Original Research Article

Drug utilization pattern in a neonatal intensive care unit at tertiary care hospital attached to a medical college in Southern Karnataka, India

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ABSTRACT

Background: Neonates and in particular preterm neonates belongs to the most vulnerable population. A neonatal intensive Care Unit (NICU) is a highly specialized unit that provides high quality skilled care to critically ill new born, premature or low birth weight babies. Apart from facilities for continuous clinical and biochemical monitoring, NICU management involves the use of wide range of medications. Irrational prescription of drug is common in clinical practice, important reason being lack of knowledge about drug prescription. Developing countries have limited funds available for health care and drugs so it becomes very important to prescribe drugs rationally. The present study was done to find out the drug utilization pattern and improve the rational use which aids in the improvement of neonatal care.

Methods: The study was retrospective study in NICU of tertiary care hospital attached to MIMS, Mandya for a duration of 6 months. Data extraction sheet were used to collect the information regarding demographic details, maternal and delivery details, indication for admission, final diagnosis and medications administered. Data collected were evaluated for the category of prescribed, based on World Health Organization Anatomical Therapeutic Committee (WHO classification system and were analyzed using SPSS. WHO drug utilization core indicators were also evaluated.

Results: Among 400 neonates admitted in NICU during the study period, 53.7% were males and 46.2% were females. There were 29.7% preterm born neonates. The maximum number of neonates were admitted in early neonatal period (87.25%). Neonatal sepsis (37.9%) and Birth asphyxia (11.6%) were the most common indications for admission. The total number of drugs prescribed was 1428 and the average number of drugs per neonate was 3.57. Preterm (<37weeks) and low birth weight (<2.5Kg) were exposed to significantly higher number of drugs. The most frequently prescribed therapeutic class of drugs was anti-infectives (60.36%), followed by drugs of central nervous system (7.84%). Among the anti-infectives, the most commonly prescribed drugs were Ampicillin (59%), followed by gentamycin (42.5%). High end antibiotics like carbapenems, colistin’s and linezolid were used in less than 5% of cases.

Conclusions: Drug use in neonates should be minimal and focus on the importance of therapeutic treatment guidelines establishment in hospital to control the over usage of antibiotics.

Keywords: Drug utilization, Neonates, Neonatal intensive care unit, Prescription, Rational drug use

INTRODUCTION

A neonatal intensive care unit (NICU) is a highly specialized unit that provides high quality skilled care to critically ill newborn infants, premature and low birth weight infants. Apart from facilities for continuous clinical and biochemical monitoring, neonatal intensive care unit involves use of a wide range of medications.¹
Very less information is available on pharmacokinetics and pharmacodynamics of drugs in newborn and infants because they are discouraged or not included in drug trials.2

Neonates and in particular preterm neonates belong to the most vulnerable population. Organ immaturity and consequently difficulties adapting to extra uterine life are reasons for premature babies being often multi morbid and in need of intensive medical care. Preterm babies initially have to survive whereas term neonates are often admitted for peri or postnatal complications and congenital diseases. Hence, they are exposed to high number of drugs.3

A growing number of pharmaceutical products are available in world market and there has been an increase both in the consumption of the drugs and in expenditure on them. Irrational prescription of drug is of common in clinical practice, important reason being lack of knowledge about drug and unethical drug promotion. Drug utilization studies and monitoring of prescriptions could identify the associated problems and provide feedback to prescribers.4

There are studies which have documented the injudicious, unnecessary and excessive use of antibiotics practices that have led to alarming rise in antibiotic resistance, which is a major threat to public health. Some studies have shown that resistance is directly associated with selection of inappropriate antimicrobials. Improved guidelines for antibiotic use in neonatal sepsis from microbial etiology and sensitivity should be drawn and enforced.5

Developing countries have limited fund available for health care and drugs, so it becomes very important to prescribe drugs rationally so that the available funds can meet the need of medicine. We have seen most of the drugs utilization studies have been carried out in adult patients with only a few being reported from neonatal population and there were no universally accepted and standardized guidelines regarding the rational prescription in neonatal intensive care.6 This study gives an insight of drug use in newborn infants admitted in neonatal intensive care unit (NICU) attached to a tertiary care hospital. The aim of the study was to assess the drug utilization pattern in neonatal intensive care unit (NICU).

METHODS

This was a retrospective study conducted over a period of 6 months (May14 to Oct 316 2017) in a level III NICU attached to medical college in southern India. All inborn and out born (babies delivered outside medical college) newborn admitted to NICU, during the study period were included in the study. Case sheets, investigations report and treatment given to all neonates admitted during the study period were reviewed after approval from institutional ethics committee. Data extraction sheet was used to collect the data regarding demographic details, maternal and delivery details, indication for admission, final diagnosis and medications administered. All drugs given to the neonates were recorded except intravenous fluids, nutritional supplements, vaccines, topical medications, oxygen and blood products. Drugs prescribed were categorized based on WHO-ATC classification system; a pharmaceutical coding system which divides drugs into different groups according to the organ or system on which they act or their therapeutic and chemical characteristics.

