Original Research Article

Evaluation of pharmacotherapy in neonatal and pediatric intensive care unit of a south Indian tertiary care hospital: a prospective observational study

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ABSTRACT

Background: Evaluating the pharmacotherapy is essential at neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU) to identify and understand pattern and variability in drug use in polypharmacy, also to promote interventions that will improve patient outcomes.
Methods: In our study, we audited pharmacotherapy of 300 neonates and 100 pediatric patients admitted to NICU and PICU from November 2018 to February 2019. WHO-CORE prescribing indicators, WHO-ATC system and WHO-ICD 10th version was used to evaluate pharmacotherapy and to understand the pattern and extent of medication use and to systematically classify drugs and diseases respectively.
Results: A total of 1207 medications containing 34 unique active ingredients were prescribed for 300 neonates with an average of 4.02 (±2.0) drugs per neonate admitted to NICU and the most prescribed drugs were anti-infectives for systemic use 799. A total of 976 medications containing 69 unique active ingredients were prescribed with an average of 9.76 (±3.81) per pediatric patients admitted to PICU with anti-infectives for systemic use 331 tops the list. More than 75% of drugs was prescribed in generic name with 98% constant availability of key drugs at intensive care unit.
Conclusions: This study substantiates the need for reinforcement of institutional antibiotic policies as antibiotics are widely prescribed and there is an increase trend of antibiotic resistance at critical care unit, assessment of WHO core prescribing indicators are reflective of quality care revealing the awareness about strict monitoring of pharmacotherapy.

Keywords: Pharmacotherapy, NICU, PICU, WHO-CORE indicators

INTRODUCTION

Pharmacotherapy, it is the usage of medication adjusted to the individual need of the patient to maximize efficacy and safety, evaluation of pharmacotherapy is essential to identify and understand pattern and variability in drug use, also to promote interventions that will improve patient outcomes.[1] Rationality in drug usage is of at most important since there is an increase in prescribed drugs (polypharmacy) which vary accordingly to condition or severity of the disease in each individual admitted to neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU).[2]

The parameters like the variation in pharmacokinetics, pharmacodynamics, organ maturity, physiological changes, therapeutic approaches based on the pathophysiology of pediatric disease, drug dose, dosage

form, frequency, duration of treatment, route of administration of drug vary in pediatric population when compared to adults. Most of the drug dose is decided based on body weight and sometimes even off -label and unlicensed drugs are used depending on physicians' decisions, only if drug use is highly effective and benefits are greater than risk.[3,4]

Based on study site demography it is very essential to know the extent and usage pattern of antibiotics particular to the pediatric population to combat increasing antibiotic resistance burden that leads to higher medical cost, prolonged hospitalization, and increased mortality.[5]

Pediatric patients admitted to the intensive care unit receive a greater number of different medications with more drug orders written compared to in-ward children. There is a paucity of studies conducted in India on the evaluation of pharmacotherapy at the pediatric critical care unit. Hence, we conducted a prospective observational study using WHO-CORE prescribing indicators, WHO-ATC system and WHO-ICD 10th version to evaluate pharmacotherapy and to understand the pattern and extent of medication use and to systematically classify drugs and diseases respectively.

METHODS

A prospective observational study was conducted at NICU and PICU of a tertiary care government teaching hospital in south India for six months (November 2018 to February 2019) after the study protocol was reviewed and approved by the Institutional Human Ethics Committee of the institution.

Neonates and pediatric patients of either sex admitted to NICU and PICU and who stay with a minimum completion of 1 ICU day and who received one or more medications were included in the study after taking informed consent from a parent/guardian. New admissions to NICU and PICU were only considered to reduce the over-representation of the same individual data. Patients admitted in the intensive care unit only for receiving phototherapy, blood and blood products, maintenance fluids with electrolytes, total parenteral nutrition, mechanical ventilation without any other medications were excluded from the study. All patients enrolled were followed until discharge from NICU and PICU.

All relevant data of the enrolled patients including demographic details like name, age, gender, body weight, clinical data such as diagnosis, past medical history, interventions made, co-morbidities, allergy status, the total number of written drug orders (new medication orders, modification orders, discontinuation orders), different medications ordered, frequency, days of therapy(start and stop date), indication and route of medication administration and cost was collected from various data sources like patient case notes, treatment

chart, by interviewing patient caretakers and was documented in a suitably designed data collection form. Any discrepancies regarding patients were resolved by consulting pediatrician.

The drugs used in ICU were coded according to the WHO anatomical therapeutic and chemical classification (ATC) system.[6] The final diagnoses were classified and coded according to the WHO international statistical classification of diseases and related health problems 10th version (ICD-10).[7] The prescribing trends and utilization of drugs were investigated using the WHO core indicators for drug utilization studies.[8] The financial burden was assessed by collecting medical costs, indirect costs involved from the patient caretaker.

The data was initially abstracted into paper data collection form and later data were entered into statistical package for social sciences (SPSS version 22). Descriptive statistical analysis was performed by calculating the percentages and frequency for the categorical variables included in the study.

