ORIGINAL ARTICLE

Outcome of 3-Day in Contrast to 7-Day Course of Intravenous Antibiotics for Suspected Early Onset Neonatal Sepsis

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ABSTRACT

Background: Neonatal Sepsis is associated with morbidity and increase risk of death. The clinical manifestation is very nonspecific and based on clinical suspicion, initial antibiotic therapy after obtaining blood culture.
Aim: To compare the frequency of failure of treatment in 3-day versus 7-day antibiotic treatment for probable early onset neonatal sepsis.
Methods: This study was Randomized controlled trial conducted at Neonatology unit of department of Pediatrics, Sir Ganga Ram Hospital, Lahore from 1st January 2015 to 30 June 2015. Total 120 neonates of probable early onset sepsis, included in the study were divided into two groups and started with antibiotics .In the intervention arm antibiotics were stopped after the 72 hours while antibiotics were continued total of 7 days in control arm.
Results: There were no significant treatment failures between the two groups (9 babies in the 7-day group versus 7 in the short course group (p=0.424).
Conclusion: There was no difference in the rates of treatment failure that could be identified between 3-day and 7-day courses in neonates with suspected early onset neonatal sepsis.
Keywords: Sepsis, early onset neonatal sepsis, antibiotics, short course

INTRODUCTION

Neonatal and infant mortality is quite high contributing to more than two thirds of deaths in less than five years of age[1]. Neonatal sepsis remains one of the leading causes of neonatal admission, morbidity and mortality in developing countries[2]. Timely case management is of critical importance and outcome can be improved with better compliance but the current standard of hospitalization for parenteral antibiotic therapy is not always feasible[3,4]. This study was conducted by looking at the ambiguity in the available literature on timely guidelines for the treatment duration in suspected (i.e. non culture proven) neonatal sepsis with a high disease burden in our setting. Early onset sepsis occurs during the first three days (72 hours) of life[5]. The major risk factors for neonatal sepsis are amniotic bag rupture, maternal colonization, chorioamnionitis and maternal fever[7]. The most common cause of neonatal bacterial sepsis is GBS. The symptoms and clinical signs of sepsis in newborns depends on severity of infections, these symptoms may be poor feeding, hypothermia, hypotension and lethargy in general Respiratory symptoms, such as, apnea, grunting, tachypnoea, intercostal recessions and flaring of ala nasi are common as pneumonia is often the presenting infection[8]. The gold standard for diagnosis is blood culture[9]. However obtaining culture from neonates can be difficult as sample volumes are small and a substantial m=numbers of cultures turn out to be contaminated or negative[10]. The other tests includes CBC, CRP and procalcitonin, other biomarkers like cytokines and chemokines can also be considered.

Received on 02-11-2019
Accepted on 17-04-2020

Treatment of neonatal infection may be divided into anti-microbial therapy for the suspected or non-pathogen and supportive care[11].

After obtaining culture specimens initial treatment of early onset bacterial infections should consist of ampicillin and aminoglycoside (usually gentamicin), or ceftriaxone. If diagnosis is delayed mortality increases. The mortality and residual neurological damage are inversely proportional to gestational age and birth weight[12].

PATIENTS AND METHODS

This randomized controlled trial was conducted at the neonatal unit of Sir Ganga Ram Hospital from January 2018, to 30 June 2018. A total of 120 newborns with probable early onset sepsis, having birth weight of more than 1 kg and aged to touch more than 30 weeks were included in the study. While newborns with major birth defects, severe HIE, culture proven sepsis, suspected orthopedic infections, cellulitis, those who were already receiving antibiotics and those with any surgical condition were not included in the study.

After moral clearance neonates were divided into two groups with 60 neonates in each group. Septic screens of all the patients were sent on the start of therapy. Group A was given antibiotics; ampicillin, third generation cephalosporins, amikacin for 72 hours. Group B was given the same antibiotics for 7 days.

Vital signs were recorded hourly, along with the daily examination for resolution of signs and symptoms. Septic screen was repeated on day 3. Antibiotics were stopped in short course group after 72 hours and continued for 7 days in the long course group, treatment failure at the completion of treatment was recorded as per operational

definition. Patients showing treatment failure were given antibiotics until treated, data was analyzed using SPSS 16. Two groups were compared for treatment failure, data was presented in the form of frequency table, charts, graphs. Chi-square test was applied.

RESULTS

There were 53 patients in group A with no treatment failure and 7 patients with treatment failure. There were 51 patients in group B with no treatment failure and 9 patients with treatment failure. Rate of treatment failure in both groups was statistically the same (P value was 0.5915, Chi-square was 0.288).

Group A: Short course Group

Group B: Long course Group

Data stratification was done with respect to gender, gestational age, weight and post stratification Chi-square test showed that there was no effect of these variables on treatment failure.

Table I: Outcome in terms of treatment failures in the study group

		Treatment Failure		Total	p-value
		Yes	No		
Treatment	Group A	7	53	104	0.5915
	Group B	9	51	16	
Total		60	60	120	

Table II: Stratification W.R.T Gestational Age of Treatment Failures in the Study Groups

Gestational Age	Group	Treatment Failure		Total	P-value
		YES	NO		
30-34 Weeks	Group A	4	13	17	0.368
	Group B	2	15	17	
34-37 Weeks	Group A	5	29	34	0.402
	Group B	3	33	36	
37-40 Weeks	Group A	1	6	7	0.849
	Group B	1	8	9	
Total		16	104	120	

Table III: Stratification W.R.T Birth Weight of Treatment Failures in the Study Groups

Birth Weight	Group	Treatment Failure		Total	P-value
		YES	NO		
1000-2000g	Group A	1	7	8	0.824
	Group B	1	5	6	
2000-3000g	Group A	5	27	32	0.647
	Group B	4	30	34	
3000-4000g	Group A	2	18	20	0.632
	Group B	3	17	20	
Total		16	104	120	

DISCUSSION

The current study of first-line antibiotic treatment across neonates shows that symptomatic infection causes exposure to adverse drug effects, nosocomial disorders and outbreaks of immune strains. The isolation of an organism on blood culture confers many benefits including a good choice and time period of antimicrobial treatment. Blood cultures are still golden in diagnosing neonatal sepsis. However, taking cultures can be difficult as the sample is small and a large number of cultures come out contaminated or negative. Groups that did not show any treatment failure were followed after two weeks and remained healthy.

