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Response: Treatment Strategy for Severe Sepsis in Newborns

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Thank you for your feedback on our article, titled "Cytokine Profiles Before and After Exchange Transfusions in Severe Late-Onset Neonatal Group B Streptococcus Meningitis: A Case Report" (Chishiki et al. 2021).

We performed two exchange transfusions (ExTs) for late-onset Group B Streptococcus (GBS) meningitis in a term infant. Although the administration of two ExTs resulted in the reduction of both the levels of cytokines and the likelihood of septic shock, meningitis already occurred. Hence, the effectiveness of the two ExTs on improving neurological outcomes was limited. Neonatal GBS meningitis has high fatality and sequela rates. Thus, it is necessary to establish a preventive strategy.

ExT is a relatively safe and effective treatment for GBS meningitis. It eradicates bacteria, bacterial toxins, and circulating pro-inflammatory cytokines, improves perfusion and tissue oxygenation, corrects the plasma coagulation system, and enhances the immunological defense mechanisms of neonates. On the other hand, polymyxin B-immobilized fiber column for direct hemoperfusion (PMX-DHP) adsorbs endotoxins and prevents septic shock, which may be caused by the gram-negative bacteria. Furthermore, PMX-DHP is effective in protecting neonates against gram-positive cocci-induced sepsis. Jaber et al. (1998) reported that PMX-DHP removed *Staphylococcus aureus* cytokine-inducing substances. Wang et al. (2000) reported that anandamide, which was generated by activated macrophages during septic shock, attached to polymyxin B. PMX-DHP also acts effectively against gram-positive cocci, which induce sepsis, by removing cytokines and anandamides (Imaizumi et al. 2001). In addition, blood purification is effective in newborns and preterm infants (Wightman and Freeman 2016). In 2013, the Guidelines for blood purification in neonatal critical care were established in Japan (Ibara et al. 2013). Nishizaki and Shimizu showed in their letter that PMX-DHP was effective and relatively safe in infants with extremely low birth weight infants and in those with gram-positive cocci-induced sepsis.

However, we had no experience in administering hemoperfusion for neonatal sepsis in our institution. Furthermore, there were problems such as shock, difficulty in securing blood access, and abnormal blood coagulation. Hence, we performed ExTs that could be prepared immediately. Since oxygenation improved and blood pressure increased during the first administration, ExTs resulted in the reduction of various cytokines. However, it might also reduce immune cells and antibiotics. Thus, ExTs might have limited effects on sepsis.

Administration of PMX-DHP to newborns has risks such as abnormal coagulation, hypothermia, and hypotension. If these risks can be avoided, PMX-DHP can be an effective treatment for neonatal sepsis caused by gram-positive cocci. However, to perform PMX-DHP safely for neonatal sepsis, it is necessary to establish an environment conducive for the rapid preparation of PMX column, blood products, and access to the route of administration. Cases continue to accumulate; hence, preventive strategies and treatment modalities for severe bacterial infectious diseases in newborns should be established.

Conflict of Interest

The authors declare no conflict of interest.

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