Antimicrobial drug utilization pattern in neonatal sepsis in a tertiary care hospital

Hardik V. Vaniya, Jitendra M. Agrawal, Nirav M. Patel, Hiren R. Trivedi, Jayesh D. Balat, Shilpa P. Jadav, Dinesh A. Chawda

Department of Pharmacology, Shri M.P. Shah Govt. Medical College, Jamnagar, Gujarat, India

Correspondence address: Dr. Hardik V. Vaniya, Department of Pharmacology, Shri M.P. Shah Govt. Medical College, Jamnagar, Gujarat, India. E-mail: hvaniya@gmail.com

DOI: 10.5455/jcer.201422

ABSTRACT

Objective: The objective of this study was to determine antimicrobial drug use in newborns at a tertiary care neonatal intensive care unit, to identify educational/research priorities in neonatal drug therapy. Materials and Methods: This prospective observational study included 713 patients of neonatal sepsis over a period of 18 months. Data like name, age, sex, birth weight, gestational age, antibiotics used were recorded in the previously prepared case record form. Results: Number of patients admitted in early neonatal period was 467 (65.5%) and number of patients admitted in late neonatal period was 246 (34.5%). The mean age of all patients being admitted in NICU was 6.23 ± 5.86 days. The majority of neonates (92.56%) were prescribed 2 to 5 antibiotics and 29.59% of neonates were prescribed 2 antibiotics. Average number of antibiotics of all patients being admitted was 3.74 ± 1.38. Most frequently used antibiotics in decreasing frequency were: Amikacin (97.19%), ampicillin + sulbactam (60.17%), vancomycin (57.64%), ceftazidime (38.71%), cefotaxime (34.22%), ciprofloxacin (26.23%), piperacillin + tazobactam (19.07%). 73% drugs were given by generic name and 53.33% drugs were prescribed from the essential drug list. Mean length of stay in NICU of all patients being admitted was 7.59 ± 5.66 days. Conclusion: The present study provides valuable insight about the overall pattern of antimicrobial drug use profile in patients of neonatal sepsis of a tertiary care hospital. It is intended to be a step in broader evaluation of safety and efficacy of drug prescription in neonatal sepsis patients.

Key words: Antibiotics, drug utilization, neonate, neonatal sepsis

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection and accompanied by bacteraemia in the first month of life.[1] Neonatal sepsis is the most common cause for increased morbidity and mortality among neonates in India, with incidence of approximately 4% in intramural live births.[2-3] The use of antibiotics is the standard of care in the treatment of paediatric patients with bacteraemia or sepsis. A variety of diagnostic tests (complete blood count, acute phase reactants) are commonly obtained, and antibiotics are continued or discontinued based on the results of the laboratory testing, degree of clinical suspicion and cultures.[4] As defined by the WHO, drug utilization is “The marketing, distribution, prescription and use of the drug in a society, with special emphasis on the resulting medical, social and economic consequences”. Very limited information is available regarding the extent and pattern of antibiotic drug use in perinatal period. Antimicrobial treatment of patients with sepsis is often predicated on the general principles of appropriate drug use and information extrapolated from other populations, rather than on evidence-based recommendations specific to these patients.[5] Currently, there are no universally accepted guidelines for the most appropriate empiric therapy in patients with sepsis.[6,7] Studies have documented the unnecessary, injudicious, or excessive use of antibiotics practices that have led to an alarming rise in antibiotics resistance, which poses a major threat to public health worldwide.
Some studies have demonstrated that resistance is directly associated with selection of inappropriate antimicrobials and increased patients’ mortality. Improved guidelines for antibiotic treatment in sepsis neonatorum from institutional etiology and microbial sensitivity should therefore be drawn and enforced.

The present study was aimed to explore and describe the current pattern of antimicrobials prescribing practices and utilization in neonates with sepsis, to know the clinical outcomes of neonates treated with various antibiotic regimens, to identify problems in drug utilization and suggest any measures if possible and to study the demographic parameters.

