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OCCURRENCE OF HYPERBILIRUBINEMIA IN NEONATES GIVEN A SHORT-TERM COURSE OF CEFTRIAXONE VERSUS CEFOTAXIME FOR SEPSIS

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Abstract

Introduction: Sepsis occurring before 28 days after birth is termed as neonatal sepsis. It is a life-threatening infection responsible for significant morbidity and mortality worldwide.

Aim: To compare the incidence of hyperbilirubinemia in neonates given a short-term course of ceftriaxone versus cefotaxime for sepsis.

Methods: A retrospective study conducted in Autonomous State Medical College, Shahjahanpur & Allied Pt. Ram Prasad Bismil Memorial Hospital. Study was carried out by evaluating 110 prescriptions of neonatal sepsis. 110 prescriptions were grouped into two, ceftriaxone prescribed cases included in group-A and cefotaxime prescribed cases included in group-B. At the time of antimicrobial administration, patients were about 15-28 days old and each received at least one dose of ceftriaxone or cefotaxime during hospital admission. Patient characteristics and bilirubin levels were compared between groups.

Results: Majority of the patients were males (68.18%), weighing 3.25kg. At initial visit, an average age of patients was 21 days. Among 110 cases, elevated bilirubin levels were observed in 96(87.27%), only 14 patients had normal bilirubin levels. After treatment with antimicrobial agents, abnormally elevated bilirubin levels were noticed in 5 patients, 2 (3.50%) in ceftriaxone and 3 (5.6%) in cefotaxime treated patients. Bilirubin levels were increased in both the groups but the mean difference was not statistically significant. ($p>0.05$)

Conclusion: In present study we had observed hyperbilirubinemia in patients received both ceftriaxone and cefotaxime. However cefotaxime received patients had shown slightly higher bilirubin levels as compared with ceftriaxone received patients, but which is not statistically significant($p>0.05$).

Keywords: Sepsis, Hyperbilirubinemia, Ceftriaxone, Cefotaxime

INTRODUCTION

Sepsis occurring before 28 days after birth is termed as neonatal sepsis[1, 2]. It is a life-threatening infection responsible for significant morbidity and mortality worldwide. The incidence of neonatal bacterial sepsis estimated to be between 1 and 12 per 1000 live births in high-income countries[1]. The incidence in low- and middle-income countries is higher, and in Asia, the incidences have been estimated to be up to 38 per 1000 live births[3–8]. In the high-income countries, neonatal sepsis has a mortality ranging from 5 to 20% and causes major disability (or death) in up to 40% of all cases despite initiation of conventional treatment[1]. Mortality rates up to 70% have been observed in some low- and middle-income countries[1, 4]. Common causative organisms associated with this infectious process include streptococcus agalactiae, Escherichia coli, listeria monocytogenes, and other Gram-negative aerobes[9].

In survivors, sepsis is associated with serious long-term morbidity such as cerebral palsy, cognitive and psychomotor delay, auditory and visual impairment, and bronchopulmonary dysplasia[10]. Depending on the time of onset, neonatal sepsis may be divided into early onset sepsis and late onset sepsis. The infection in early onset sepsis is usually acquired vertically from a colonised mother, while the infection in late onset sepsis is usually acquired horizontally, e.g. from the community or a nosocomial (hospital-acquired) infection[11, 12].

Due to the non-specific signs and symptoms and potential for severe consequences with untreated neonatal sepsis, the American Academy of Pediatrics recommends the initiation of broad spectrum antimicrobial therapy consisting of ampicillin plus either a third-generation cephalosporin or gentamicin until infectious etiology can be ruled out[13]. Ceftriaxone and cefotaxime are third-generation parenteral cephalosporins with broad-spectrum activity against Gram-positive and Gram-negative organisms. Favorable pharmacokinetic and pharmacodynamics properties (long serum half-life, tissue and central nervous system penetration, and simple dosing regimen) make these agents appealing options in neonatal infections[14]. Cefotaxime is recommended over ceftriaxone because ceftriaxone may cause bilirubin displacement, potentially leading to serious adverse events associated with unconjugated hyperbilirubinemia such as kernicterus. An additional concern with ceftriaxone use is that high drug concentrations in the biliary system can result in ceftriaxone-calcium complexation, thereby increasing concerns for cholestasis, pseudolithiasis, and biliary sludging[15]. Present study had been designed to compare the incidence of hyperbilirubinemia in neonates given a short-term course of ceftriaxone versus cefotaxime for sepsis.

MATERIAL AND METHODS

A retrospective study was conducted after approval from institutional ethical committee at Autonomous State Medical College, Shahjahanpur & Allied Pt. Ram Prasad Bismil Memorial Hospital, from January 2023 to July 2023. Study was carried out by evaluating 110 prescriptions of neonatal sepsis.

Inclusion criteria:

- ✓ 15 to 28 days old at the time of antimicrobial administration
- ✓ Received at least 1 dose of ceftriaxone or cefotaxime.