RESULTS

Patients' descriptive

A total of 300 patients, comprising 42% (n=127) females and 58% males (n=173) from NICU admissions and a total of 100 patients comprising 53% (n=53) females and 47% (n=47) males from PICU were included in the review. The demographic data and patient characteristic studied are presented in (Table 1).

Table 1: Demographic data and patient characteristics.

Variables	NICU	PICU
Gender N (%)	Male: n=173 (58)	Male: n= 47 (47)
	Female: n=127 (42)	Female: n=53 (53)
Age distribution (%)	Pre-term: 36.7	1 month to 2 years: 47
	Full-term: 62.3	2-12 years: 38
	Post-term: 1	12-18 years: 15
Mean age	37±3.60 weeks	4.8±4.6 years
Length of stay	6.51± 4.5 days	5.06±2.3 days
Mechanical ventilation (%)	34	40

Overall medical conditions were seen among neonate's majority were certain conditions originating in the perinatal period (n=158) were the most common conditions and certain infectious and parasitic diseases (n=40) were the major medical condition seen and in

pediatric patient's disease of the nervous system (n=23) and respiratory system (n=22) were majorly seen.

A total of 1207 medications containing 34 unique active ingredients were prescribed for 300 neonates with an average of 4.02 (±2.0) drugs per neonate admitted to NICU and the most prescribed drugs were anti-infectives for systemic use (799) among them amikacin (166), gentamycin and ampicillin (153) followed by cefotaxime (123) were most frequently used antibiotics. Blood and blood-forming organs (163) among which the majority of drugs prescribed were multivitamin drops (108) and followed by drugs of cardiovascular system (87) that includes inotropes in which dopamine and dobutamine and adrenaline was frequently used in neonates. A total of 976 medications containing 69 unique active ingredients were prescribed with an average of 9.76 (±3.81) per pediatric patients admitted to PICU and most prescribed drugs were anti-infectives for systemic use (331) and ceftriaxone (76) amikacin and meropenem (44) followed by vancomycin (43). Drugs of the nervous system (157) especially anti-epileptics were second-most prescribed category of drugs among them fosphenytoin (27) and levetiracetam (26) was most prescribed followed by phenobarbitone and sodium valproate and rest of the drug category prescribed are shown in (Table 2).

Table 2: Systematic classification of prescribed drugs according to ATC classification among study population of NICU and PICU.

Medications	Medications use in NICU N (%)	Medications use in PICU N (%)
Alimentary tract and metabolism	37 (3.07)	149 (15.27)
Blood and blood-forming organs	163 (13.50)	127 (13.01)
Cardiovascular system	87 (7.21)	105 (10.76)
Genitourinary system and sex hormones	1 (0.08)	0 (0.00)
Anti-infectives for systemic use	799 (66.20)	331 (33.91)
Nervous system	105 (8.70)	157 (16.09)
Respiratory system	6 (0.50)	53 (5.43)
Systemic hormonal preparation excl. sex hormones and insulin	9 (0.75)	51(5.23)
Anti-parasitic	0 (0.00)	1 (0.10)
various	0 (0.00)	2 (0.20)
Total	1207 (100)	976 (100)

Assessment of WHO-CORE indicators for drug utilization are reflective of quality care provided in the critical care unit depicted in (Table 3).

Table 3: WHO core indicators.

WHO core indicators	Value (NICU) (%)	Value (PICU) (%)
Prescribing indicators		
Average number of drugs per encounter (mean drug use)	4.02	9.76
Percentage of drugs prescribed by generic name	76.38	83.09
Percentage of encounters with an antibiotic prescribed	99.66	99.6
Percentage of encounters with an injection prescribed	93.28	88.93
Percentage of drug from Indian Academy of paediatrics (IAP) list of essential medicines for children of India 2011	68.2	69
Health indicators		
Availability of copy of essential drugs list or formulary	Yes	Yes
Availability of key drugs	98	98

The majority of drugs were administered by intravenous route in both neonates 93.45% and pediatric 88.93% followed by oral, nebulization, and intramuscular route. A total of 1,681 drug orders comprised of 1,207 (71.80%) new orders, 43 (2.56%) modification orders and 431 (25.64%) discontinuation orders were prescribed among neonates and in pediatric patients a total of 1,180 drug orders comprised of 976 (82.71%) new orders, 62 (5.25%) modification orders and 142 (12.03%) discontinuation orders were prescribed.

The calculation of direct medical, non-medical and indirect cost revealed an average of ₹4,803 and ₹4,506 was the economic burden imposed on a caretaker for an average length of stay of 6.51±4.5 days and 9.76±3.81 days among neonates and pediatric patients respectively on admission to the intensive care unit.

