the mucosal samples and samples obtained for the diagnosis of infection was considered to indicate concordant findings.

Statistical analysis

SPSS statistics software (version 21; IBM-SPSS Inc, Armonk, NY) was used for the analysis. Mann-Whitney *U* test was used to compare the differences between the quantitative values. Fisher exact test was used for the comparison of the qualitative analysis. *P* values < .05 were considered to be statistically significant.

RESULTS

A total of 3,928 samples were collected from 600 patients during the investigation period, with 2,321 and 1,607 samples obtained from the oropharynx and rectum, respectively. *Staphylococcus* species were mainly detected from the cultures of the oropharynx (Fig 1A), and enterobacterium was the most prevalent in the samples obtained from the rectum (Fig 1B). Half of *Staphylococcus aureus* detected in samples from the oropharynx was methicillin-resistant *S aureus* (MRSA).

The patients' characteristics and demographic data are shown in Table 1. During the investigation period, 20 patients (3.3%) developed a late-onset bacterial infection. Compared with the patients who did not develop a late-onset bacterial infection, these patients had lower gestational age, birth weight, and Apgar score, and higher rates and longer durations of mechanical ventilation and central venous catheter, the introduction of intravenous hyperalimentation, as well as a higher rate of surgery.

Of 20 patients who developed late-onset bacterial infection, 11, 5, and 1 patient were diagnosed with bacteremia, urinary tract infection, and pneumonia, respectively. Of the remaining 3 patients, 2 were diagnosed with both bacteremia and pneumonia and 1 patient was diagnosed with bacteremia and a urinary tract infection. The causative pathogens are shown in Table 2. Gram-positive cocci (80%) were predominantly detected in the patients. In particular, *S aureus* was the most common cause of bacterial infection (35%). None of these patients died due to infectious diseases during the investigation period.

The causative pathogens of 15 patients (75%) diagnosed as having late-onset bacterial infection (bacteremia [n = 11], urinary tract infection [n = 3], and pneumonia [n = 1]) were also detected from the last surveillance culture. When the causative pathogen was identical to the bacteria detected from the last surveillance cultures in patients who developed late-onset bacterial infection, the patients were classified as the identical group. The result of the antimicrobial susceptibility test was also the same between the

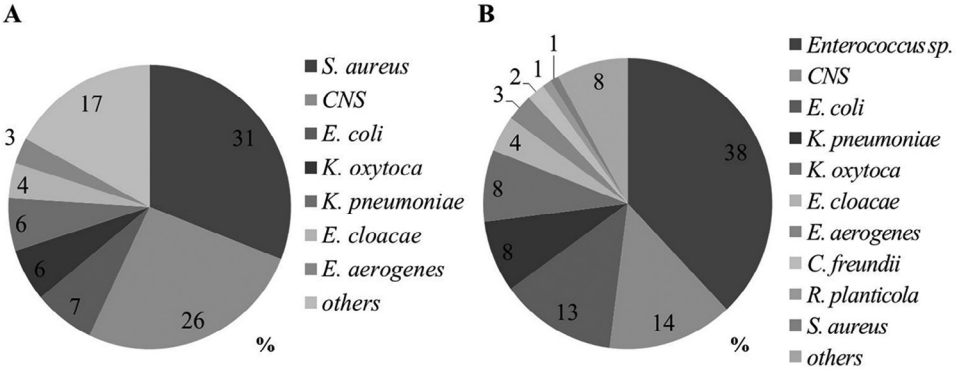

Fig 1. The proportions of bacteria detected by periodic surveillance cultures. (A) Result of the oropharyngeal swab. (B) Result of the rectal swab. Approximately 52% and 29% of *Staphylococcus aureus* (*S aureus*) and *Escherichia coli* (*E coli*) identified from the oropharyngeal swab was methicillin-resistant *S aureus* and extended-spectrum β-lactamase-producing *E coli*, respectively. All *S aureus* identified from the rectal swab was methicillin-resistant. *CNS,* coagulase-negative staphylococci; K oxytoca, *Klebsiella oxytoca*; K pneumoniae, *Klebsiella pneumoniae*; E cloacae, *Enterobacter cloacae*; E aerogenes, *Enterobacter aerogenes*; Enterococcus *sp*, *Enterococcus* species; C freundii, *Citrobacter freundii*; R planticola, *Raoultella planticola.*