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Prevention of healthcare-associated infections in neonates: room for improvement

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SUMMARY

Infants in neonatal intensive care units (NICUs) are highly susceptible to infection due to the immaturity of their immune systems. Healthcare-associated infections (HCAIs) are associated with prolonged hospital stay, and represent a significant risk factor for neurological development problems and death. Improving HCAI control is a priority for NICUs. Many factors contribute to the occurrence of HCAIs in neonates such as poor hand hygiene, low nurse–infant ratios, environmental contamination and unnecessary use of antibiotics. Prevention is based on improving neonatal management, avoiding unnecessary use of central venous catheters, restricting use of antibiotics and H2 blockers, and introducing antifungal prophylaxis if necessary. Quality improvement interventions to reduce HCAIs in neonates seem to be the cornerstone of infection control.

Introduction

Healthcare-associated infections (HCAIs) cause substantial harm to hospitalized neonates. They have considerable health and economic consequences, including increased morbidity and mortality, prolonged length of stay (LOS) and increased medical costs.[1] In North America, it is estimated that each episode of sepsis prolongs the duration of a neonate's hospital stay by two weeks, resulting in an incremental cost of US$25,000 per episode. In a recent study of very-low-birthweight (VLBW) infants, nosocomial BSIs were found to increase hospitalization costs by 26% for infants weighing 401–750 g and by 80% for infants weighing 1251–1500 g. This study also showed that the LOS increased by four to seven days in all VLBW categories with nosocomial bloodstream infections.[2] Infants admitted to neonatal intensive care units (NICUs) are at high risk of HCAIs. They are exposed to specific and non-specific risk factors that increase the risk of bacterial and fungal sepsis, including the frequent use of broad-spectrum antimicrobial drugs, parenteral nutrition, acid inhibitors and steroids, as well as the systematic and long-term use of invasive devices such as central venous catheters (CVCs) and endotracheal tubes.[3] Preterm neonates in NICUs are at greater risk of infection due to low birth weight and intestinal disorders with proliferation of a pathogenic microflora. Moreover, nursing in incubators may delay or impair normal intestinal colonization. Neonates are more susceptible to infection because they lack an effective skin barrier, and

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have immature or ineffective immune systems, allowing invasion by many organisms from various colonized sites.[4,5]

Epidemiology

In 1999, the Pediatric Prevention Network national point prevalence survey in the USA found that 11.4% of infants in NICUs had an HCAI.[6] The most common HCAIs in this survey were BSIs (53% of HCAIs, overall prevalence 7.4%) and respiratory infections (13% of HCAIs, prevalence 1.8%). Pneumonia rates reported by others show considerable variation (7–32% of HCAIs), perhaps reflecting differences in the definitions used. Gram-positive pathogens account for up to 70% of cases of neonatal sepsis, with sepsis due to Gram-negative organisms accounting for 15–20% of infections. A study conducted between 2006 and 2008 reported the frequency of pathogens causing BSIs [coagulase-negative staphylococci (CoNS), 28%; *Staphylococcus aureus*, 19%; *Candida* spp., 13%] and the frequency of pathogens causing ventilator-associated pneumonia (VAP; *Pseudomonas aeruginosa*, 16%; *S. aureus*, 15%; *Klebsiella* spp., 14%).[7]

CoNS are the main pathogens involved in late-onset neonatal sepsis.[8] Within the first week of life, neonates are colonized rapidly by micro-organisms from the hospital environment.[9] During this period, the risk of CoNS infection increases substantially with the use of CVCs, mechanical ventilation, parenteral nutrition, and exposure to other invasive skin or mucosa-breaching procedures.[10] CoNS are common inhabitants of the skin and mucous membranes. Although a small proportion of neonates acquire CoNS by vertical transmission, acquisition is primarily horizontal by cross-transmission.[11] Consequently, infants admitted to a hospital acquire most of their micro-organisms from the hospital environment, their parents and staff.[12] Transmission via the hands of hospital staff can lead to endemic strains circulating for extended periods. As CoNS are ubiquitous skin commensal bacteria, it has been assumed that colonization of the skin and of indwelling catheters are important sources of sepsis.[13] However, recent studies have suggested that epithelial loci other than the skin, such as the nares, may be important access points of infection.[13] Antibiotic resistance in skin-residing strains has been found to be low at birth, but increases rapidly during the first week of hospitalization.[14] Therefore, selective pressure as a result of perinatal antibiotic exposure is a major factor influencing the spectrum and antibiotic resistance pattern of micro-organisms isolated from neonates.

