Is prophylactic antibiotic treatment justified in neonates?

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Infections are second leading cause of mortality preceded only by cardiovascular diseases.[1] Neonates in particular are at a high-risk of developing bloodstream infections because of their immature immune system and mucosal surfaces.[2,3] In neonates, sepsis has repeatedly been indicated to be an important cause of mortality, with preterm and very low birth weight (<1500g) infants being at the highest risk.[3] Nosocomial bloodstream infections, are vital reasons for neonatal morbidity and mortality. According to a study 64% were caused due to gram-positive organisms, 27% due to gram negative organisms and 8% due to fungi, the most common of the infectious agents being the coagulase negative staphylococci.[4] The first microbial colonization in a newborn occurs during the passage through the birth canal and therefore the empiric treatment for early onset sepsis is based on the most common organisms detected at birth and that of late onset sepsis depends on presenting clinical signs.[5]

Factors that specifically increase neonatal susceptibility to infections include maternal fever during delivery, premature rupture of membranes, preterm labour and maternal urinary and genital tracts colonization.[3,6] Clinical signs of sepsis include "temperature instability, respiratory distress, vomiting, abdominal distension, poor feeding, lethargy or irritability, hypotension, tachycardia, pallor, petechiae, cyanosis and jaundice."[6] It is a common practice amongst paediatricians to administer antibiotics to at risk neonates, without evidence of clinically or microbiologically proven sepsis.[6]

The choice between prophylactic versus selective antibiotics in newborns at risk of sepsis still remains a dilemma in paediatric medicine. The American Academy of Pediatrics in 1997 recommended prophylactic antibiotic treatment of all at-risk infants whereas Lopez in 2001 recommended against it.[6] Currently, the practices vary widely depending on hospital settings as there's insufficient data from randomized controlled trials to guide practice.[6]

There is not enough evidence to believe that

prophylactic antibiotics should be administered to neonates.[7] Even for neonates with established bacterial infections, the empiric treatment may have its demerits because there's evidence that epidemiology of the type of organisms isolated in early-onset infection is changing, with gram negative bacilli increasing, taking over classical group B streptococci.[6] For early onset sepsis, administration of intrapartum antibiotics doesn't provide a solution either because it too, results in resistant strains and change in epidemiology.[6] Furthermore, the results of culture sensitivity tests are not rapidly available for timely diagnosis, adding to the complication. Also, in a developing country like Pakistan, microbiological diagnosis is not accessible to 80% of the population.[8] Many newborns receive antibiotics for presumed infection unnecessarily for every proven case of infection.[2] Such unnecessary antibiotic usages results in generation of resistant microbial strains, super infections and drug toxicity.[9] Very few trials to address the issue are available and because of the fact that they are under-powered, they don't provide any evidence for or against its use[6] and hence, their results cannot be generalized. Moreover, there's a total lack of relevant trials on the long-term neurodevelopmental effect of preventive antibiotic therapy.[7]

In stark contrast to above body of evidences, a study revealed that prophylactic Vancomycin was effective in prevention of sepsis in pre term neonates with central venous catheters.[10] Interestingly, another study showed that even in asymptomatic neonates, morbidity and mortality is increased if the prophylactic treatment is not started timely.[6] The temptation shown by paediatrician to initiate the prophylactic antibiotics regime prior to getting the lab results could possibly be due to high morbidity and mortality associated with neonatal sepsis. As recommended, the empiric treatment is subjected to review after culture sensitivity results are available.[3]

In light of above discussion, it is very clear that significant evidence needs to be established and randomized controlled trials need to be made on the subject in order to decide in favour of, or against the administration of prophylactic antibiotics to neonates. One primary reason for lack of such studies, especially in Pakistan, could be ethical, where selection and choice of cases and controls is a difficult task to be completed. Despite all difficulties and limitations, it is obligatory to establish the required evidence so that use/no use of prophylactic antibiotics in neonates can be justified. At the moment, it remains an unanswered question that needs due debate in order to generate a well accepted generalized opinion.

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