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ORIGINAL ARTICLE

Empirical antimicrobial therapy for late-onset sepsis in a neonatal unit with high prevalence of coagulase-negative *Staphylococcus*☆,☆☆

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KEYWORDS
Sepsis;
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Abstract
Objective: The aim of this study was to compare two different empiric treatments for late-onset neonatal sepsis, vancomycin and oxacillin, in a neonatal intensive care unit with a high prevalence of coagulase-negative *Staphylococcus*.
Methods: A cross-sectional study was conducted in an neonatal intensive care unit from 2011 to 2014. Data from the medical records of at-risk newborns were collected daily. Infections were defined according to the National Health Surveillance Agency criteria. Data analysis was performed using an internal program.
Results: There was a significant reduction in the number of *Staphylococcus aureus* infections ($p = 0.008$), without endocarditis, meningitis, or lower respiratory tract infection, as well as a reduction in the frequency of deaths related to *S. aureus* infection. There were no significant changes in the incidence of Gram-negative bacterial or fungal infections. An increase in coagulase-negative *Staphylococcus* infections was observed ($p = 0.022$). However, there was no

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measured increase in related morbidity and mortality. There was a reduction in the median number of days of treatment with oxacillin from 11.5 to 6 days ($p < 0.001$) and an increase of one day in the median number of days of treatment with vancomycin ($p = 0.046$).
Conclusions: Modification of the empiric treatment regimen for neonatal late-onset sepsis with use of oxacillin showed a significant reduction in *S. aureus* infections, as well as a reduction in the frequency of infections with major organ system involvement and mortality due to infection with this microorganism. As a result, oxacillin can be considered as an effective treatment for late-onset sepsis, making it possible to avoid broad-spectrum antibiotics.

PALAVRAS-CHAVE
Sepse;
Recém-nascido;
Staphylococcus;
Oxacilina;
Vancomicina

Terapia antimicrobiana empírica para sepse tardia na unidade neonatal com alta prevalência de *Staphylococcus* coagulase negativo

Resumo
Objetivo: Comparar dois períodos com diferentes esquemas empíricos para tratamento de sepse neonatal tardia, incluindo vancomicina ou oxacilina respectivamente, em Unidade Neonatal de referência com alta prevalência de *Staphylococcus* coagulase negativo.
Métodos: Estudo transversal, realizado em Unidade Neonatal de referência, de 2011 a 2014. A coleta de dados foi realizada diariamente por vigilância ativa em prontuário de recém-nascidos de risco. As infecções foram notificadas conforme critérios definidos pela Agência Nacional de Vigilância Sanitária. O banco de dados e a análise foram realizados em programa interno.
Resultados: Ocorreu redução significativa da notificação de infecções por *Staphylococcus aureus* (p = 0,008), sem notificações de endocardite, meningite e infecções de vias aéreas inferiores, além de redução na frequência de óbitos pelo micro-organismo e sem alteração significativa nas incidências de infecções por bactérias Gram negativas e fungos. Houve aumento de infecções *S. coagulase negativo* (p = 0,022), mas sem aumento de morbidade e mortalidade. Ocorreu redução na mediana do tempo de uso de oxacilina, de 11,5 para 6 dias (p < 0,001), com aumento de mediana de um dia de uso de vancomicina (p = 0,046).
Conclusões: A modificação do esquema empírico com utilização de oxacilina revelou redução significativa das infecções por *S. aureus*, além da redução na frequência de infecção de foco profundo e mortalidade pelo micro-organismo. Considera-se que oxacilina pode ser utilizada como esquema de tratamento de sepse neonatal tardia, evitando-se o uso de antibióticos de largo espectro.

Introduction

The most prevalent microorganisms in late-onset neonatal sepsis described in international literature are coagulase-negative *Staphylococcus* (CoNS).[1–6] While rates of laboratory-confirmed sepsis due to these microorganisms vary from 30% to 60%,[1] higher rates have also been reported. These microorganisms account for 77.9% of late-onset neonatal sepsis in industrialized countries and 46.5% in developing regions.[2] However, infections caused by these commensal microorganisms are often questioned due to difficulties in confirmation and differences in notification criteria.[1,7]

It should also be considered that CoNS are minimally invasive microorganisms that colonize infants after birth and are normally present in the microbiomes of different body sites. They have the beneficial effect of stimulating the innate immune response and improving the defense against other pathogens.[2] However, defense mechanisms can be inadequate in newborn infants, increasing their susceptibility to infection by these microorganisms.[3] On the other hand, although they are considered to be microorganisms responsible for sepsis in newborn infants, they present insidious evolution and low morbidity and mortality.[2,5,8–11]

It is known that the resistance profile of CoNS can exceed 90% for isoxazolyl penicillin.[3] As a result, vancomycin has been considered the standard treatment.[1,12] However, vancomycin restriction as empiric therapy for late-onset neonatal sepsis has been indicated in literature.[9–11,13]

The objective of this study was to compare, epidemiologically, two different empiric treatments for late-onset sepsis in a neonatal intensive care unit (NICU) with a high prevalence of CoNS and oxacillin-sensitive *Staphylococcus aureus*.

Methods

This observational prospective study was conducted at Hospital das Clínicas, at the Federal University of Minas