Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20183026

Original Research Article

Drug utilization study in a neonatal intensive care unit of a government tertiary care hospital in Western Maharashtra

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Received: 25 May 2018
Accepted: 26 June 2018

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ABSTRACT

Background: Presently drug utilization studies (DUS) are in an evolving era. Current literature search has shown paucity of epidemiological studies in the field of paediatric pharmacology. Hence the present study was designed to assess the drug utilization pattern in neonatal intensive care unit to improvise the current prescription practices, if required and to determine areas in neonatal pharmacology in need of further research.
Methods: A prospective, observational study spanned for a period of one year from January 2015 to December 2015 was conducted at the neonatal intensive care unit (NICU), Government teaching tertiary care hospital, Maharashtra. Data of prescribed drugs was collected. WHO prescribing indicators were used for evaluating DUS. Assessment of exposure rates of different class of drugs in different gestational age groups was done. Data were analysed using descriptive studies.
Results: Data of 205 neonates, showed male preponderance (53.17%) over female neonates (46.83%). With regard to the gestational age, 47.31% were term, 52.68% preterm. Average number of drugs per encounter was 6.69. 76.29% drugs were prescribed by generic name and 69.80 % drugs were from IAP list of essential medicines for children. Mean drug use was 6.23±3.34 per patient. Most common class of drug to which neonates were exposed was antibiotics (96.10%) and amikacin topped the list with exposure rate of 91.22%.
Conclusions: The present study substantiates the need for implementation of institutional antibiotic policies, awareness regarding IAP list of essential drugs for children, prescription by generic name and rational drug use.

Keywords: Drug utilization study, Exposure rate, Mean drug use, Neonates, NICU

INTRODUCTION

Drug utilization (DU) study is an effective mechanism to identify individual variability in drug use and to promote interventions that will improve patient outcomes.[1] Presently DU studies are in an evolving era. Their scope is to evaluate the present practices and future trends of drug usage, to estimate disease prevalence, drug priorities which will help the hospital administration in improving the availability of required drugs.[2]

A current search of literature in the area of paediatric pharmacoepidemiology has shown paucity of studies in the field of paediatric pharmacology with very few studies being published.

Neonates in particular preterm and very preterm belong to the most vulnerable population whereas term neonates are often admitted to the Neonatal Intensive Care Unit (NICU) because of congenital diseases and peri- or post-natal complications. Organ immaturity and consequently difficulties in adapting to extra-maternal life are reasons

for very preterm neonates being often multi-morbid and in-need of intensive and complex medical care.[3]

Hence the present study was designed to assess the drug utilization pattern in neonatal intensive care unit to improvise the current prescription practices, if required and to determine areas in neonatal pharmacology in need of further research.

METHODS

It was a prospective, observational and spanned for a period of one year from January 2015 to December 2015, conducted with the approval of the Institutional Ethical Committee in the NICU, Government teaching tertiary care hospital, Maharashtra. A written informed consent from parent / legal guardian was taken. Neonates of either sex admitted in the NICU ward were enrolled in the study. Neonates whose parents were not willing to consent for the study and death of neonates occurring within 24 hrs of admission in NICU were excluded from the study.

Data collection

Detailed information about drugs prescribed to each neonate during hospital stay namely number of drugs prescribed per prescription, use of generic/brand names, drug dose, dosage form, frequency, duration of treatment, administration of drugs in adherence to the prescription order was retrieved from parents/guardians, medical and nursing charts.