DISCUSSION

In this study, we have examined the pharmacological treatment provided in neonatal and pediatric intensive care unit to know the pattern and extent of widely used

medications at critical care. The present study includes the neonatal population of 300, out of which 42%.

were female and 58% were male. The sex distribution in our study showed the male preponderance which was also found in a similar study conducted by Warrier et al, reporting 53.78% of male and 46.22% of female and Amir et al, reporting 68% of males and 32% of female neonates.[9,10] We also include the pediatric population of 100, female patients 53% outnumbered males 47%. The prevalence of preterm born neonates in our study was 36.7% which is higher than the study conducted by Chauthankar et al, 27.8% of preterm babies and lower than the study conducted by Chatterji et al, 54.8% preterm born.[11,12]

In our study the mean length of stay in NICU was 6.51±4.5 days, lesser than the study conducted by Neubert et al, that is, 10±6 days and higher than the study conducted by Amir et al, with the mean length of stay of 3.15±2.8 days.[10,13] The discrepancy in the length of stay of our study may be due to more neonates were full-term born which makes less vulnerable to co-morbidities than the pre-term born. The mean length of stay in PICU was 5.06±2.3 days, for a total of 506 ICU days for 100 patients.

The most common diagnosis found in NICU was belonging to certain conditions originating in the perinatal period 52.67% that include respiratory distress syndrome, jaundice, birth asphyxia, meconium aspiration syndrome, hypoxic-ischemic encephalopathy (HIE), neonatal seizures and second most diagnosed conditions belongs to certain infections and parasitic disease 13.33% which includes neonatal sepsis followed by endocrine, nutritional and metabolic diseases 11.33% that includes conditions like nutrition and supportive care (N and S), in born errors of metabolism.

The clinical conditions encountered in our study were most frequently found and reported in studies conducted by Chatterjee et al, and Kumbar et al, there was no other rare diagnosis found for admission to NICU.[12,14]

The analysis of clinical diagnosis for the admission to PICU showed that the majority of the diagnosis was related to diseases of the nervous system which includes, seizure disorder with status epilepticus followed by diseases of the respiratory system that includes, bronchopneumonia, aspirational pneumonia, and disease of the digestive system that includes, acute cholecystitis, intestinal obstruction and the similar pattern of diagnosis condition was seen in a study conducted by McDonnell et al.[15]

We systematically classified the most common class of drugs to which neonates were exposed in our setup according to ATC code in which anti-infective for systematic use was 66.20%, blood, and blood-forming agents 15.16%, cardiovascular drugs 7.21% drugs, and nervous system drugs were encountered frequently. In our study among 66.2% of antibiotics prescribed amikacin 21.15%, gentamicin and ampicillin 19.49%, and cefotaxime 15.67% top the list.

The pattern of drug use and the most common drug found in our study was similar to studies done by Amir et al, and Bonati et al, whereas the study conducted by Grohskopf et al and Fonseca et al reports gentamicin, ampicillin and vancomycin as most commonly antibiotics, the usage of different antibiotics are due to different antibiotics policy followed, race, antibiotic resistance pattern found in that particular area.[10,16-18]

Among pediatric patients anti-infectives for systemic use 33.91%, nervous system 16.09%, alimentary tract and metabolism 15.27% were encountered frequently. Ceftriaxone, amikacin, and meropenem, vancomycin topped among antibiotics. Nervous system drugs like paracetamol, fosphenytoin, levetiracetam were most commonly used.

Alimentary tract and metabolism drugs ranitidine, ondansetron, thiamine was found most common which is not similar to study conducted by Mcdonnell et al evaluating pharmacotherapy in PICU with a sample size of 100 patients with a total of 851 ICU days of stay and who received 4419 drug orders with most frequent orders found were morphine, furosemide, potassium, lorazepam, and albuterol.[15] The most commonly prescribed drugs in our study and study conducted by Grohskopf et al and Blanco-Reina et al are similar.[17,21]

Blanco-Reina et al, conducted a similar study, in which the mean drug prescribed per patient was 7.4±6 drugs less than our study showing of 9.7±81 drugs and the major clinical diagnosis were similar to our study that includes disease of the nervous system, respiratory disease.[21]

The WHO essential list of medicine for children categorizes antibacterial into 3 groups as ACCESS, WATCH, and RESERVE based on observed antibiotic resistance patterns and monitoring requirements globally. Analysing antibiotics prescribed in intensive care unit, most of the antibiotics like meropenem, vancomycin, ceftriaxone, piperacillin-tazobactam, ciprofloxacin comes under WATCH group that has higher resistance potential and are recommended as first or second choice treatments only for a specific, limited number of indications. These medicines should be further prioritized as key targets of stewardship programs and monitoring.[19,20]

The limitation of our study are as follows, it is a single-centre study and some of the WHO core and complementary indicators could not be assessed due to the limitation in sample size, special nature of patient population included and study being carried in inpatient critical care unit. Patients included in our study stayed for at least 24 hours in the critical care unit, drug use pattern may vary by including patients stayed less than 24 hours.

CONCLUSION

The assessment of WHO core prescribing indicators for drug utilization is reflective of quality care provided in the critical care unit. The percentage of antibiotics encountered in both populations was high and our study shows each patient admitted to the critical care unit was exposed to a minimum of one antibiotic to a maximum of six antibiotics during the length of stay. The chance of developing antibiotic resistance and failure of therapy is high among pediatric patients that necessitates the changing pattern of antibiotics prescription and it can be corrected by reinforcement of institutional antibiotic policies and by strict adherence to it by health care professionals.

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