Statistical analysis

Recorded data was entered in Microsoft excel sheet and analysed using SPSS-20. Results were expressed in terms of descriptive statistics

RESULTS

Demographic characteristics

The study includes a total of 400 neonates, comprising 215(53.75%) male and 185 (46.25%) female. Among the 400 admitted babies in NICU, 341(85.25%) neonates survived.

Table 1: Morbidity pattern observed in neonatal intensive care unit.

| Morbid condition                                      | Frequency |
|------------------------------------------------------|-----------|
| Neonatal sepsis                                      | 360       |
| Respiratory distress syndrome                        | 87        |
| Birth asphyxia                                       | 110       |
| Neonatal jaundice                                    | 97        |
| Small for gestational age                            | 47        |
| Low birth weight (1-2.49kg)                          | 8         |
| Prematurity (28-<37 weeks)                           | 69        |
| Transient tachypnoea of new-born                     | 5         |
| Congenital pneumonia                                 | 15        |
| Neonatal aspiration of meconium                      | 62        |
| Haemolytic disease of meconium                       | 10        |
| Convulsion of new-born                               | 8         |
| Congenital malformation                              | 43        |
| Miscellaneous <0.5%                                  | 10        |
| Any other diagnosis                                  | 20        |

The majority of neonates were term (>37 weeks) accounting for 70% followed by preterm 28.5% and 1.25% were extreme preterm. The group maximum exposed to the drugs are neonates weighing more 2.5 kilograms which constitutes 45.58% of the total prescription followed by weight group of 2-2.5 kilogram constituting 23.17%, 1.5-2kg weight group constitutes 16.80%, similarly 8.6% and 5.7% in 1-1.5kilograms and less than 1kilogram respectively.

The spectrum of morbidity pattern which is depicted in Table 1, included neonatal sepsis (37%), birth asphyxia
(11.6%), neonatal jaundice (10.2%), respiratory distress syndrome (9.1%), prematurity, neonatal aspiration of meconium, small for gestation, neonatal convulsions, congenital malformation etc. Out of 400 neonates admitted during the study period, 59 (14.75%) died and the common condition associated with mortality were moderate to severe birth asphyxia, followed by respiratory distress syndrome and neonatal sepsis.

**Medication/prescription descriptive**

According to WHO-ATC (World health organization-anatomical therapeutic committee) classification system, 60.36% (n-862) of drugs were anti-infectives for systemic use, followed by 7.84% (n-112) of drugs for nervous system, 4.83% (n-69) of drugs for alimentary tract, 3.15% of drugs for respiratory system and 2.8% of drugs for cardiovascular system as depicted in Table 2.

Among the Anti-infectives, the drug most often prescribed is ampicillin accounting for 59% (239) followed by gentamycin of 42.5% (170), cefotaxime 19.2% (77), Amikacin 18.2% (73), ciprofloxacin, Piperacillin-Tazobactum, Meropenem, Fluconazole.

Similarly, among drugs used for nervous system most frequently prescribed drugs were Phenobarbinte accounting for 17.5% followed by Midazolam 17.5% and Phenytoin 5%.

In respiratory drugs, Salbutamol respiratory solution, Aminophylline and Caffeine citrate and in drugs used for alimentary canal and cardiovascular system included ranitidine, dopamine, dobutamine and furesimide. Table 3 depicts most frequently prescribed drugs in neonatal intensive care unit.

| Table 2: Drug use according to WHO-ATC classification system. |
|---------------------------------------------------------------|
| **Total medicines** | **WHO-ATC category** |
| 1428 | Anti-infective for systemic use (%) | Respiratory system | Nervous system | Alimentary tract | Cardiovascular system | Other system and oral supplements |
| 862 (60.36%) | 45 (3.15%) | 112 (7.84%) | 69 (4.83%) | 40 (2.8%) | 300 (21.0008%) |

| Table 3: Most frequently prescribed drugs in neonatal intensive care unit. |
|---------------------------------------------------------------|
| **Group** | **Name of drugs** | **Number of neonates receiving drugs (n=400)** |
| Anti-infectives | Ampicillin | 236 (71.02%) |
| | Gentamycin | 170 (42.5%) |
| | Cefotaxime | 77 (19.2%) |
| | Amikacin | 73 (18.2%) |
| | Ciprofloxacin | 62 (15.5%) |
| | Piperacillin-tazobactum | 38 (9.5%) |
| | Meropenem | 31 (7.7%) |
| | Fluconazole | 21 (5.25%) |
| Respiratory system | Aminophylline | 45 (11.25%) |
| | Caffeine citrate | 32 (8%) |
| | Salbutamol respiratory solutions | 20 (5%) |
| Nervous system | Midazolam | 55 (13.75%) |
| | Phenobarbitone | 70 (17.5%) |
| | Phenytoin | 20 (5%) |
| Alimentary tract | Ranitine | 43 (10.75%) |
| Cardiovascular system | Dopamine | 32 (8%) |
| | Dobutamine | 20 (5%) |
| | Furosemide | 30 (7.5%) |

The less frequently used drugs which constitutes less than 5% in total prescription has been included in Table 4. It includes high end antibiotics like Linezolid, Imipenem, Vancomycin, Netilmicyn, surfactant, Ipratropium bromide, Levetiracetam, Sildenafil, Digoxin etc.