The neonates were categorized, and sub categorised according to gestational age (GA) in weeks as follows: very preterm: 28 to <32 weeks, late preterm: 32 to <37 weeks and term: ≥37 weeks.[4]

The neonates were categorized and sub categorised according to birth weight as follows: extremely low birth weight (ELBW): <1000grams, very low birth weight (VLBW): 1001 to <1500grams, low birth weight (LBW): 1501 to <2500grams and Normal weight (NW) ≥2500grams.[5]

The WHO core drug use indicators were used for evaluating DU study were:[6]

- Average number of drugs per encounter
- Percentage of drugs prescribed by generic name
- Percentage of encounters with an antibiotic prescribed
- Percentage of encounters with an injection prescribed

Percentage of drugs prescribed from Indian Academy of pediatrics (IAP) list of essential medicines for children of India 2011.[7]

Assessment of exposure rates of different class of drugs in different gestational age groups.

Statistical analysis

Data was collected in a predesigned Microsoft® Excel sheet 2008. Data were analyzed using descriptive statistics.

RESULTS

Data of 205 neonates were analysed in the present study. The sex distribution of the admitted neonates showed male preponderance (53.17%) over female babies (46.83%). With regard to the GA, 47.31% were term, 52.68% preterm. The mean GA was 36±3 weeks and the range was 28 to 40 weeks. The mean birth weight was 2.08±0.64kg and the range was 0.685 to 3.8kg. The mean duration of hospital stay was 8±6 days. In total, 79.02% neonates were alive at the time of discharge or transfer (Table 1).

Table 1: Demographics of study population (n=205).

Characteristics			n	%
Gender	Male		109	53.17
	Female		96	46.83
Gestational Age (weeks)	Mean±SD	36±3	--	--
	Range	28 to 40	--	--
	<37 (Preterm)		108	52.68
	≥37 (Term)		97	47.31
Birth weight (Kg)	Mean±SD	2.08±0.63	--	--
	Range	0.68 to 3.8	--	--
Length of hospital stay(days)	Mean±SD	8±6	--	--
	Range	2 to 32	--	--
Survival rate	--		162	79.02

n = Number of patients, %= percentage

Analysis of the clinical indication for admission at the NICU showed that neonatal sepsis (15.61%) followed by Respiratory distress syndrome (RDS) (13.17%), meconium aspiration syndrome (12.20%), neonatal hyperbilirubinemia (12.20%) and birth asphyxia (11.22%) were the common clinical disorders (Table 2).

Analysis of the WHO Core drug-prescribing indicators is summarized in Table 3. Average number of drugs per encounter was 6.69. Percentage of drugs prescribed by generic name and from IAP list of essential medicines for children was 76.29 and 69.80 percent respectively. Percentage of encounters with an antibiotic prescribed was 96.10 and percentage of encounters with an injection prescribed was 99.51.

Mean drug use was 6.23±3.34 per patient, when all patients were included. The average number of drugs administered varied depending on gestational age and birth weight. The highest drug use 8.21 was in the 28 to <32 weeks gestational age, followed by 7.24 in the 32 to <37

weeks and 5.89 in the ≥37 weeks gestational age (Figure 1).

Table 2: Different diagnosis in study population.

Diagnosis*	Number of patients	Percentage
Neonatal sepsis	32	15.61
Respiratory distress syndrome	27	13.17
Meconium aspiration syndrome	25	12.20
Neonatal hyperbilirubinemia	25	12.20
Birth asphyxia	23	11.22
Congenital anomalies	13	6.34
Intrauterine growth restriction	11	5.37
Hypoxic ischaemic encephalopathy	7	3.41
Pneumonia	3	1.46
Convulsions	3	1.46
Hepatitis B	1	0.48
Excessive cry	1	0.48
Pustular rash	1	0.48

*Diagnosis are not mutually exclusive

Table 3: WHO core drug prescribing indicators.