Central-line-associated bloodstream infection

BSIs are the most common HCAIs in NICUs. BSIs are the result of interaction of several factors related to clinical care practices and characteristics of the patient population.[15] The presence of a CVC is a major risk factor for BSI. The 1999 prevalence survey in the USA found that infants with central intravascular catheters had a birthweight-adjusted relative risk of 3.8 [95% confidence interval (CI) 2.32–6.26, $P<0.001$].[6] CoNS are responsible for 50% of catheter-related infections. Interpretation of a positive blood culture is difficult as CoNS are skin commensals. The diagnosis is usually uncertain due to the non-specific signs of sepsis in this population and the definition of central-line-associated bloodstream infection (CLABSI) used in neonates. The diagnosis is often based on a single positive blood culture and clinical signs, despite the fact that many experts recommend obtaining both central line and peripheral blood cultures. A recent systematic review found significant variability in the reporting of BSI and CLABSI rates in NICUs, and confirmed that CLABSI rates are more challenging to collect.[16] As such, it may be more appropriate to use BSI rates to monitor HCAIs in some NICU settings.

Central line infections are generally a result of poor insertion technique, or failures in the hygiene protocol at the time of catheter placement and during ongoing care at the catheter site. Data suggest that the hub is the common source of contamination and subsequent infection.[17] The risk of CLABSI is related to the duration of catheter use and the frequency of catheter manipulation.[18] Many strategies have been developed in adults to prevent and reduce these HCAIs by using care bundles.[19] Reducing CLABSI should be based on implementation of clinical practice guidelines for the insertion and maintenance of catheters. Improvement consists of five care steps: maximal barrier precautions upon insertion; chlorhexidine skin antisepsis; optimal catheter site selection; optimal catheter site selection; and daily review of the need for the line, with prompt removal of unnecessary lines.[20] Several institutions have published the results of multi-faceted interventions to reduce CLABSI rates. A NICU centre conducted an educational programme aimed at reinforcing hand hygiene, and developed and implemented a checklist for care of the catheter hub. This led to a decrease in the CLABSI rate from 23 to 12 infections per 1000 catheter-days [odds ratio (OR) 0.33; 95% CI 0.20–0.90], and a decrease in the umbilical CLABSI rate from 15 to 5 infections per 1000 catheter-days (OR 0.47; 95% CI 0.17–0.91).[21] A recent literature review[20] showed that bundle implementations are effective for the reduction of CLABSI in NICUs.

Healthcare-associated pneumonia

Healthcare-associated pneumonia (HAP) represents 6.8–32.3% of HCAIs in NICUs, and is the second most common hospital-acquired infection in critically ill neonates.[22] Rates of VAP vary between 0.7 and 2.2 per 1000 ventilator-days.[23] However, as for CLABSI, rates varied between NICUs depending on birth weight and gestational age. Indeed, the risk of VAP is significantly higher below 28 weeks of gestation. Many risk factors for the development of HAP in NICU patients are similar to those identified in adult patients, such as prolonged duration of mechanical ventilation, severe underlying cardiopulmonary disease and previous thoraco-abdominal surgery.[23] Most bacterial healthcare-associated lower respiratory tract infections occur due to aspiration of bacteria from the oropharynx or the gastrointestinal tract. Uncuffed endotracheal tubes facilitate access of micro-organisms to the lower respiratory tract. Neonates with bronchopulmonary dysplasia and those who have impaired swallowing mechanisms are at increased risk of aspiration.[24]

Preventive proposed interventions include early extubation strategies and switching to non-invasive respiratory support. General concepts of prevention include: staff education and training; microbiological surveillance; prevention of cross-transmission (improving hand hygiene); and early removal of mechanical ventilation. In adult populations, a bundle including various steps for ventilator care has been developed successfully[25]: hand hygiene and compliance with use of gloves and gowns; elevation of the head-end of the bed by 30–40°;