



PRESCRIPTION PATTERN OF ANTIMICROBIAL DRUGS USED IN NEONATAL INTENSIVE CARE UNIT [NICU]: A SINGLE CENTRE, OBSERVATIONAL STUDY IN A TERTIARY CARE HOSPITAL.

Pharmacology

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KEYWORDS

INTRODUCTION

Neonates by definition are new-borns up to 28 days post-partum or 4 weeks post-partum and up to 4 weeks post expected date of delivery in case of Premature Infants. Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries hence early diagnosis and treatment with antimicrobials is must. Antimicrobials are the key drugs for treatment of sepsis and are among the most commonly prescribed drugs in neonatal intensive care unit (NICU) [1,2].

The use of antimicrobial agents, especially antimicrobials has become a routine practice for the treatment of neonatal illnesses. Also, there is practice of prescribing drugs off label and unlicensed and the absence of dose guidance in this population hence Neonates require more attention while prescribing antimicrobials to avoid the drug resistance, adverse drug reactions and drug-drug interactions [3].

Prescription pattern studies have been done previously in Neonatal intensive care unit (NICU) but not on Antimicrobial drugs. Since literature pertaining to prescription pattern studies of the antimicrobial drug use in NICU is lacking. We have designed the present study to bridge the gap in the knowledge in that aspect. The aim of this study is to provide the description of current prescribing practices in the NICU for antimicrobial drugs.

AIMS AND OBJECTIVES

Primary Objective:

To determine the Prescription pattern of Antimicrobial drugs used in Neonatal Intensive Care Unit [NICU] at a Tertiary Care Hospital.

Secondary Objectives: Includes The Following Parameters Studied As

- Number of Antimicrobial drugs prescribed per subject.
- Route of Antimicrobial drugs prescribed.
- Percentage of Antimicrobial drugs prescribed as Single drug, FDCs of Antimicrobials
- To find out percentage of Antimicrobial drugs prescribed by Generic name and Brand name.
- To assess if the prescription has any drug-drug interactions.
- Percentage of Antimicrobial drugs prescribed from Hospital Drug Formulary.

MATERIALS AND METHOD

The present study was an observational, single centre study conducted in the Neonatal Intensive Care Unit (NICU). Study was conducted for a period of 18 months from 1st April 2017 to 30th September 2018. Approval of the Institutional Ethics Committee was sought before commencing the study.

At our tertiary care hospital, the department of NICU runs separately besides Department of Paediatrics. All neonates visiting to this NICU getting admitted for any reason were screened on the day of discharge by observing their prescriptions and those who met the inclusion criteria were offered to participate in the study.

The Inclusion Criteria is as follows:

- All neonates of either sex receiving at least one anti-microbial drug.
- Subjects who's legally acceptable representative (LAR) are giving written informed consent.

1. Enrolment Data was collected as:

- General particulars included were subject initials, gender and age.
- The subject symptomatology and diagnosis.
- Drug details noted were dose, route, brand name or generic name (nomenclature) and availability on hospital formulary. The above data was recorded using a Case Record Form.[CRF]

2. Data Analysis: Parameters that were studied are:

- Antimicrobial drugs prescribed.
- Fixed Dose Combinations of antimicrobials (FDC) or Multi-drug antimicrobial treatment prescribed.
- Use of Brand name or Generic name in prescription.
- Off label analysis of Antimicrobial drugs prescription.
- Outcome of the antimicrobial treatment.
- To assess the drug-drug interactions, the prescription will be screened by Medscape drug interaction checker.
- Number of Antimicrobial drugs available on the hospital drug formulary.

Statistical Analysis:

The observations pertaining to baseline demographics and clinical profile of the subjects were expressed as frequency percentages. The age of subjects was expressed as percentages.

RESULTS

The present study was an Observational, Single centre study conducted in the Neonatal Intensive Care Unit (NICU) of a Tertiary care hospital. 294 subjects who fulfilled the inclusion criteria were enrolled in the study. The observations made during the eighteen months study period are presented in this section.