Prescribing indicators	Value
Average number of drugs per encounter (Mean drug use)	6.69
Percentage of drugs prescribed by generic name	76.29%
Percentage of encounters with an antibiotic prescribed	96.10%
Percentage of encounters with an injection prescribed	99.51%
Percentage of drug from Indian Academy of pediatrics (IAP) list of essential medicines for children of India 2011	69.80%

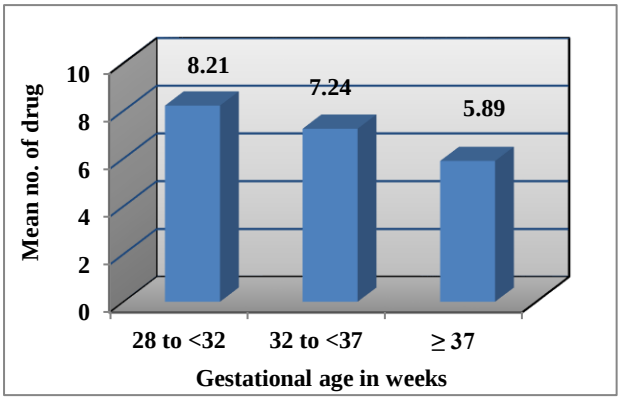


Figure 1: Mean drug use in different gestational age groups.

Based on birth weight, the highest mean drug use 8.125 was in ≤1000gm category followed by 7.86 in 1001 to 1500gm category. Least mean drug use 5.17 was seen in ≥3000gm category (Figure 2).

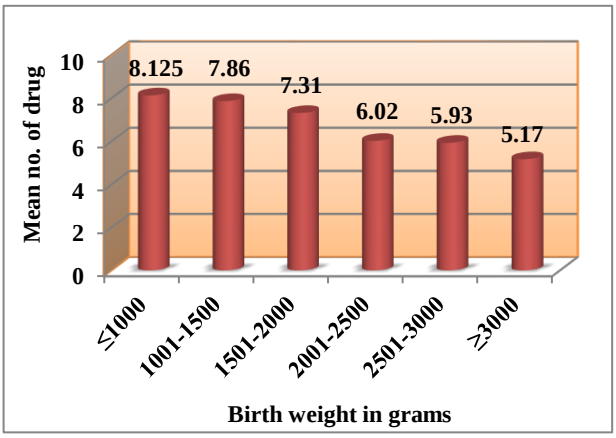
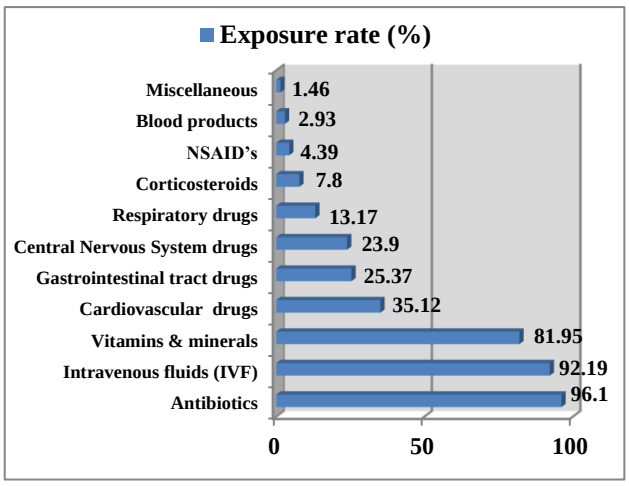


Figure 2: Mean drug use in different birth weight groups.

Most common class of drug to which neonates were exposed were antibiotics (96.10%) followed by intravenous fluids (92.19%) and vitamins and minerals (81.95%). Other classes were cardiovascular drugs (35.12%), gastrointestinal tract drugs (25.37%), Central Nervous System drugs (23.90%), and Respiratory drugs (13.17%) respectively (Figure 3).



*The sum total of percentage exceeds 100 as some patients received more than one drug class

Figure 3: Exposure rates of different class of drugs in study population.

The top 15 drugs used in all infants are listed in Table 4 and 5. The antibiotics amikacin (91.22%) and ceftriaxone (87.32%) were the 2 most widely prescribed drugs, with rates of exposure far outstripping exposure to any other drug. This was followed by intravenous fluid 10% Dextrose (73.17%) and vitamin K for prophylaxis with exposure rate of (71.71%) (Table 6).

