

Staphylococcal Infections in the Newborn

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INTRODUCTION

Bacterial infection in the neonatal period causes a high morbidity and mortality and in developing countries is responsible for 26 % of death [1,2]. In neonatal intensive care unit the most prevalent bacterial are the *Staphylococcus aureus* (*S. aureus*) [3,4], and *Staphylococcus* coagulase negative (SCoN). Among the SCoN, the *S. epidermidis* is responsible for much of the late neonatal sepsis. Other species such as *Staphylococcus capitis*, *Staphylococcus hemolyticus*, *Staphylococcus hominis* and *Staphylococcus saprophyticus* has been identified as the cause of sepsis in the newborns [5].

Colonization always preceded the Staphylococcal infections. The initial sites of colonization by *S. aureus* are the nostrils and umbilical stump and subsequently the oropharynx. This colonization is observed in 50-70 % of infants already during the first week of hospitalization. This microorganism also colonizes the young adults in 30 to 50% persistently and in 10 to 20 % transiently. The SCoN account for 50 % of late sepsis, and the disease usually appears around the third week of hospitalization [3,5].

Study in Unit Neonatal Intensive Care (NICU) at tertiary level in the city of São Paulo (Brazil), showed that between 2000 and 2005 the prevalence of staphylococcal infection was 3.1%. *S. aureus* 1.7% and SCoN 1.4 %. The acquisition of SCoN was predominantly nosocomial and *S. aureus* acquired in the community [6].

In a city in southern of Brazil the CoNS was the agent found in blood cultures and as a colonizer in the NICU. Prematurity was the most frequent reason for hospitalization [7].

RISK FACTORS

The increase in the number of infections in neonatal age group is due largely to increased survival of infants with gestational ages smaller than remain in the NICU by longer periods. The lower the gestational age, the greater the number of infections⁸

Staphylococcal infection in newborns occurs also by others factors than prematurity and length of hospital stay, mentioned below:

Bacteria's Own Factors

They are related to the specific virulence of a particular strain of *Staphylococcus* their viability in the environment and its antibiotic sensitivity profile. Staphylococci are divided into two groups: coagulase producers represented by *S. aureus* and coagulase negative, the SCoN.

The easier of *S. aureus* produce systemic infection in healthy newborns reflects the ability of this pathogen to alter the immune mechanisms of lightening and preventing the spread by epithelial surface. The components of your wall are related to decreased activity of the complement system, inactivation of neutrophils and difficulty of connecting the Fc fraction of immunoglobulin.

The virulence factors of *S. aureus* includes the production of: epidermolytic toxins A and B, which cause dissociation of epithelial desmosomes, causing skin lesions and erythema; exotoxins and TSST-1 TSST-2, responsible for the toxic shock syndrome; Hyaluronidase, an enzyme which causes lysis of hyaluronic acid in the extracellular matrix of connective tissue, facilitating the spread of the bacterium through the soft tissue; coagulase, an enzyme that is potent triggering of the coagulation cascade; catalase, which converts hydrogen peroxide (used as a natural microbicide) into water and oxygen; enterotoxin, thermo stable proteins carried by food, and responsible for digestive frames (nausea, diarrhea and vomiting) [8,9].

The lipoteichoic acid and peptidoglycan are potentially toxic components of the cell wall of Gram positive bacteria. These components stimulate the production of inflammatory mediators such as cytokines, triggering the inflammatory cascade, which may cause the patient to shock, multiple organ failure and death [10].

SCoN infections have increased in the neonatal period due to two main factors: the increase of antimicrobial resistance in this group and to advances in medicine and the use of invasive devices for newborn care mainly of very low birth weight. These bacteria have a glycocalyx

capsule containing polysaccharide adhesin, thereby facilitating adherence to hydrophobic surface catheters and probes with progression to biofilm formation. In addition to membership function, biofilms can protect the antibiotic action of CoNS and also the newborn's immune cells such as macrophages. Prolonged parenteral nutrition with lipid emulsions in central venous catheters with attached CoNS, helps in the growth of colonies and invasion of the bloodstream by a number of factors such as mechanical blockage, nutrition of these agents and macrophages function change [11,12].

The gene "mec", is responsible for the resistance of staphylococci to beta-lactams and is present in most strains of CoNS. The resistance mechanism involves modification of linker binding to penicillin binding proteins, thus decreasing the affinity for these antibiotics and due to this the antimicrobial treatment have become more difficult [13,14].

