e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(2); 101-104

Original Research Article

Observational Research to Evaluate the Use of C-Reactive Protein in Deciding Duration of Antibiotics Therapy in Neonatal Bacterial Infection

Prem Kumar[1], Nand Kishor Singh[2], Akhilesh Kumar[3]

[1]Senior Resident, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India

[2]Senior Resident, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India

[3]Professor, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India

Received: 16-10-2023 Revised: 21-11-2023 / Accepted: 20-12-2023
Corresponding author: Dr. Nand Kishor Singh
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess the role of C-reactive protein in deciding duration of antibiotics therapy in neonatal bacterial infection.

Methods: The present study was conducted in the Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India and 50 patients were included in the study. The duration of study was about two years.

Results: Clinical features of infected neonates were 39 (78%) born by vaginal delivery 3 (6%) had history of maternal fever, 6 (12%) had history of PROM, 20 (40%) refusal of feeds, 16 (32%) lethargy, 10 (20%) poor cry, 10 (20%) Tachypnea, 6 (12%) jaundice, 7 (14%) conjunctivitis, 6 (12%) vomiting, 3 (6%) excessive cry, 2 (4%) pyoderma, 2 (4%) abdominal distension, 2 (4%) hypothermia, 1 (2%) fever, 2 (4%) diarrhea, 2 (4%) umbilical sepsis in the study. Study of organism observed in 21 (42%). In the gram negative 16 (32%) neonates: 6 had klebsiella, 4 had E Coli, 4 had pseudomonas, 2 had acinetobacter. The neonates had gram positive bacilli – 3 staphylococcus aureus, 1 Coagulase Negative Staphylococci (CoNS), 1 had Haemolytic streptococci. CRP guided distribution of treatment, relapse rate in two groups and correlation with blood culture. In group A (23) had CRP value was <6 -duration of therapy was <3 days and No. bacilli, No relapse was observed. In group B CRP value was >6 in 32 neonates, 2 patients treated for 5 days, 14 patients for 7 days and 11 patients for 11 days. Blood culture was positive for 12 neonates with 7 days therapy, for 10 neonates with 11 days duration therapy and no relapse was observed. Overall duration of treatment for <7 days observed in group I were 23, and group II were 2 and total number were 25. Duration of > 7 days therapy observed in group 1 was 14 and group 2 was 11 and total number was 25.

Conclusion: The role of CRP is significant in deciding the duration of antibiotics therapy in neonates. It is safer as compared to other, but still further study is required for other marker because CRP cannot influence gestation age infections, non-infectious confounders.

Keywords: Sepsis, PROM, C - reactive protein, neonates, antibiotic therapy

Introduction

Neonatal bacterial infection (septicaemia) remains a significant cause of neonatal morbidity and mortality globally. The incidences of neonatal sepsis vary between 11 to 25 per thousand live births in India. [1] Its clinical manifestations vary from being specific to subtle, testing the skills of a pediatrician. The inability to be certain of infection coupled with non-specific signs of the life threatening illness in neonates have resulted in wide spread use of antibiotics, [2] aggravating the problem of antibiotics resistance. There is an increasing need for careful evaluation of indications and duration of treatment which in turn would shorten the length and cost of hospital stay and diminish the trauma and side effects of antibiotics. [3] C-reactive protein (CRP) an acute phase reactant is synthesized in liver in response to inflammatory cytokines and may rise more than 1000 times during acute phase responses. It falls quickly after efficient elimination of microbial stimulus, due to its short half of life of 19 hours. [4]

Globally sepsis is one of the most typical causes of newborn mortality and fatality. [5] According to the National Neonatal Perinatal Database (NNPD), 2002-2003, episodes of neonatal sepsis (NS) in India is seen in 30 per 1000 live births. [6] Worldwide, approximately 3,000,000 infants per year suffer from NS (2202/100,000), and India has a very high

level of occurrence of clinical sepsis (17,000/100,000 live births). [7] NS is a clinical syndrome described as a microbial infection in the bloodstream of a neonate in the presence of a fever. It is a life-threatening condition in the initial 28 days of an infant. [8,9] It comprises varying clinical manifestations including septicemia, pneumonia, meningitis, osteomyelitis, and urinary tract infections. [10] NS is a most conventional problem associated with considerable mortality and morbidity. Most neonates present with atypical symptoms of NS, and others mimic the symptoms, making it difficult to differentiate between them.