Exclusion criteria:

- ✓ Incomplete medical records
- ✓ Who received both ceftriaxone and cefotaxime during hospital admission
- ✓ History of hyperbilirubinemia
- ✓ Lack of subsequent total bilirubin levels beyond the baseline result.

A total of 110 prescriptions were reviewed and grouped them into two, ceftriaxone prescribed cases included in group-A and cefotaxime prescribed cases included in group-B. From all the medical records, the following information was extracted like, age in days at initial hospital admission, sex, gestational age, history of hyperbilirubinemia and hospital LOS (length of stay).

RESULTS

In the present study we have evaluated a total of 110 prescription of neonatal sepsis after meeting inclusion and exclusion criteria. Majority of the patients were males (68.18%), weighing 3.25kg. At initial visit, an average age of patients was 21 days. During the course of treatment, 41.8% of neonates were admitted in hospital (Hospital LOS) for 3 days, 22.72% of neonates were hospitalized about 3-5 days and remaining patients (35.45%) were stayed for more than 5 days. Among 110 cases, elevated bilirubin levels were observed in 96(87.27%) only 14 patients had normal bilirubin levels. At end of the study, abnormally elevated bilirubin levels were noticed in 5 patients, 2 (3.50%) in ceftriaxone and 3 (5.6%) in cefotaxime treated patients. Average 0.55±0.1 mg/dl of elevated bilirubin was noticed overall. Bilirubin levels were increased in both the groups but the mean difference was not statistically significant.($p>0.05$)

Table-1: Patients characteristics and bilirubin levels

Variables	All patients (n=110)	Ceftriaxone (n=57)	Cefotaxime (n=53)	P value
Age at initial visit in days	21.0	20.0	22.0	0.723
Gestational age in weeks	38.5	38	39	0.702
Sex n (%) males	75(68.18%)	39(68.4%)	36(67.92%)	0.987
Weight(Kg)	3.25	3.1	3.4	0.502
Hospital LOS <3 days 3 -5days >5 days	46(41.8) 25(22.72) 39(35.45%)	19(33.3) 18(31.57) 20(35.08)	27(50.94) 7(13.20) 19(35.84)	-----
Baseline bilirubin mg/dl	2.25(n=110)	2.1(n=57)	2.4(n=53)	0.625
Abnormal bilirubin, n (%), mg/dl	96(87.27)	51(89.47)	45(84.90)	0.724
Abnormal bilirubin mg/dl	2.85(n=96)	2.4(n=57)	3.3(n=53)	0.356
Increase in bilirubin: baseline to abnormal, n (%)	5(4.5)	2(3.50)	3(5.6)	0.502
Difference in bilirubin values abnormal versus baseline, mean ± SD	0.55 ±0.1 (n=96)	0.15±0.001 (n=57)	0.4± 0.01 (n=53)	0.316

Significant - P<0.05***

DISCUSSION

A total of 110 patients were included in the present study after meeting inclusion and exclusion criteria. Majority of study participants were males (68.18%), weighing 3.25kg. At initial visit, an average age of patients was 21 days. During the course of treatment, 41.8% of neonates were admitted in hospital (Hospital LOS) for 3 days, 22.72% of neonates were hospitalized about 3-5 days and remaining patients (35.45%) were stayed for more than 5 days. Among 110 patients, initially 96 (87.27%) shown hyperbilirubinemia. Overall 5 patients had shown elevated bilirubin levels after receiving ceftriaxone (n=2) and cefotaxime (n=3), but which was not statistically significant ($p>0.05$). High mean elevation in bilirubin levels were noticed in patients received cefotaxime as compared with ceftriaxone group, but which was not statistically significant. These results are consistent with previously published studies[16].

Neonatal sepsis is a major cause of morbidity and mortality. It is the third leading cause of neonatal mortality and constitutes 13% of overall, global neonatal mortality. In the high-income countries,

neonatal sepsis has a mortality ranging from 5 to 20% and causes major disability (or death) in up to 40% of all cases despite initiation of conventional treatment. Mortality rates up to 70% have been observed in some low- and middle-income countries. Sepsis is associated with serious long term morbidity such as cerebral palsy, cognitive and psychomotor delay, auditory and visual impairment, and bronchopulmonary dysplasia[17]. For early onset neonatal sepsis, the risk factors are multiple gestation, maternal intrapartum fever, maternal urinary tract infection or chorioamnionitis, prolonged labour, preterm rupture of the membrane (PROM), prolonged PROM > 18 h, and meconium aspiration syndrome[18].

CONCLUSION

In present study we had observed hyperbilirubinemia in patients received both ceftriaxone and cefotaxime. However cefotaxime received patients had shown slightly higher bilirubin levels as compared with ceftriaxone received patients. The data of present study suggest that neonates below 28 days treated with a short-term course of ceftriaxone for neonatal sepsis did not have a higher likelihood of developing hyperbilirubinemia compared with those receiving a short-term course of cefotaxime.

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