Newborn Factors

Due to the decreased production and maturation of precursors of neutrophils; newborns are more susceptible to staphylococcal infections when compared to larger or adult children. More over there is reduced function of neutrophils such as diapedesis across the endothelium and activation of the complement system, interleukins, chemotaxis and phagocytosis.

S. aureus infections in the complement system and opsonization agent are more effective in destroying agent than the production of specific antibodies or the role of T cells.

The more susceptible infants are preterm infants, especially those of very low birth weight (less than 1500g). These are the most immunologically immature (phagocytes, complement, humoral and cellular system) have decreased inflammatory response and often receive less breast milk; require longer hospital stays, and more invasive care, leading to the breakdown of physical barriers such as the skin and provide the entry microorganism [5,6,17,18]. Among the invasive care are:

Mechanical ventilation noninvasive and invasive

- Airway aspiration
- Punctures venous or arterial
- Prolonged parenteral nutrition
- Invasive diagnostic procedures
- Use of catheters and probes

The large, early use of antibiotic therapy is strongly associated with outbreaks in neonatal units mainly by CoNS. The incidence of late sepsis in very low newborns that evolves without infection in the first days of life in developed countries is approximately 16% with an average of 17 days of occurrence to life. Studies show a higher incidence of early-onset sepsis, low weight and late-onset sepsis in african descendants newborns; attributed to maternal factors as socio-

economic condition, nutrition, presence of chorioamnionitis. The male this more associated with sepsis and meningitis, among the contributing factors described the delay in lung maturation increasing the likelihood of respiratory distress and pulmonary infections syndromes [21].

Others factors associated with late infection by staphylococci are: perinatal asphyxia, hypothermia, delayed hyperbilirubinemia, Inborn Errors of Metabolism, localized infection in the umbilical stump.

There is an association report of therapy with ranitidine and increased late neonatal sepsis, whose mechanism is still incerto [22].

TRANSMISSION

The environment of the newborn is of great importance in the transmission of disease, since this will be colonized by germs existing there.

The neonatologist must know the most prevalent bacteria in their unit, as well as the standard sensitivity to these antibiotics in order to provide the most appropriate treatment. Moreover, it must be taken into account the number of inpatients; the relationship between the number of health professionals and patients; and the level of knowledge of health professionals.

The colonization of the newborn umbilical stump, nasal mucosa and skin by *S. aureus*; on the fifth day of life may reach 90% of infants in NICU. Usually the umbilical stump is the first place, requiring less inoculum in relation to other sites. We emphasize that colonization by *S. aureus* in 85% of cases is due to the handling of health professionals team involved in newborns service.

It is essential the importance of hand washing, hygiene umbilical stump, the isolation care, environmental hygiene, equipment and surfaces and tracking the presence of health professionals carriers of staphylococcus strains resistant to met icilin.

The prevalence of *S. aureus* resistant to met icilin in the NICU is the most important predictive factor for acquisition of the bacteria by inpatients. One-person transmission has a critical role in disseminating bacterial [16-18].

The SCoN are commonly in human milk and mucous membranes; It is considered a member of the normal flora of the nasal mucosa and umbilical stump of the newborn; present on the fourth day of life in 83% of newborns in UCIN [19,20]. The observation that SCoN are important agents of nosocomial infection in newborns mainly with low birth weight is explained by the need for invasive procedures, leading to breaking barriers physical host. In addition to low weight, nutritional factors, delayed enteral feeding, and comorbidities such as bronchopulmonary dysplasia, arteriosus ductus and extensive intraventricular hemorrhage; increase the risk of infection SCoN [21].

Stable team, with the adoption of protocols, training and retraining in the passage and care of catheters and probes is essential for the prevention of infection by CoNS in the NICU.

CLINICAL MANIFESTATIONS

Staphylococcal infection should be suspected in infants with the risk factors mentioned the most relevant is the prematurity, weighing less than 1500g, hospitalization for more than 14 days, and the use of venous catheters and or arterial, parenteral nutrition, and use of broad-spectrum antibiotics.

Early sepsis by staphylococcus is rare, and is related to acute infectious complications in late pregnancy or in childbirth colonization leading to clinical symptoms in the first 48-72 hours of life.

