PATTERN OF DISEASE AND DRUG USE AMONG NEONATES: RESULTS FROM A NEONATAL INTENSIVE CARE UNIT IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

BACKGROUND

Evidence-based pharmacological treatment is inadequate among neonates due to difficulties in performing clinical trials. Also, medication errors in neonates are frequent because of their unique pharmacokinetics. The aim of this study was to analyse the pattern of disease and prescription pattern using applicable WHO indicators in neonatal intensive care unit (NICU) of a tertiary-care hospital.

METHODS

Prescriptions of neonates admitted to NICU over a period of 4 months were studied prospectively. Rational drug use, drug interactions, off label use and adverse effects were taken into consideration. Drug prescription parameters were analysed in relation to birth weight, gestational age at birth and co-morbid conditions.

RESULTS

Prescriptions of 622 neonates were analysed. The total number of drugs prescribed was 2352. The average number of drugs per prescription was 4.9. Respiratory distress and neonatal jaundice were the most common causes for admission. 79.7% of the drugs were prescribed with generic name. 52% of the total drugs prescribed were antimicrobials.

CONCLUSIONS

Prescription of maximum drugs was by their generic name and was dispensed free of cost to the patients from the hospital pharmacy. Almost all the drugs prescribed were present in the NLEM, India 2017 and off-label antibiotics use were common. The study helped in assessing drug needs of neonates, rational usage and also guided the administration in drug procurement.

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BACKGROUND

Neonates have unique pharmacokinetics and pharmacodynamics due to immaturity of various organ functions such as kidney, liver and gastric motility.[1] Lack of data makes selection of appropriate drug-dose further complicated in high-risk neonates such as premature, low birth weight (LBW) or critically ill.[2] Accordingly, caution is required while exposing such neonates to various medications. Evidence-based pharmacological treatment is inadequate among neonates due to difficulties in performing clinical trials in this population.[3]

Drug utilization studies are a part of the medical audit and are useful to monitor and evaluate prescribing practices and help to provide necessary suggestions and modification to make drug use most effective.[4] Data on the prescription pattern helps in assessment of the risk-benefit profile of drugs, nature of the health care delivery system.[5] Most of the studies published were performed in developed countries and also focused on single active substances and their status in terms of unauthorized or off-label use.[6] Few studies on drug-related toxicity concentrated especially on renal damage.[6,7] The observational data collected from multiple centers is varied because of potential heterogeneity of patients.[8] We have limited data that investigates the drug prescription trends in our neonatal population especially in Kadapa, Andhra Pradesh. The present study aims to understand the pattern of disease, prescription pattern, safety of drugs in relation to toxicity and possible drug interactions. The study shall be helpful to understand the disease pattern and drug needs of neonates in Kadapa and guide the healthcare providers.

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METHODS

A prospective observational study was conducted in NICU of Government medical college hospital, Kadapa with prior permission from institutional ethics committee. The consent of parents of neonate was obtained. All neonates admitted to NICU and receiving more than one medication were included in the study. Neonates admitted due to mother illness and those receiving only vaccines, blood and blood products, electrolyte solutions, and phototherapy, were excluded from the study. Medical records of all neonates admitted in NICU over a period of 4 months were analysed. A total of 622 case sheets were scrutinized prospectively.

They were divided into 4 groups based on birth weight. Analysis included drug exposure, duration of therapies, and co-administration of drugs with potential adverse effects. Descriptive analysis of drug use was performed and included: exposure, defined as the number of unique active substances reported for each neonate, total exposure for a particular therapeutic class which was calculated based on no. of doses of a particular drug class in a course and no. of courses. The World Health Organization (WHO) core indicators for drug utilization were also evaluated.[4,9]

RESULTS

During the study period the prescriptions of 622 neonates were analysed. The male babies outnumbered females in a ratio of 60:40. (Figure 1) 21% of cases were born preterm at a gestational age of <34 weeks. With regards to birth weight, the results show that only 2% of the cases are born with ELBW <1000 grams. Birth asphyxia, respiratory distress and neonatal jaundice were the leading causes for admission followed by hyaline membrane disease and septicaemia. The other causes were meconium aspiration syndrome, hypoxic ischemic encephalopathy and congenital malformations. (Figure 2, 3) (Table 1)

In our study, the most common group of drugs as per Anatomical therapeutic class were antibacterial drugs (47%), NSAIDS (21%), and respiratory drugs (9.4%). Among diuretics, furosemide and spironolactone were used commonly. (Table 2) Surfactant was used in most of the preterm cases by Insure technique. The most commonly used antiepileptic drug was phenobarbitone followed by phenytoin and midazolam. All the neonates were uniformly advised calcium, vitamin D and multivitamin supplements at discharge. Fluconazole was used frequently in preterm and ELBW babies not responding to antibacterial drugs. Amikacin with Cefotaxime was the most commonly used antibacterial combination. In cases of septicaemia the other drugs used include Piperacillin with tazobactam, Vancomycin, Meropenem and linezolid.