**MATERIALS AND METHODS**

A prospective observational study was carried out in NICU of paediatric department of Guru Gobindsingh hospital, Jamnagar. Prior permission of the Institutional Ethics Committee and Head of Paediatrics department was obtained for conducting the study. An appropriate study protocol and performa were developed and discussed with teaching staff members of the Pharmacology department and head of Paediatrics department

**Inclusion/Exclusion criteria:**

Neonates with confirmed or suspected cases of neonatal sepsis in patients aged 0-28 days, admitted to the NICU were included in the study. Neonates with other serious complications were excluded from the study.

**Collection of data:**

During the study period neonates (0 to 28 days of age) admitted with suspected diagnosis of early onset sepsis (0-7 days of age) and late onset sepsis (>7-28 days of age) were investigated. Written informed consent was obtained from their parents/guardians. Data of patients matching inclusion criteria were recorded. Admitted neonates who didn’t fulfill the above clinical criteria were excluded from the study. Total 713 cases were collected. The study was carried out for 18 months duration from January 2012 to July 2013. Data like name, age, sex, birth weight, gestational age, antibiotics used were recorded in the previously prepared case record form.

**RESULTS**

Number of male patients with neonatal sepsis admitted in NICU was 449 (62.97%) and number of female patients admitted in NICU was 264(37.03%). Number of patients admitted in early neonatal period was 467(65.5%) and number of patients admitted in late neonatal period was 246(34.5%). The mean ± SD of age of all patients being admitted in NICU was 6.23 ± 5.86 days. Number of pre-term, term and post term patients with neonatal sepsis was admitted in NICU was 246(34.5%), 461(64.66%) and 6(0.84%) respectively. Number of patients admitted in NICU with normal birth weight, low birth weight, very low birth weight and extremely low birth weight was 293(41.09%), 263(36.89%), 150(21.04%) and 7(0.98%) respectively.

Majority of neonates (92.56%) were prescribed 2 to 5 antibiotics) neonates were prescribed 2 antibiotics. Mean of number of antibiotics of all patients being admitted was 3.74 ± 1.38 [Table 1].

In our study, 8.98% of encounters have duration less than 3 days, 28.89% of encounters have duration in range of 3-5 days, 35.90% of encounters have duration in range of 6-8 days, 16.97% of encounters have duration of 9 to 14 days.

<table>
<thead>
<tr>
<th>No. of drugs</th>
<th>No. of encounters</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>211</td>
<td>29.59</td>
</tr>
<tr>
<td>3</td>
<td>88</td>
<td>12.34</td>
</tr>
<tr>
<td>4</td>
<td>157</td>
<td>22.02</td>
</tr>
<tr>
<td>5</td>
<td>204</td>
<td>28.61</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>7.57</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>0.70</td>
</tr>
<tr>
<td>Total</td>
<td>713</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Most commonly prescribed antibiotics were amikacin (97.19%), ampicillin + sulbactam (60.17%), vancomycin (57.64%), ceftazidime (38.71%), cefotaxime (34.22%), ciprofloxacin (26.23%) and piperacillin + tazobactam (19.07%). [Figure 1] Combinations of ampicillin and penicillin/cephalosporin were prescribed most commonly. Out of 15 drugs used, 8 drugs were prescribed from WHO Model List of Essential Medicines for children April 2013. So, 53.33% drugs were given by generic name and 27% were prescribed by brand name.

In our study, 8.98% of encounters have duration less than 3 days, 28.89% of encounters have duration in range of 3-5 days, 35.90% of encounters have duration in range of 6-8 days, 16.97% of encounters have duration of 9 to 14 days.
days and 9.4% of encounters have duration of more than 14 days. [Table 2] Mean ± SD of length of stay in NICU of all patients being admitted was 7.59 ± 5.66 days. Out of total 713 neonates 657(92.14%) neonates survived, 41(5.75%) neonates died and 15(2.10%) neonates were discharged against medical advice.

**DISCUSSION**

We have collected data of 713 neonates matching inclusion criteria admitted in neonatal intensive care unit (NICU) of Guru Gobindsingh Government Hospital, a tertiary care teaching urban hospital attached to Shri M. P. Shah Government Medical College, Jamnagar. Data of the patients like age, sex, birth weight, gestational age, antibiotics used were analyzed. There should be at least 600 encounters included in cross-sectional survey describing current treatment practices.[9] In our study sample size was 713.