1| Demographic Details Of The Subjects

A| Gender of the subjects: Out of the 294 subjects encountered during the study period, 50% subjects (147) were males and 47% (139) subjects were females while 3% (8) were having ambiguous genitalia so the gender was undetermined. Male to Female ratio in our study was 1.05: 1 (M: F)

B| Birth weight wise distribution of subjects: Mean birth weight was found in our study was 1690 gm. Out of 294 studied subjects it was found out to be Maximum percentage of subjects were falling under VLBW (Very low birth weight) group i.e. 128 (44%). Followed by Group LBW (Low birth weight) group i.e. 114 (39%), then group Normal birth weight i.e. 30 (10%), followed by ELBW (Extremely low birth weight) i.e. 19 (6%), and last group consisting of 3 (1%) overweight babies.

2| Clinical Profile Of The Subjects

A| Diagnosis of subjects: Of the all 294 subjects encountered in NICU maximum diagnosed cases that is 189 (64.30%) of RDS (Respiratory Distress Syndrome) followed by 53 (18%) cases of Sepsis followed by 13 (4.4%) cases of Hypoglycaemia, Rest of the cases also include diagnosis was Prematurity Apnoea 8 (2.7%), Meningitis 5 (1.7%). Rest of all other cases were of Congenital Syphilis, Dengue Prophylaxis, Fever, HIV Prophylaxis, Home Delivery Prophylaxis, Hydrocephalus, Hypothermia, Meconium aspiration, Pneumothorax, Polycythaemia, Premature rupture of membranes prophylaxis, Prophylaxis of Fall from height, Septic arthritis, T.B. prophylaxis, Transient tachypnoea.

B| Antimicrobials prescribed per subject: Of 294 subjects total no. of

prescriptions of antimicrobials were 757. Maximum no. of subjects 188 (63.9%) received 2 Antimicrobials per prescription, followed by 32 (3%) received 3 antimicrobials per patient, followed by 29 (9.9%) then 17 (5.8%) received single drug prescription, while 16 (5.4%) received 5 antimicrobials per prescription, while 12 (4.1%) received more [$>$] than 5 antimicrobial drugs per prescription.

3| Pattern Of Drug Use

A| Type of Antimicrobial Agents Prescribed: Out of the 294 subjects we studied Amikacin was the most commonly prescribed in 262 (89.1%) prescriptions, Amoxycillin plus Clavulanic Acid combination is given Second most Commonly in 227 (77.2%) prescriptions, in 80 (27.2%) prescriptions Meropenem was prescribed, Colistin was prescribed in 63 (21%) of prescriptions, Piperacillin plus Tazobactam combination was given in around 45 (15.3%) prescriptions, about 32 (10.9%) prescriptions were found to be prescribed for Linezolid and 12 (4%) prescriptions had Ampicillin plus Sulbactam combination prescribed, Vancomycin was prescribed in 10 (3.4%) and Fluconazole in 9 (3%) cases was prescribed. Rest of the prescriptions included drugs like imipenem, Isoniazid, Netilmicin, Benzyl Penicillin G, Ciprofloxacin, Cefotaxime, Nevirapine, Metronidazole, Ofloxacin prescribed in the range of 0.003% – 0.01%.

B| Prescription by Brand/ Generic Name: Out of 757 antimicrobials prescribed, 290 (38%) were prescribed by Brand name and 467 (62%) were prescribed by Generic name. Most common Brand name used was Augmentin for (Amoxycillin + Clavulanic acid) combination followed by Amoxiclav another Brand name for same, following these two next most common was Piptaz for (Piperacillin + tazobactam) and least common was Ampisulbactam (Ampicillin + Sulbactam).

Table 1: Antimicrobials prescribed by Brand name & Generic name and as percentage [%]

Brand name	290	38%
Generic name	467	62%

C| Doses prescribed for each antimicrobial drug: In present study we observed that recommended doses of antimicrobial drugs were given in 100% of the encounters. No prescription was found to be not given according to the standard recommended doses of these drugs.

D| Route of Antimicrobials prescribed: The antimicrobials were in almost all 291 prescriptions prescribed exclusively by intravenous route. Only exception to that were of 3 cases where the oral route was used in along with intravenous route for use of the agents for prevention of Tuberculosis from mother to neonate.

E| Number of Antimicrobials prescribed per subject: In NICU department, total 294 subjects were encountered. Total 757 drugs were prescribed to these subjects. Hence on an average 2.57 Antimicrobials were accounted per prescription.

