Indian Journal of Pediatrics (April 2022) 89(4):323–324
https://doi.org/10.1007/s12098-021-04063-2

EDITORIAL COMMENTARY

Fine-Tuning the Duration of Antibiotic Therapy for Neonatal Sepsis

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Received: 6 December 2021 / Accepted: 13 December 2021/Published online: 18 January 2022

Sepsis accounts for a third of deaths during the first 28 d of life in India and other low- and middle-income countries [1]. Early diagnosis of neonatal sepsis is often a challenge because of nonspecific symptoms and signs. Moreover, blood culture results are often delayed and positive only in a small percentage of cases treated for sepsis. Infection in neonates could be early-onset (within the first 72 h) or late-onset (after 3 d of life). Early-onset sepsis is acquired during the delivery process and is often caused by organisms acquired from maternal genital flora. Late-onset sepsis is often nosocomial. Any delay in initiating treatment will result in complications with increased mortality and morbidity. In a British Columbia referral hospital, almost 75% of very-preterm and low-birth-weight babies received antibiotics. They could reduce antibiotic administration beyond 48 h from 50% to 7.2% auditing blood culture reports for continuing antibiotics [2]. Indiscriminate use of antibiotics for longer periods than required will result in drug resistance, side effects related to medication, and superimposed infection with other bacteria and fungi. Hence, the treating physician should carefully balance between delayed treatment and inappropriate treatment with regard to antibiotic choice and duration of therapy. Although there are earlier studies on this issue, none of them could come out with definite guidelines.

Choudhury et al. have studied 7 d versus 14 d of antibiotics therapy for culture-positive sepsis. Infants with culture-positive sepsis were randomized if they were asymptomatic on day 5 of therapy to one of the study groups. Blood culture was collected 24 h after stopping therapy and neonates were observed for 72 h in the hospital. Cases were followed up for 28 d. They observed treatment failure among 5 cases in the 7 d group compared to 1 in 14 d treatment group [3]. Rohatgi et al. have conducted a randomized controlled trial (RCT) comparing 7 d versus 10 d among culture-positive sepsis neonates. Klebsiella was isolated in 40.9% and *Staphylococcus aureus* in 22.7% of cases. They administered ceftriaxone with amikacin initially, and modified treatment based on the sensitivity pattern of the organisms. Treatment failure was observed in 1 neonate in each group [4]. Gathwala et al. in their study of 10 d versus 14 d therapy among culture-positive neonates concluded that outcome was similar in both study groups with 1 treatment failure in each group [5]. In all these studies, more than 50% of cases were symptomatic or the screening tests were positive during pre-recruitment assessment and could not be randomized [5]. In an earlier retrospective study from Salt Lake City, only 2.3% of newborns treated for early-onset sepsis had blood-culture positivity. Neonates with culture-positive early-onset sepsis received a mean duration of 12 d antibiotics, while the late-onset 11 d [6]. Thus, it appears that duration of therapy cannot be fixed for all culture-positive neonatal sepsis cases since the duration may vary based on condition of the infant, type of the organism, and the administration of appropriate antibiotics.

Reddy et al. [7] in this issue of the Journal, published a randomized controlled trial among culture-proven sepsis comparing 10 d versus 14 d of antibiotic therapy. The primary outcome was the occurrence of sepsis with the same organism or clinical sepsis with negative culture during 28 d of life and similar to earlier studies [3–5]. This was a pilot study with 35 neonates weighing > 1.5 kg birth weight and > 32 wk of gestation in each group. They observed treatment failure in one infant in the 10 d treatment group and none in the other group. However, they had excluded infants who were clinically symptomatic after 7 d, those with deeper infection like meningitis or bone infection, and those caused by *Staphylococcus aureus*. This makes the study applicable for a selected group of neonates. They could not blind the study because of the nature of the study. Moreover, when the neonate is asymptomatic, blood culture and screening tests are negative, it may not be justifiable to continue antibiotics beyond next 48 h [7].

In an earlier RCT using multiplex PCR-based diagnostic test-the syndromic evaluation system (SES) was compared with the identification of causative organism by blood

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culture using BACTEC method. Identification of causative organism was 4 times higher in the SES group. The results were available in 7 h in the SES method compared to 72 h in BACTEC. Major part of time in the SES method of testing was needed for transporting the blood sample from the hospital to the designated laboratory. Treatment based on SES resulted in administration of appropriate antibiotics, reduced mortality, shorter duration of hospital stay, and reduction in readmission rate. SES testing has many benefits but appears to be costly for routine use. Cost can be reduced by making the test available on a larger scale and in many hospitals [8].

The duration of treatment for uncomplicated neonatal sepsis may vary from a minimum duration of 7 d to a maximum of 14 d depending on the causative organism and the severity of illness. The choice of empirical antibiotic therapy should be based on the prevalence of organisms and their sensitivity pattern in the hospital. Antibiotics can be escalated or de-escalated based on the blood culture report. It will be safer to stop antibiotics if the infant becomes asymptomatic with negative screening tests and blood culture. However, neonates with deeper infections like meningitis and bone infection will require a longer duration (3–4 wk) of therapy. The treating physician should carefully review each case at regular intervals in order to individualize and fine-tune the duration of therapy. Antibiotic stewardship should also be in place in all hospitals caring for infants and children [9].

Declarations

Conflict of Interest None.

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