Table 4: Exposure rates (percentage) of different class of drugs in different gestational age groups.

	Gestational Age in weeks		
Drug class	**28 to <32 n=19**	**32 to <37 n=89**	**≥37 n=97**
Antibiotics	100	97.75	93.81
Intravenous fluids (IVF)	100	95.50	87.63
Vitamins and minerals	94.74	85.39	76.29
Cardiovascular drugs	52.63	40.45	26.8
Gastrointestinal tract drugs	42.11	30.34	17.53
Central Nervous System drugs	31.58	21.35	24.74
Respiratory drugs	26.32	15.73	8.25
Corticosteroids	0	11.24	6.19
NSAIDs	5.26	4.49	4.12
Blood products	5.26	4.49	1.03
Miscellaneous	0	1.12	2.06

Table 5: Exposure rates (percentage) of most often prescribed drugs.

Name of drug	No of patients	Exposure rate (%)*
Amikacin	187	91.22
Ceftriaxone	179	87.32
10% Dextrose	150	73.17
Vitamin K	147	71.71
Isolyte-P	90	43.90
Oral calcium	70	34.15
Dopamine	52	25.37
Adrenaline	42	20.49
Piperacillin + Tazobactum#	42	20.49
Atropine	33	16.10
Multivitamin	31	15.12
Ranitidine	31	15.12
Calcium gluconate	28	13.66
Dobutamine	28	13.66
Phenobarbitone	25	12.20

*The sum total of percentage exceeds 100 as some patients received more than one drug class # only two Fixed dose combination are prescribed, which are Piperacillin + Tazaobactum and Salbutamol + Ipratropium bromide

DISCUSSION

Importance of drug utilization studies in pharmacoepidemiology has been increasing due to their close association to other areas of public health like pharmacovigilance, pharmacoeconomics and pharmacogenetics.[8] It is essential to assess the drug utilization pattern in NICU to improvise the current prescription practices, if required and to determine areas in neonatal pharmacology which are in need of further research.

Table 6: Exposure rates (percentage) of most often prescribed drugs in different gestational age groups.

	Gestational age in weeks		
Drugs	**28 to <32 n=19**	**32 to <37 n=89**	**≥37 n=97**
Amikacin	100 (19)	96.63 (86)	84.54 (82)
Ceftriaxone	100 (19)	93.26 (83)	79.38 (77)
10% Dextrose	94.74 (18)	83.15 (74)	59.79 (58)
Vitamin K	94.74 (18)	77.53 (69)	61.86 (60)
Isolyte-P	36.84(7)	46.07 (41)	43.30 (42)
Oral calcium	15.79(3)	33.71 (30)	38.14 (37)
Dopamine	42.11(8)	32.58 (29)	15.46 (15)
Adrenaline	36.84 (7)	22.47 (20)	15.46 (15)
Piperacillin + Tazobactum	36.84 (7)	52.84 (23)	12.37 (12)
Atropine	36.84 (7)	16.85 (15)	11.34 (11)
Multivitamin	5.26 (1)	13.48 (12)	18.56 (18)
Surfactant	21.05 (4)	11.24 (10)	1.03 (1)
Calcium gluconate	21.05 (4)	16.85 (15)	11.34 (11)
Ranitidine	10.53 (2)	15.73 (14)	15.46 (15)
Dobutamine	26.32 (5)	12.36 (11)	12.37 (12)

In the present study, sex distribution of the admitted neonates showed male preponderance (53.17%) over female neonates (46.83%). Similar results were found in study by Warrier I et al. In which, 53.78% male neonates were admitted compared to females (46.22%).[9]

The mean gestational age was 36±3 weeks and the range were 28 to 40 weeks. This in concordance with the previous study results by Warrier I et al, with mean gestational age of 35±5 weeks.[9]