In our study, overall off-label use was 14.2%, while 36% neonates received at least one off-label drug. Majority were avoidable off label prescriptions in terms of dose, duration and frequency. There was no use of unlicensed preparations. Highest numbers of off label prescriptions were antimicrobials, antiepileptics followed by anti-emetics.

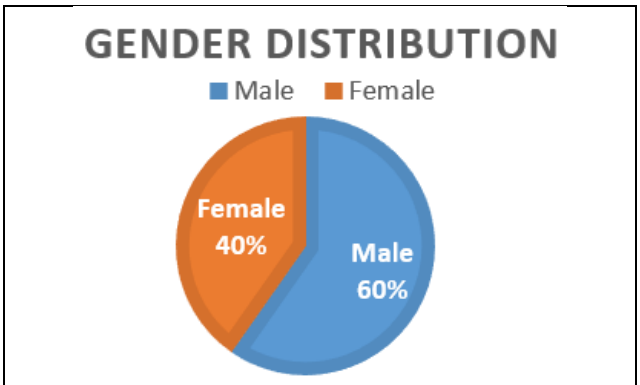

Figure 1. Gender Distribution

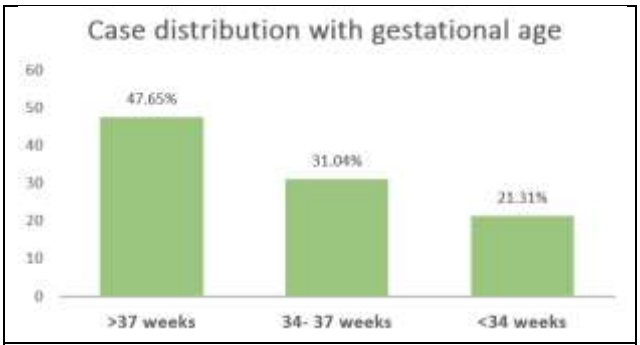

Figure 2. Case Distribution in Relation to Gestational Age

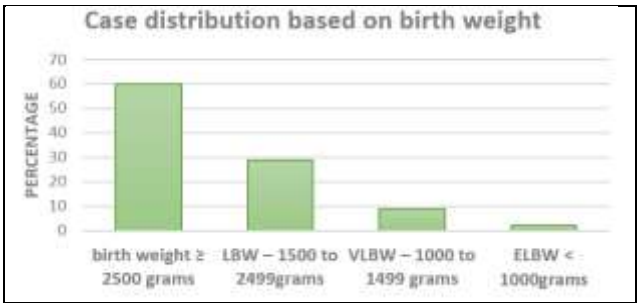

Figure 3. Case Distribution Based on Birth Weight

Sl. No.	Name of Disease/ Illness	Number of Cases	Percentage
1.	Respiratory distress	151	24.27
2.	Moderate –severe birth asphyxia	74	11.89
3.	Neonatal jaundice	138	22.18
4.	Hyaline membrane disease	78	12.54
5.	Sepsis/pneumonia/meningitis	81	13.02
6.	Meconium aspiration syndrome	29	4.66
7.	HIE- hypoxic ischemic encephalopathy	14	2.25
8.	Major congenital malformation	9	1.44
9.	Congenital heart disease	11	1.76
10.	Hypoglycaemia	5	0.8
11.	Others	32	5.14

Table 1. Disease Pattern

Drug Group	N	(%)	Commonly Used Drugs
Respiratory System	221	9.41	Surfactant, aminophylline
Gastrointestinal System	51	2.16	Ranitidine, domperidone, ondansetron
Cardiovascular System	50	2.10	Digoxin, dopamine
Diuretics	53	2.27	Furosemide, spironolactone
Antibacterials	1110	47.2	List enclosed separately
Antifungals	101	4.2	Fluconazole
NSAIDS	382	16.24	Paracetamol, indomethacin
Antiepileptics	87	3.7	Phenobarbitone, phenytoin
Topical Preparations	153	6.52	Mupirocin, tobramycin
Calcium Gluconate	64	2.7	Birth asphyxia, preterm
Others	80	3.46	

Table 2. Therapeutic Class of Drugs Prescribed

Drugs Usage Pattern (WHO)	Number/ Percentage
Average no. of drugs per prescription	4.9
Percentage of drugs prescribed from EDL	96
Percentage of drugs prescribed by generic name	92
Percentage of drugs prescribed from hospital pharmacy	98
Percentage of prescriptions containing an injection	100