Hence, distinguishing the infants who have NS from those with suspected sepsis becomes challenging. The most common diagnostic method is the blood culture, also thought about as the touchstone, but the demerit is that it takes at least 48-72 hours for the results to be available. [11] Moreover, the positive findings of blood culture are low and are afflicted by the blood volume inoculated, level of bacteremia and laboratory capableness, and most importantly, prenatal antibiotic use. [12]

The aim of the present study was to assess the role of C-reactive protein in deciding duration of antibiotics therapy in neonatal bacterial infection.

Materials and Methods

The present study was conducted in the Department of Pediatrics, NMCH, Patna, India and 50 patients were included in the study. The duration of study was about two years.

Inclusive Criteria: Neonates <28 days of life having birth weight more than 1500 grams with suspected septicaemia were included in the study.

Exclusion Criteria: Neonates undergone surgery due to wound infection Neonates diagnosed as meningitis (because it requires longer treatment of antibiotics) were excluded from study.

Method: After admission blood culture and sensitivity, Routine blood investigations, urine culture and sensitivity, chest x-ray, CRP were done. CRP was estimated within 24-48 hours of admission. Then neonates were classified as per the levels of CRP serum levels. Neonates were kept up to 48 hours after stopping the antibiotics to observe the recurrence of clinical features of septicaemia. If there is no recurrence of symptoms of septicaemia within four weeks of discharge or the baby required antibiotics for different diagnosis other than septicaemia. In the case of relapse the baby needed another course of antibiotics for suspected or proved septicaemia within 4 weeks after discharge. To estimate the value of CRP as a parameter for guiding the duration of antibiotic therapy, the negative predictive value with respect to further treatment was determined.

Statistical Analysis: Different clinical features, CRP levels, micro organisms were classified with percentage. The statistical analysis was made in SPSS software.

Results

Table 1: Clinical features of suspected infected neonates

Particular	No. of neonates	Percentage
Vaginal delivery	39	78
Material fever >100.4 F	3	6
PROM > 18 hrs (premature Rapture of Membrane)	6	12
Refusal feeds	20	40
Lethargy	16	32
Poor Cry	10	20
Tachypnea	10	20
Jaundice	6	12
Conjunctivitis	7	14
Vomiting	6	12
Excessive Cry	3	6
Pyoderma	2	4
Abdominal distension	2	4
Hypothermia	2	4
Fever	1	2
Diarrhoea	2	4
Umbilical Sepsis	2	4

Clinical features of infected neonates were 39 (78%) born by vaginal delivery 3 (6%) had history of maternal fever, 6 (12%) had history of PROM, 20 (40%) refusal of feeds, 16 (32%) lethargy, 10 (20%) poor cry, 10 (20%) Tachypnea, 6 (12%) jaundice, 7 (14%) conjunctivitis, 6 (12%) vomiting, 3 (6%) excessive cry, 2 (4%) pyoderma, 2 (4%) abdominal distension, 2 (4%) hypothermia, 1 (2%) fever, 2 (4%) diarrhea, 2 (4%) umbilical sepsis in the study.

Table 2: Study of Micro Organism

Particular	Organism	No. of cases
Gram Negative (n=16) (32%)	Kelbesiella E. Coli Pseudomonas Acinetobacter	6 4 4 2
Gram Positive (n=5) (10%)	Staphylococcus Aurous CONS and α Hemolytic streptococci	3 1 1

Study of organism observed in 21 (42%). In the gram negative 16 (32%) neonates: 6 had klebesiella, 4 had E Coli, 4 had pseudomonas, 2 had acinetobacter. The neonates had gram positive bacilli – 3 staphylococcus aureus, 1 Coagulase Negative Staphylococci (CoNS), 1 had Haemolytic streptococci.