Both symptomatic and asymptomatic neonates with maternal risk factors were included in this study. Neonates with very low birth weight were excluded as they often have subtle symptoms of sepsis that can be missed in the clinic and some serious adverse reactions can mimic sepsis, which makes the diagnosis of treatment failure extremely difficult. In this study, we used CRP at inclusion as a sign of sepsis; serial CRP values have not been used to determine the time to stop treatment with antibiotics, so that, the results obtained can be transferred to lower-level hospitals and clinics, where these laboratory facilities are not readily available.

In our study, treatment was stopped in the whole group only after the neonates were already completely asymptomatic. In neonates with symptoms it would not be possible to rule out a continuous infection for sure and therefore it would not be a good idea to discontinue treatment. There is no other way to predict that neonates who will become symptomatic again at the time of the arrival of the culture report are active again which is why randomization did not occur at the beginning of the antibacterial course. The study also highlighted the nature of the clinical problem (regarding the continuation of antimicrobial drugs) that pediatricians experience after a neonate suspected of sepsis with elevated CRP and other symptoms of infection, becomes asymptomatic soon after starting treatment.

A further 3-day limit was determined based on observations made in previous studies.[13] As this study leads to a new type of life-threatening neonatal disease, special measures to ensure that the treatment failure were not missed. The insignificant trend of major treatment failure in the 7-day group confirmed, that even in this

sample determined the state of short-term study was better than the 7-day regimen. The reason for the increased treatment failure in the 7-day group may be the presence of IV cannula for a long time when it is not needed, in addition to the long stay of neonates in the neonatal unit leading to an increased risk of nosocomial infection. It is possible that the first negative symptoms may have been caused by neonatal sepsis as shown by a false tradition. Both groups were equally equal in basic flexibility, so that thinking due to these differences were reduced.

To the best of our knowledge, no such research focused on short-term antibiotic treatment for neonatal sepsis has been published in our program to date. A similar study was conducted in India in 2009 by Saini et al in which 52 neonates were randomly assigned to give a short / 7-day (n-26 each) first course of antibiotic treatment for neonatal sepsis. The fundamental differences were equal in both groups. There was a small difference in treatment failure in both groups (three who were in the 7-day vs zero group in the short study group presented treatment failure, p = 0.23) .[14] Another similar study was conducted in Iran in 2014 by Pasha et al. in which 2 groups of neonates were included. There were 30 patients in each group. One group received a three-day course of antibiotic therapy and the other group was given 5 days of treatment. Only one neonate in 3 days showed no treatment failure as opposed to treatment failure in the 5-day group (P = 0.5).[15] The study had some drawbacks. Due to the small sample size in the study there was no conclusion that a short anti-bacterial course does not reduce the 7-day study. In addition, the results apply only to a specified subgroup of preterm neonates weighing more than one kilogram of birth and acquisition over 30 weeks. Blinding could not be included in the study as it was not effective to prepare placebos that looked similar to a wide range of antibiotics, and to plan similar antibiotic administration for a short study group. CRP quantitative assay would be very effective as a evidence of sepsis. In this study, there was no statistically significant difference in treatment failure rates between the 3-day period and the 7-day in preterms of more than 30 weeks and one kilogram with suspected sepsis, who were asymptomatic within 2 days of antibiotics therapy. The above discussion shows that the results of the study are consistent with other previous studies. The purpose of the study is clear, namely: it is possible that at the onset of primary sepsis, the 3-day model works in the same way as 7 day. More studies are needed to strengthen the validity of this study. This will be beneficial in a number of areas; First, a short course of antimicrobials will lead to a shorter hospital stay leading to a decrease in nosocomial infection cases. This short hospital stay will also be beneficial in terms of cost effectiveness, it will reduce the burden of neonatal services in our set up where most of the city's hospitals have to admit patients beyond their bed capacity. Another benefit of such a short-term regimen will be reduced administration of unnecessary toxic substances that can pose another threat to the liver and kidneys.

Despite the lack of well-designed trials that evaluate the appropriate duration of treatment for sepsis, it is recommended that the duration of antimicrobial treatment be two to three days pending the culture results of possible sepsis.

A similar study was conducted in India in which 52 infants with undiagnosed sepsis were randomly assigned to any short course (48-96 hours) or long (7 days) course of antibiotic treatment.[16] There was no difference in the rate of treatment failure (defined by repetition of clinical signs and laboratory evidence) between both groups.

CONCLUSION

The study reveals that there was no difference in the outcome of neonates receiving either short course (3-day), or long course (7-day) of antibiotic treatment for suspected early onset neonatal sepsis. The rates of treatment failures were comparable between both the groups of neonates more than thirty weeks and more than one-kilogram with suspected sepsis. This gives us the possibility of shortening the duration of antibiotic therapy in uncomplicated suspected early onset neonatal sepsis.

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