A total of 1428 drugs were prescribed for 400 study population during the period of hospital stay.

The average number of drugs administered per neonate were 3.57 (Table 5).
A total of 1428 drugs were prescribed for 400 study population during the period of hospital stay. The average number of drugs administered per neonate was 3.57 (Table 5).

### Table 4: Drugs prescribed with a frequency of less than 5%.

| Groups                     | Drug used      | Frequency |
|----------------------------|----------------|-----------|
| Anti-infectives            | Linezolid      | 19 (4.75%)|
|                            | Imipenem       | 19 (4.75%)|
|                            | Vancomycin     | 18 (4.5%) |
|                            | Natilmicyn     | 16 (4%)   |
|                            | Colistin       | 12 (3%)   |
| Respiratory system         | Surfactant     | 19 (4.75%)|
|                            | Ipratropium bromide | 14 (3.5%) |
| Nervous system             | Levetiracetam  | 18 (4.5%) |
| Alimentary tract and metabolism | Metronidazole | 18 (4.5%) |
| Cardiovascular system      | Sildenafil      | 18 (4.5%) |
|                            | Adrenaline     | 17 (4.25%)|
|                            | Digoxin        | 2 (0.5%)  |

### Table 5: WHO core indicators.

| WHO core indicators | % of patients |
|---------------------|---------------|
| Total number of prescripts in items | 1428 |
| Average number of drugs per neonates | 3.57 |
| Prescription with antibiotics | 60.3 |
| Prescription with injections | 86.97 |
| Percentage of drug prescribed by generic name | 78 |
| Percentage of drug prescribed from EML 2015 (children) | 71.2 |
| Percentage of drug prescribed from NLEMI 2011 | 74 |

### DISCUSSION

In present study, pattern of total 1428 drugs prescribed over a period of 6 month for a total of 400 newborns admitted in Neonatal Intensive Care Unit were assessed. Out of 400 neonates admitted in NICU, 53.75% were male which is in consistent with study done by Brijal et al, and Choure et al, in which 60.92% and 54.3% were male neonates respectively. This shows that the gender discrimination in term of access to public health care and need for immediate awareness against gender discrimination in early stage of life.

In present study 87.25% of neonates were admitted in early neonatal period. This is similar to a study by Vaghela JP et al, in patients admitted in early neonatal period were 86.3%. Neonates are hostile to the influences of several conditions like asphyxia infection complications of premature birth in early neonatal period which demands special attention.

Majority of neonates admitted in NICU were for neonatal sepsis (37.9%) which is comparable to study done by Brijal et al, where they found this as a major cause for death in neonates.7 Few strategies given by WHO to assess the drug utilization and establish the certain baseline in management of disease or selection of drugs observed and illustrated in Table 5 as WHO-core indicators. It shows that average number of drugs per neonate as 3.57 which is similar to a study by Choure et al, and yet another reported average number of drugs per encounter as 4.8. Of the total 1428 drugs prescribed during the study period, majority of prescriptions were accounted by antibiotics (60.36%), followed by CNS drugs (7.84%) and alimentary system (4.83%) which is comparable to study done Neubert et al, where 90% of the drugs prescribed were anti-infectives followed by nervous system drugs and respiratory drugs. The total encounter of antibiotic were 862 which accounts 60.36% of total drug prescription which is similar to a study done by Brijal et al, where 65.07% of neonates were exposed to antibiotics and yet another study showed 64.5% of antibiotic exposure. Higher incidence of antibiotic exposure in NICU could be due to the common practice of instituting empirical therapy and can be attributed to higher incidence of infections due to poor sanitation or lower rate of literacy.

In present study most commonly prescribed antibiotics were Ampicillin (59%), gentamycin (42.5%), cefotaxime (19.2%) and amikacin(18.2%) which is comparable to another study in India by Vaghela et al. Similar findings were observed in other studies in which penicillins and aminoglycosides were commonly prescribed. And other less frequently used drugs which constitutes less than 5% in total prescription included linezolid, vancomycin, surfactant, levetiracetam, sildenafil, digoxin etc.

Drug utilization studies helps in framing hospital formulary and standard treatment guidelines as per the diagnosis and also helpful in rational use of drugs making treatment cost effective and beneficial to patients and to the countries with poorly funded health system. The strength of present study is that, it is a step further in the broader evaluation of safety and efficacy of drug prescription in NICU. Sample size, administrative data for analysis is our limitation as this type of study should be broadly studied and present study is confined to only one teaching hospital.

### CONCLUSION

To conclude, periodic survey should be conducted over the time to facilitate rational usage of drugs in neonates because of their immature body functions and to avoid adverse drug reactions. Most importantly the therapeutic treatment guidelines should be established to control the over usage of antibiotics and to rationalize the drug usage.
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