Table 3. WHO Indicators

Sl. No.	Name of Antimicrobial	Number	Percentage
1.	Cefotaxime	288	25.9
2.	Amikacin	422	38.1
3.	Piperacillin with tazobactam	88	8.5
4.	Linezolid	34	3.2
5.	Metronidazole	76	6.8
6.	Meropenem	48	4.2
7.	Vancomycin	40	3.6
8.	Ampicillin	42	3.7
9.	Immunoglobulins	32	2.8
10.	Others	44	3.3

Table 4. Pattern of Antimicrobial Use

DISCUSSION

The study provided baseline data about disease pattern and prescribing habits in NICU of a tertiary care hospital. Male (60%) preponderance observed in our study is consistent with study of Brijaletal[9] and Mangal et al.[10] The factor responsible might be due to more gender discrimination prevalent in rural population attending our centre. The gender discrimination in terms of access to healthcare is an issue of serious concern and there is an urgent need to further improve awareness against gender discrimination.

The incidence of disease and disease pattern was similar to earlier studies of Girardi et al[7] and Chatterjee et al.[8] The incidence of ELBW neonates was only 2% which indicates good health of the mother, better ante natal care provided and also increased awareness and nutritional status of people. The cases of respiratory distress especially transient tachypnoea of new born were most common and this group required less number of drugs and less duration of stay of 1-2 days. Cases admitted with severe birth asphyxia, hyaline membrane disease, HIE required longer stay and multiple drugs. Also, multiple comorbid conditions were reported in cases of ELBW babies and preterm babies with gestational age of <34 weeks. The highest numbers of drugs per day were given in the 1st week in NICU and ELBW infants were exposed to a higher number of drugs compared to other neonates and were more likely to receive associations of drugs with multiple toxicities.

In this study, the average number of drugs per encounter was 4.9 and higher when compared with study of Brijal et al[10] and Mangal et al.[11] This could be because of variation in disease pattern and specific protocols followed in different hospitals and regions. Prescription of maximum drugs was by their generic name and was dispensed free of cost to the patients from the hospital pharmacy, which is an encouraging sign and needs to be encouraged. The absence of the latest National essential list of medicines at the neonatology unit was noted. Secondly an antibiotic usage policy for the unit depending on the local microbial sensitivity pattern should have been in place.

Antimicrobial use was similar to other studies in India done by Chatterjee et al.[8] Antibacterials together with antifungal drugs were the highest prescribed drug class constituting 52% followed by respiratory system drugs. Antimicrobials commonly used were especially cefotaxime and amikacin, which were usually co-administered in ELBW for prophylactic purposes starting from the first postnatal day. Amikacin, ampicillin, cefotaxime, ceftazidime, piperacillin, and vancomycin have potential nephrotoxicity and they were used either alone or in combination. Vancomycin in addition can cause nerve deafness. Linezolid has haematological toxicity which can manifest as neutropenia, thrombocytopenia and anaemia. Great caution and care to be taken while using these drugs to avoid residual damage in neonates. Also, furosemide was frequently used, usually starting later, in case of specific cardio-vascular impairment. Combination of drugs with potential nephrotoxicity i.e. antibacterials and furosemide did not exceed 5.5 days. Arora et al. reported that age group 2 months-6 months had highest percentage cases of ADRs (17.68%) emphasizing young infants are the most vulnerable group and extra efforts (clinical, social and economic) should be undertaken for care of these children.[12]

Off-label prescribing does not necessarily constitute negligent practice; on the contrary, the off- label use of drugs could be necessary to provide the most appropriate treatment for a patient.[13] The extent and variation in off label drug use can be explained based on the setting and disease pattern in that particular area. Our results are similar to the results published by Jain et al[6] and Dos Santos et al.[14] The errors in off label drug use can be minimized by increasing awareness and making adjustments on a daily basis in relation to the health of neonate like renal function, birth weight and other factors.

Regular educational interventions like sensitization on pharmacovigilance shall further promote rational prescribing. Since pharmaco-epidemiological studies detailing prescribing patterns in NICU patients are very few from developing countries, the present study will help to promote rational usage, decrease medication errors, improve therapeutic outcome and cost control of various medications used.

CONCLUSIONS

Prescription of maximum drugs was by their generic name and was dispensed free of cost to the patients from the hospital pharmacy. Almost all the drugs prescribed were present in the NLEM, India 2017 and off-label antibiotics use were common. The study helped in assessing drug needs of neonates, rational usage and also guided the administration in drug procurement.

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