Late sepsis by staphylococcus is well documented, the second most common agent in large centers in newborn with very low weight. The clinical signs of infection are the most frequent hypothermia (common in preterm infants) or hyperthermia, tachypnea, tachycardia and other non-specific signs such as lethargy, irritability, episodes of apnea, abdominal distension, and vomiting, gastric waste between others. Apnea and bradycardia are frequent signs in infants with very low weight, while tachypnea, retractions and cyanosis are seen in term newborns. In infants who have skin lesions as bullous impetigo, mastitis or abscesses, bone lesions such as osteomyelitis and pyoarthritits, and other organs such as endocarditis, pneumonia and enterocolitis, the most prevalent pathogens are Staphylococcus aureus, which often cause more localized infections. However, these can spread and cause severe sepsis and septic shock, necrotizing fasciitis on where mortality may reach 60 to 70% of cases. Endocarditis should be investigated in infants with bacteremia S aureus always and this mortality increases to close to 40% of newborns [22].

Recently they have been observed in previously healthy patients with no identifiable risk factors for staphylococcal infections, infections by resistant staphylococci to meticilin acquired in the community. The most affected newborns are male, aged seven to fourteen days old. The most common clinical presentation are skin lesions described above, but invasive infections such as bacteremia , urinary tract and soft tissues have also been described . It is common for the mother or intimate contact of people with the RN also present skin lesions with the same agent²³. Stable team, with the adoption of protocols, training and retraining in the passage and care of catheters and probes is essential for the prevention of infection by CoNS in the NICU.

LABORATORY DIAGNOSIS

Laboratory diagnosis is made by isolation of the agent in blood culture, cerebrospinal fluid, urine and skin lesions. If the blood culture collected by the catheter is positive have greater clinical significance when associated with periphery blood culture [5,6,19].

Isolated catheter culture does not allow easy distinction between colonization and infection. The semi-quantitative or quantitative blood culture allows better discrimination diagnóstica [21]. Generally the average time of growth of bacterial contamination is greater than 48 hours.

Currently it is possible to perform the typing of staphylococci by electrophoresis test medium gel, especially in periods of increased infection in Service to be able to identify patients colonized and infected.

TREATMENT

The treatment of choice for staphylococcal infections is methicillin, and should always be used when the germ is sensitive to this antibiotic, even if the initial empiric treatment was started with another antibiotic. However, due to the resistance methicilin of staphylococci, especially the CoNS, when the infection is nosocomial the drug of choice are vancomycin. In this sense it is also very important to know the microbiota of neonatal units to prevent the inappropriate use of antibiotics.

Rifampicin, given orally can be combined with vancomycin to provide a synergistic effect in treatment for infections such as meningitis and endocarditis. Teicoplanin has similar efficacy to vancomycin. Linezolid and oxazolidone seem to have a satisfactory effect against staphylococci, streptococci and enterococci resistant to vancomycin and are well tolerated by children. However, it is rare to use in infants. The use of vancomycin in patients should have serum control during use due to its ototoxicity and nephrotoxicity.

PREVENTION

Breastfeeding, early use of the Kangaroo (skin to skin contact of the mother and the newborn) and the reduction of unnecessary interventions are measures that reduce all types of hospital infection.

Hand washing is the single most effective measure to reduce hospital infections, as well as other strategies supported by Control of infection Commission existing in the hospital, as the rational use of antibiotics and maintenance of continuing education of health professionals, especially those involved with vascular access.

During insertion of catheters it is recommended to use sterile barrier (field, surgical clothes, cap, mask, sterile gloves) and antiseptic skin with chlorhexidine. The catheter insertion site must always be monitored for the presence of erythema, induration or purulent discharge. You must remove the catheter as soon as possible.

The infection can only be related to the catheter if it has been entered for at least 48 hours. This is manifested by clinical signs of infection and no apparent focus and the presence of the catheter, growing blood cultures collected by the catheter with more than 15 colony forming units and peripheral blood cultures with the same micro-organism and the same antibiotic sensibility. In this case it is necessary to remove the catheter and continue the systemic antibiotic administration [22-29].

Once having been detected colonization by Staphylococci, whether in patients or health professionals can try bacterial eradication. [29,30].

CONCLUSIONS

The infections caused by staphylococci in the neonatal age group are associated with high morbidity and mortality. Early diagnosis and the use of adequate antibiotic therapy contribute to the reduction of infection. However non-pharmacological measures such as hand washing, rational use of antibiotics, continuing education of insertion practices and manipulation of catheters, breastfeeding and the minimum patient handling is the indispensable prevention.

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