In the present study, 47.31% of neonates belong to term and 52.68% belong to preterm gestational age group. Previous study by Warrier I et al, found similar results i.e. 48% term and 51.5% preterm neonates.[9]

In the present study the mean birth weight of the neonates is 2.08±0.637kg with a range of 0.685 to 3.8kg, this is comparable with study done by Neubert et al, and Chatterjee S et al, reported mean birth weight of 2.13 and 2.21kg respectively.[3,10]

In the present study, the mean length of stay in hospital was 8±6 days, this is relatively less as compared to the study done by Neubert A et al, in which the author have reported mean length of hospital stay as 19.4 days.[3] The discrepancy may be because of majority (47.31%) of neonates in the present study were term born as compared to 31.10% term born reported by Neubert A et al, which

may make them less vulnerable to morbidity and reduces the hospital stay.[3]

The survival rate in the present study at the time of discharge or transfer was 79.02%. Chatterjee S et al, have reported 85.80% of survival rate in NICU.[10]

In the present study, neonatal sepsis (15.61%) was the most common clinical indication for admission at the NICU followed by RDS (13.17%), MAS (12.20%), neonatal hyperbilirubinemia (12.20%) and birth asphyxia (11.22%). Treatment was initiated on the basis of admitting diagnosis and investigations carried out to arrive at a final diagnosis. The treatment given was in accordance with treatment guidelines outlined in standard textbooks of neonatology.[11,12]

The WHO core drug prescribing indicators are efficient tools to assess and detect potential problems in drug use in health care setting. In the present study, average number of drugs per encounter was 6.69. This was higher as compared to previous study reported 4.8 reported by Chatterjee S et al.[10] The higher value of average number of drugs per encounter in the present study could be attributed to empirical use of antibiotics, inclusion of IV fluids and vitamin supplements prescription in the study.

In present study, percentages of encounters with an antibiotic prescribed were 96.10. Chaterjee S et al, had reported, encounters with antibiotic as 30.20%.[10] This deviation could be due to difference in the institution-wise antibiotic policy and availability of drugs in that region.

In the present study, percentage of drugs prescribed by generic name was 76.29% and 69.80% of drugs prescribed were from IAP list of essential medicines for children 2011. These percentages are lower than those reported in similar study by Chatterjee S et al, (88.70 and 79.7% respectively).[10] Lower percentage of drugs from national essential drug list in the present study reinforces need for implementation of rational drug use policy. The less percentage of drugs prescribed by generic name has pharmacoeconomic implications as cost of treatment needs to be considered in setting like tertiary care government hospital.

In the present study, the total percentage of encounters with an injection prescribed was 99.51%. This is in concordance with Chaterjee S et al, study which has reported 92.10% encounters with an injection prescribed.[10]

The mean number of drugs used varied depending on gestational age. Previous comparable studies have not classified the data as per this classification. Overall mean drug use in the present study population was 6.69±3.34 per patient. Neubert AJ et al, had reported mean drug use as 11.1±9.56 drugs per patient.[3] The lower value of overall mean drug use may be explained by the lesser number of preterm and very preterm neonates in the present study (43.41 and 9.26%) as compared to Neubert AJ et al, (54.7 and 14.2%).[3] Premature neonates are known to have high rates of medical complications necessitating prolonged NICU stay periods, which ultimately result in higher drug use and exposure rates.

In the present study, the highest drug use of 8.21 was seen in the 28 to <32 week GA group, followed by the 32 to <37 week GA group at 7.24 and ≥ 37 weeks GA group at 5.89. Warrier I et al, have reported mean drug use of 2.4 in ≥37 weeks GA group. The higher values in the present study could be because of inclusion of use of intravenous fluids (IVFs) and prophylaxis of vitamin K in the present study. Use of IVFs and prophylaxis of vitamin K were not included in the previous study by Warrier I et al.[9]

The highest mean drug use of 8.125 was seen in ≤1000gm birth weight group. It is comparatively lower than the similar study by Warrier I et al.[9] The authors have reported mean drug use of 11.1 in ≤1000gm birth weight neonates. This difference could be explained due to higher survival rate and longer mean lengths of hospital stay in their study (97% and 15 days) as compared to (37.5% and 8 days respectively) in the present study.