Table 3: CRP guided distribution of treatment relapse rate in two groups and correlation with blood culture results

CRP Value	Groups	Duration of therapy No of cases	Blood culture +ve	Relapse	Negative predicative value (%)
<6	Group A	<3 days	Nil	Nil	100
>6	Group B	5 days (2) (4%)	Nil	Nil	100
		7 days (14) (28%)	12	Nil	100
		> 11 days (11) (21%)	10	Nil	100

CRP guided distribution of treatment, relapse rate in two groups and correlation with blood culture. In group A (23) had CRP value was <6 -duration of therapy was <3 days and No. bacilli, No relapse was observed. In group B CRP value was >6 in 32 neonates, 2 patients treated for 5 days, 14 patients for 7 days and 11 patients for 11 days. Blood culture was positive for 12 neonates with 7 days therapy, for 10 neonates with 11 days duration therapy and no relapse was observed.

Table 4: Over all durations of treatment with CRP guided treatment

Group	Duration of treatment	
	< 7 days	> 7 days
Group 1	23	14
Group 2	2	11
Total	25	25

Overall duration of treatment for <7 days observed in group I were 23, and group II were 2 and total number were 25. Duration of > 7 days therapy observed in group 1 was 14 and group 2 was 11 and total number was 25.

Discussion

Neonatal septicemia remains a significant cause of neonatal morbidity and mortality. The incidence of neonatal sepsis varies between 11 to 24.5 per thousand live births in India. [13] Its clinical manifestations vary from being specific to subtle, testing the very skills of a pediatrician. The inability to be certain of infection, coupled with non-specific signs of the life threatening illness in neonates have resulted in widespread use of antibiotics, aggravating the problem of antibiotic resistance. There is an increasing need for careful evaluation of indications and duration of treatment, which in turn would shorten the length and cost of hospital stay and diminish the trauma and side effects of antibiotics.

Clinical features of infected neonates were 39 (78%) born by vaginal delivery 3 (6%) had history of maternal fever, 6 (12%) had history of PROM, 20 (40%) refusal of feeds, 16 (32%) lethargy, 10 (20%) poor cry, 10 (20%) Tachypnea, 6 (12%) jaundice, 7 (14%) conjunctivitis, 6 (12%) vomiting, 3 (6%) excessive cry, 2 (4%) pyoderma, 2 (4%) abdominal distension, 2 (4%) hypothermia, 1 (2%) fever, 2 (4%) diarrhea, 2 (4%) umbilical sepsis in the study. Study of organism observed in 21 (42%). In the gram negative 16 (32%) neonates: 6 had klebesiella, 4 had E Coli, 4 had pseudomonas, 2 had acinetobacter. The neonates had gram positive bacilli – 3 staphylococcus aureus, 1 Coagulase Negative Staphylococci (CoNS), 1 had Haemolytic streptococci. As Bacterial infections stimulate the hepatocytes to produce CRP a non-specific immune response, which is useful clinical marker for the individual host-pathogen interaction. Since the half life of CRP is less than 3 days a rapid fall is seen with successful antibiotic therapy. [14] The diagnosis of neonatal septicaemia is difficult to

establish based on the clinical criteria alone because of its subtle, variable and non-specific signs and symptoms. The use of safe and effective antibiotics has significantly contributed to decrease neonatal mortality. [15]

CRP guided distribution of treatment, relapse rate in two groups and correlation with blood culture. In group A (23) had CRP value was <6 -duration of therapy was <3 days and No. bacilli, No relapse was observed. In group B CRP value was >6 in 32 neonates, 2 patients treated for 5 days, 14 patients for 7 days and 11 patients for 11 days. Blood culture was positive for 12 neonates with 7 days therapy, for 10 neonates with 11 days duration therapy and no relapse was observed. Overall duration of treatment for <7 days observed in group I were 23, and group II were 2 and total number were 25. Duration of > 7 days therapy observed in group 1 was 14 and group 2 was 11 and total number was 25. The comparison of both CRP and micro-ESR with positive blood cultures was statistically significant ($p < 0.05$). There was no relapse in any of the cases in which antibiotics were stopped following normalization of CRP giving a negative predictive value of 100%, which was similar to the observation claimed by Ehl S et al. [15] A similar study by Squire, et al [16] revealed that authors were able to stop antibiotics in 66.5% of cases within 72 hours and could reduce the duration of treatment by 20% in suspected neonatal septicemia cases. However, the fear of missing a case of neonatal septicaemia, with its serious outcome had led to overuse of antibiotics in this age group of neonates. It is also reported any bacterial infection may ultimately turned to septicaemia, if the mother was infected during pregnancy or before delivery. [17]