Largest proportions of patients admitted in NICU were males (62.97%). This is in accordance with study done by Kumar P et al in which 57% of patients were male.[10] In our study number of patients admitted in NICU with normal birth weight, low birth weight, very low birth weight and extremely low birth weight was 41.09%, 36.89%, 21.04% and 0.98% respectively. It is quite evident that significantly large (58.91%) numbers of neonates were low birth weight. The mean birth weight in our study was 2053.08 ± 516.13 g. This is in accordance with study done by Uppal R et al.[11] Number of pre-term neonates admitted were 34.5%. This is in consonance with study done by Shrestha S et al in which number of pre-term neonates admitted were 33%.[12] It is clearly evident from the observations that low birth weight babies are more susceptible to these morbid conditions. In our study mean duration of stay in NICU for all patients being admitted was 7.59 ± 5.66 days. In previous studies, mean duration of stay in NICU was 17±16.4 days and 21.1±24.8 days respectively.[10,11]

The average number of antibiotics per encounter was 3.74 in our study with range of 1 to 7. The majority of neonates were prescribed 2 to 5 antibiotics. In a study done by Schellack N and Gous A 3.4 antibiotics were given to neonates on an average.[13] As severely ill patients are admitted in NICU and there are multiple causative organisms which are resistant to a number of drugs, use of multiple antibiotics is quite relevant. Most commonly prescribed antibiotics were amikacin (97.19%), ampicillin + sulbactam (60.17%), vancomycin (57.64%), ceftazidime (38.71%), cefotaxime (34.22%), ciprofloxacin (26.23%) and piperacillin +
tazobactam (19.07%). The results are in accordance with study conducted by Schellack N and Gous A.[13] The frequency and intensity of the use of these drugs appears to be directly related to the severity of the clinical status, and inversely related to birth weight and gestational age. Majority of the neonates received at least 2 antibiotics. Around 58% neonates were prescribed 4 or more than 4 antibiotics. As antibiotics were given as life saving measures it is difficult to focus on their irrationality.

It is generally established that combination therapy of penicillin/cephalosporin and aminoglycoside is effective. Due to emerging resistance to ampicillin, cephalosporin and aminoglycoside combination is recommended as first line therapy.[14] This is evident from our study as majority of patients were receiving amikacin and cefotaxime/cefazidime simultaneously. Number of neonates exposed to ampicillin and cefotaxime were highest in study done by Warrier et al.[15] From the previous studies done by Italian collaborative study group[15] and Lesko et al, it was concluded that penicillins and aminoglycosides were the most commonly used antibiotics.[16] Ampicillin and gentamicin were commonly prescribed antibiotics in a study done by Clark et al.[17]

In our study all neonates received drugs via parenteral route. This result complies with prospective study done by Chatterjee et al. who reported 92.1% of drugs were given by parenteral route.[18] Out of 15 drugs used 8 drugs were prescribed from WHO Model List of Essential Medicines for children, April 2013.[19] So, 53.33 % drugs were prescribed from the list. WHO has given a Fourth Model List of Essential Medicines for Children in April 2013 which is intended for use for children up to 12 years of age. In our study, 73% drugs were given by generic name and 27% were given by brand name. It is clearly evident that about 1/3rd of drugs were prescribed by brand name which unnecessarily adds to the cost of therapy. Increasing generic prescribing would rationalize the use and reduce the cost of drugs.[20]

Mortality rate during study period in our study was 5.75%. These results are in consonance with study done by Mhada TV et al in which it was 15%.[21]

CONCLUSION

To sum up, all though this study had a small sample size it gave us an overall pattern of antimicrobial drug use profile in patients of neonatal sepsis in a tertiary care NICU. This report is also intended to be a step in the broader evaluation of safety and efficacy of drug prescription in NICU. Neonates are a very vulnerable group due to immaturity of their body functions and great care needs to be taken to use the minimum number of drugs. Data reported here on the use of different antibiotics for neonates admitted for intensive care and should be helpful in establishing priority agendas for future drug studies in this population. Neonatal drug utilization is a dynamic process and the reported use of drugs changes over time. Our report should enable decisions to be made by those charged with creating specific priorities about which drugs should be studied specifically for neonates.

REFERENCES