972. Impact of Genetic Polymorphisms on the Risk of Sepsis in Premature Neonates

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Background. Despite significant advances in supportive care, neonatal sepsis continues to be a major cause of morbidity and mortality, particularly among premature infants. Susceptibility to, and the severity and outcome of sepsis depend on various factors, including environmental exposure, host immune status and inflammatory responses. Identifying single nucleotide polymorphisms (SNPs) in the genes involved in sepsis may help to clarify the pathophysiology of neonatal sepsis. The aim of this study was to evaluate the relationships between sepsis in preterm neonates and genes potentially involved in the response to invasion by infectious agents.

Methods. The study involved all 101 pre-term neonates born between June 2008 and May 2012 with a diagnosis of microbiologically confirmed sepsis, 98 pre-term neonates with clinical sepsis and 100 randomly selected, otherwise healthy pre-term neonates born during the study period. During the study, 47 SNPs in 18 candidate genes were genotyped on Guthrie cards using an ABI PRISM 7900 HT Fast real-time and MAssARRAY for nucleic acids instruments.

Results. Genotypes CT and TT of rs1143643 (the *IL1β* gene) and genotype GG of rs2664349GG (the *MMP-16* gene) were associated with a significantly increased overall risk of developing sepsis ($p = 0.03$, $p = 0.05$ and $p = 0.03$), whereas genotypes AG of rs4358188 (the *BPI* gene) and CT of rs1799946 (the *DEFβ1* gene) were associated with a significantly reduced risk of developing sepsis ($p = 0.05$ for both). Among the patients with bacteriologically confirmed sepsis, only genotype GG of rs2664349 (the *MMP-16* gene) showed a significant association with an increased risk ($p = 0.02$). Genotypes GG of rs2569190 (the *CD14* gene) and AT of rs4073 (the *IL8* gene) were associated with a significantly increased risk of developing severe sepsis ($p = 0.05$ and $p = 0.01$). Genotype AG of rs1800629 (the *LTA* gene) and genotypes CC and CT of rs1341023 (the *BPI* gene) were associated with a significantly increased risk of developing Gram-negative sepsis ($p = 0.04$, $p = 0.04$ and $p = 0.03$).

Conclusion. These results show that genetic variability seems to play a role in sepsis in pre-term neonates by influencing susceptibility to and the severity of the disease, as well as the risk of having disease due to specific pathogens.

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