Table 2: Average number of antimicrobials prescribed per subject [n = 757]

Total number of Subjects	294
Total number of antimicrobials prescribed	757
Average no. of antimicrobials per Subject	2.57

F| No. of Antimicrobials Prescribed as FDCs: Out of 757 antimicrobial drugs prescribed to the subjects 289 were prescribed as FDCs. Most Commonly prescribed FDC is Amoxicillin + Clavulanic Acid combination given in 228 (78.9%) subject prescription, followed by Piperacillin + Tazobactam prescribed in 46 (15.9%) cases encountered, followed by Ampicillin + Sulbactam was given in 12 (4.2%) subjects and least commonly prescribed was Imipenem + Cilastatin which was prescribed in only 3 (1%) subjects.

Table 3: Number of antimicrobials prescribed as FDCs [n = 289] and as percentage [%]

Amoxicillin + Clavulanic acid	228	78.9 %
Piperacillin + Tazobactam	46	15.9 %
Ampicillin + Sulbactam	12	4.2 %
Imipenem + Cilastatin	3	1 %

4| Prescription from Hospital Formulary

Almost all the drugs were prescribed from the hospital formulary. Out of the 757 antimicrobial drugs prescribed only 1 Antimicrobial agent Inj. Nevirapine was found to be prescribed outside from Pharmacy. Rest 756 antimicrobial agents were prescribed from the hospital drug formulary.

5| Prescriptions involving Drug – Drug Interaction

Out of 294 Cases we encountered in our study no single prescription was found to contain any potential Drug-Drug interactions.

DISCUSSION

The present study was conducted in Neonatal Intensive Care Unit (NICU) of a Tertiary care teaching hospital. This study was carried out to observe the prescription pattern of Antimicrobial drugs and assess their use in Neonates. Prescription data was collected from 294 subjects over a period of 12 months

50% of the subjects those visited to the Neonatal Intensive Care Unit (NICU) in our Neonatology department were Males. While Female subjects were 47% and remaining 3% subjects the gender was undetermined. Male to Female ratio in study was 1.05 : 1. Our study results correlates well with the findings conducted in Neonatology department by Ali SR, Ahmed S, Lohana H in Pakistan, by Demisse AG, Alemu F, Gizaw MA, Tigabu Z in Ethiopia, by Hoque M, Haaq S, Islam R. in South Africa, by Anand K et al in uttarakhand India and Hardik V vaniya et al from India, etc that have all been shown to have a male preponderance towards the admission in Neonatal Intensive care unit. [4]. In some studies, this discrepancy between birth rate of boys and girls is interpreted as a natural selection response to differential survival prospects [6]. Additionally, cultural and social factors could contribute to male babies getting more attention by parents than females.

In our study the percentage of LBW (Low birth weight) neonates were 39% which was slightly higher when correlated with Demisse AG, Alemu F, Gizaw MA, Tigabu Z in Ethiopia, Ali SR, Ahmed S, Lohana H in Pakistan, Hoque M, Haaq S, Islam R. in South Africa, by Anand K et al in Uttarakhand India, by Tekleab AM, Amaru GM, Tefera YA in Ethiopia and by Hardik V Vaniya et al from India [54-59]. The incidences found in these studies ranged from 29% to 37.7%. Although there are numerous factors associated with LBW and prematurity, the major contributors are low socioeconomic status, maternal infection, maternal undernutrition, and anaemia [7].

Of the all 294 subjects encountered in NICU most common cases that is 64.30% were of RDS (Respiratory Distress Syndrome) followed by 18% cases of Sepsis followed by 4.4% cases of Hypoglycaemia. Inese Sviestinaa, Dzintars Mozgisc in Latvia suggest similar findings that Lower respiratory tract infections (LRTI) were most common in Neonates. These results are in consistent with studies done by Suryawanshi S, Pandit V, Suryawanshi P, Panditrao A. in Pune, India. These findings were higher as compared to the studies performed elsewhere; for instance, neonatal infection was 20.3% in Pakistan and 21% in South African studies [4,5].