In the present study, antibiotics top the list with the highest exposure rate of 96.10%. This is in concordance with previous studies published in the past and is probably due to empirical administration of antibiotics for prophylaxis in neonates and it is not a true reflection of the incidence of bacterial infection.[3,13] Next common groups of drugs with high exposure rates were IVFs (92.19%) followed by vitamins and minerals (81.95%). Bonati M et al, in a multicenter NICU study have reported similar results.[14]

In the present study, antibiotics followed by IVFs, vitamins and minerals are having the highest exposure rate in all the gestational age groups. All the patients from the age group 28 to <32 weeks were given antibiotics and IVFs. Apart from empirical use, the vulnerability to infection, dehydration and the organ immaturity in this age group explains the high use of antibiotics and IVFs. Similar results were reported by Neubert AJ et al.[3]

In the present study, amikacin (91.22%) was the most commonly prescribed drug followed by ceftriaxone (87.32%) with exposure rates far outstripping exposure to any other drug. Previous study by Warrier I et al, had reported higher exposure to antibiotics like ampicillin (94.22%) and cefotaxime (92.24%).[9] This discrepancy could be due to institutional-wise change in antibiotic policy.

A total of 71.71% neonates were administered vitamin K as prophylaxis for hemorrhagic disease of newborn. Study by Neubert AJ et al, had reported higher exposure of vitamin K in neonates (90.06%).[3] The possible explanation for lower exposure rate of Vitamin K in the present study could be, as the data of neonatal administration of vitamin K in labor room before shifting to NICU was not included.

Hypocalcemia is a frequently observed clinical and laboratory abnormality in neonates. Birth asphyxia and prematurity are the high-risk factor for neonatal hypocalcaemia requiring calcium supplementation.[15] In the present study the percentage of neonates with birth asphyxia was 11.22 and preterm was 52.68. This was reflected in the exposure rate to oral calcium supplementation (34.15%) and intravenous calcium gluconate (13.66%). With the exceptions of oral calcium, piperacillin + tazobactum and ranitidine, the exposure rates to all other most often prescribed drugs decline with the increase in the GA. Exposure rate to oral calcium increases as the GA increases and to intravenous calcium gluconate decreases as the gestational age increases.

Limitations of the study were small sample size and single center study. Some of the prescribing indicators could not be assessed due to the special nature of the population and the study being inpatient in nature. Authors recommend larger sample size study at multicenter for the interpretation of results, to arrive at a definite conclusion and to address the untouched research areas of neonatal pharmacology.

CONCLUSION

In the present study, average number of drugs per encounter was on the higher side as compared with previous studies. It is clear that the trend towards polypharmacy continues in neonates in the NICU. Neonates, especially premature/low birth weights, as there is immaturity of drug-metabolizing pathways are more prone to adverse events due to polypharmacy. Antibiotics constituted the major class of drugs prescribed and amikacin was the most commonly prescribed drug. Relatively lower percentages of drugs from national list of essential medicine and generic medicine have been prescribed. This reinforces need for implementation of rational drug use policy. There is lower exposure rate of surfactant in the present study, probable reason being availability and cost issue.

To conclude the present study substantiates the need for implementation of institutional antibiotic policies, awareness regarding IAP list of essential drugs for children, prescription by generic name and rational drug use.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kumbhar AV, Halasawadekar NR, Ramanand SJ, Ramanand B, Patil PT, Shah RD, et al. Drug utilization study in a neonatal intensive care unit of a government tertiary care hospital in Western Maharashtra. Int J Basic Clin Pharmacol 2018;7:1572-8.