Commentary

Dosing Guideline Variation Evaluation and Consequences

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ABSTRACT

Neonatal bacterial sepsis is a major common disease that threatens the life of newborns, not only has a high incidence rate but also has a high mortality. After the diagnosis of neonatal sepsis, the rational use of antibiotics is the primary treatment measure. In cases where antibiotics are indicated, treatment should be based on the dosing guidelines. Standard dosing guidelines are systematically developed statements to help practitioners or prescribers to make decisions about the appropriate treatment for specific clinical conditions. Even though guidelines are available for the optimal management compliance is a problem and varies from country to country due to significant variation. Such variations in current dosing recommendations and non-compliance may result in selection of inadequate doses or inappropriate dosing intervals for the treatment ultimate result in under dosing, over dosing and therapeutic failures. Since neonates are immune-compromised and are suspected to infections, such consequences can be more fatal.

Key words: Neonatal sepsis, Dosing guidelines

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INTRODUCTION

Sepsis is a host immune response to infection and considered as a potentially life-threatening condition. Neonatal bacterial sepsis is a bloodstream infection in newborns and significant cause of reported neonatal mortality and morbidity. Newborns with neonatal sepsis might show nonspecific sign and symptoms including temperature instability, lethargy, seizures, respiratory distress, hypotension, tachycardia or bradycardia, feeding intolerance, abdominal distension and bleeding. Since neonates are immune-compromised and are suspected to infections, such consequences can be more fatal. Thus, the objective of this study was to evaluate variations in cefotaxime dosing regimen for the treatment of neonatal sepsis and their possible consequences.

DISCUSSION

Cefotaxime dosing regimen and interval for the treatment of neonatal sepsis in different dosing guidelines were evaluated using model-based analysis. We have observed noticeable differences between total daily dose and the frequency of administration time in the final model.

Cefotaxime was discovered in 1976 and available for commercial purposes in 1980. Cefotaxime is FDA-approved for use in pediatric patients as young as neonates. It is available as a generic medication. Cefotaxime is a beta-lactam antibiotic belongs to third-generation cephalosporin has broad antimicrobial spectrum against gram-negative species and is more active than earlier generations of cephalosporins. Cefotaxime is commonly used in neonates for enteric gram-negative meningitis and sepsis. Cefotaxime is also used in the treatment of serious bacteremia, bone and joint infections, urinary tract infections, pneumonia, intra-abdominal infections, and skin and skin structure infections. Variation in dosing guidelines has significant consequences. Variation in dosing guidelines may result in selection of inadequate doses or inaccurate dosing intervals for the treatment indicate some infants are under dosed while others are over dosed. Neonates are possibly sensitive to the drug actions because they are not mature enough. Consider this issue in mind, choosing an inappropriate dose and dosing interval can have serious consequences. Medication underdosing and overdosing can result in adverse patient outcomes including therapeutic failures, drug toxicity, polypharmacy, harmful and undesirable adverse drug reactions (ADRs), emergency room visits, increase hospital stay, and increase out-of pocket payments. It can also result in the emergence of antibiotic resistance, increasing burden of disease, and prolonged disease state and even mortality in chronic diseases (20, 21). Given the immune-compromised status to neonates special considerations are needed in caring for this population.

CONCLUSION

Although advancement in the medical care has been improved dramatically in the last decades but bacterial infections known as sepsis, still remain a main reason of neonatal deaths and morbidity around the globe. An additional problem is that prescribers find themselves in much difficult in prescribing drugs in neonates. Lack of standardization in dosing recommendations and miscellaneous guidance has resulted in large variation in dosing guidelines. Such large variations in current dosing recommendations may result in selection of inadequate doses or inappropriate dosing intervals for the treatment ultimate result in under-dosing, over-dosing and therapeutic failures. Giving immune-compromised status to neonates, such consequences can be more fatal.

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