Of 294 subjects total no. of prescriptions of antimicrobials were 757. Majority of subjects that is 69.7% received either 1 to 2 Antimicrobials per prescription, while 4.1% received more than 5 antimicrobials per prescription. These results differ slightly with the results of studies done by Suryawanshi S, Pandit V, Suryawanshi P, Panditrao A. in Pune, India where 55.9% of subjects received 1 to 2 antimicrobials, while 6.7% received more than 5 antimicrobials. However, both the results correlates with study done by Hardik V. Vaniya et al in India where majority of neonates had received 2 anti-microbial agents.

In our study among antimicrobials, Amikacin, Amoxycillin plus Clavulanic Acid and Meropenem were the FDC and drugs most often prescribed. In our study Amikacin was given in 89.1% of subjects followed by Amoxicillin plus Clavulanic acid in 77.2% subjects. These results correlates with study done by Suryawanshi S, Pandit V, Suryawanshi P, Panditrao A. in Pune, India where Amikacin was the largest prescribed drug. Amoxicillin belongs to group Aminoglycosides. The second most common drug differ being a cephalosporin rather than Amoxicillin + Clavulanic acid as in our study but both belongs to Beta lactam group of drugs in our study. Another study done by Haftey Berhane Mezagbe, Blen Tadasse, Befikadu Legesse in northern Ethiopia administered Ceftriaxone, Gentamycin, Amikacin most commonly suggesting of use of Beta lactam drugs and aminoglycosides are the most commonly used.

Out of 757 antimicrobials prescribed, in our study 38% were prescribed by Brand name and 62% prescribed by Generic name. Most common Brand name used was Augmentin for (Amoxycillin + Clavulanic acid). The World Health Organization (WHO)

recommends the use of a generic, non-proprietary name [68]. Several factors contribute to the persistent use of brand name medications, including scepticism toward generic drugs [8].

In our study it has been seen that the antimicrobials in 291/294 subjects prescribed exclusively by intravenous route that is 99%. These findings are in consistent with study done by Inese Sviestinaa, Dzintars Mozgisc in Latvia where intravenous route was used in majority 85% patients. There were 3 cases in which the oral route was used in along with intravenous route. The oral route used in our study was for prophylaxis of Tuberculosis infection transmission from infected mother to her neonate. These findings correlate well with study done by Linakis MW et al. Intravenous administration is the preferred route of administration in severely ill neonates.

Out of 757 antimicrobial drugs given to 294 subjects, 289 were prescribed as FDCs. Most Commonly prescribed FDC was (Amoxicillin + Clavulanic Acid) combination given in 78.9% subject prescription and least commonly prescribed was (Imipenem + Cilastatin) which was prescribed in only 1% subjects. These findings well correlate with studies done by Hardik V. Vaniya et al in India, Ashraf H, Handa S, Khan NA in Moradabad in India showing similar results with one of the most commonly used combination FDC being (Amoxicillin + Clavulanic Acid).

Almost all the drugs were prescribed from the hospital drug formulary. Out of the 757 antimicrobial drugs prescribed only 1 Antimicrobial agent i.e. Inj. Nevirapine was found to be prescribed from outside the Hospital pharmacy. Rest 756 antimicrobial agents were prescribed from the hospital drug formulary. This can be considered as a good practise as the price difference between both is significant which is important in the developing countries like India since the drugs available from hospital drug formulary are economical than purchased from outside pharmacy [9].

SUMMARY AND CONCLUSION

The present observational study assessed the prescription pattern of the antimicrobial drugs in NICU (Neonatal Intensive Care Unit) of a tertiary care hospital. We encountered 757 antimicrobial drugs prescribed to 294 subjects. Majority of patients were Male neonates. Majority of them fall in Low Birth Weight (LBW) category. Respiratory Distress Syndrome (RDS) followed by Sepsis were the cause of majority of admissions to NICU. Amikacin followed by Amoxycillin plus clavulanic acid were the most commonly prescribed antimicrobial drugs. Trend of prescribing more drugs with Generic name than that of Brand name was notified in our study. Standard treatment guidelines for the dose and route of prescription were followed for all of the antimicrobial drugs. Number of antimicrobials prescribed per patient was 2.57 which was well within recommended limit. We observed that almost all of the antimicrobial agents prescribed were from hospital drug formulary with exception of only one agent which was a sign of good practice.

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