Conclusion

The role of CRP is significant in deciding the duration of antibiotics therapy in neonates. It is safer as compared to other, but still further study is required for other marker because CRP cannot influence gestation age infections, non-infectious confounders. Moreover exact mechanism of elevation and decrease of CRP values during infections is still unclear.

References

1. Poul VK, Singh M. Neonatal sepsis. In: M S, editor. Medical emergencies in children 2nd Edn. New Delhi: Sagar Publication; 1998. p. 115–8.
2. Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, et al. Trends in neonatal morbidity and mortality for very low birthweight infants. Am J Obstet Gynecol. 20 07;196(2):147.e1–8.
3. Murray BE. Can antibiotic resistance be controlled? J Med. 1994;330(17):1229–30.
4. Vigushin D, Pepys M, Hawkins PN. Metabolic and scintigraphicstudies of radio-iodinated human C-reactive protein in health and disease. J Clin Invest. 1993;1 (2): 1351–57.
5. Wattal C, Kler N, Oberoi JK, Fursule A, Kumar A, Thakur A. Neonatal sepsis: mortality and morbidity in neonatal sepsis due to multidrug-resistant (MDR) organisms: part 1. The Indian Journal of Pediatrics. 2020 Feb ;87:117-21.
6. National Neonatal Perinatal Database Report 2002-03: Indian Council of Medical Research, New Delhi; 2003.
7. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. The Lancet Respiratory Medicine. 2018 Mar 1;6 (3):223-30.
8. Davies PA. Maternal and fetal infection. InFetal Physiology and Medicine 1984 Jan 1 (pp. 353-395). Butterworth-Heinemann.
9. Ershad M, Mostafa A, Cruz M. Dela, Vearrier D. Neonatal Sepsis. Curr Emerg Hosp Med Rep . 2019;7(3):83-90.
10. Singh M, Alsaleem M, Gray CP: Neonatal sepsis. StatPearls [Internet]. StatPearls Publishing, Treasure Island (FL).
11. Zea-Vera A, Ochoa TJ. Challenges in the diagnosis and management of neonatal sepsis. Journal of tropical pediatrics. 2015 Feb 1;61(1) :1-3.
12. Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal infectious diseases: evaluation of neonatal sepsis. Pediatric Clinics. 2013 Apr 1;60(2):367-89.
13. Paul VK, Singh M. Neonatal Sepsis. In: Singh M (ed). Medical Emergencies in Children. 2nd edn. New Delhi: Sagar Publication, p. 115.
14. Jaswal RS, Kaushal RK, Goel A, Pathania K. Role of C-reactive protein in deciding duration of antibiotic therapy in neonatal septicemia. Indian pediatrics. 2003 Sep 1;40(9):880-3.
15. Ehl S, Gering B, Bartmann P, Högel J, Pohlandt F. C-reactive protein is a useful marker for guiding duration of antibiotic therapy in suspected neonatal bacterial infection. Pediatrics. 1997 Feb 1;99(2):216-21.
16. SQUIRE JR EN, REICH HM, MERENSTEIN GB, FAVARA BE, TODD JK. Criteria for the discontinuation of antibiotic therapy during presumptive treatment of suspected neonatal infection. The Pediatric Infectious Disease Journal. 1982 Mar 1;1(2):85-90.
17. Gerdes JS, Polin RA. Sepsis screen in neonates with evaluation of plasma fibronectin. Pediatr Infect Dis J. 1987;6(5):443–6.