



DRUG UTILIZATION STUDY IN PATIENTS OF NEONATAL INTENSIVE CARE UNIT OF TERTIARY CARE HOSPITAL IN PUNJAB, INDIA

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ABSTRACT

Introduction: Drug utilization study (DUS) is a method for drug evaluation in which it evaluates qualitative and quantitative aspect of the drug use. The main aim of DUS is to increase rational use of the drugs in population. In neonatal intensive care unit (NICU), premature infants are treated with many drugs. Hence, DUS in NICU was planned to study prescription pattern and pharmaco-economic analysis.

Methods: A cross-sectional observational study was carried out for six months in NICU in Medical College and Hospital of Punjab after approval by Institutional Ethics Committee. Patients of both gender were enrolled after taking written informed consent and patients discharged/died within 24 hours of admission were excluded.

Results: In this study, 100 patient's data was collected during the study period in which 67 patients were preterm, 32 were term and 1 was post term. Males were more frequently admitted than the females. Preterm babies had more duration of hospitalization (11.2 days) as compare to term and post term (7 days). Respiratory Distress Syndrome (RDS) was major disease prevailing in preterm 63 out of 67 but only 22 from 32 term neonates were suffering from RDS. The average number of drugs prescribed in preterm (2.7) were much higher than the term (2.01) infants Amikacin, an antibiotic was the most commonly prescribed drug among all the groups, but the costliest drug prescribed in group A and group B was Cefoperazone. Among the antibiotic combinations most affordable were amikacin + cefotaxime to all the patients.

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INTRODUCTION

World health organization (WHO) defined drug utilization study (DUS) in 1977 as “the marketing, distribution, prescription and use of drugs in society, with special emphasis on the resulting medical, social and economic consequences”¹ DUS is a method for drug evaluation in which it evaluates qualitative and quantitative aspect of the drugs. There are various methods for qualitative DUS but most commonly used are ‘the potential therapeutic value’ and ‘the expected degree of use’. The quantitative study can be of various types also but mainly used methods are ‘cost’, ‘number of units’, ‘prescriptions’ and ‘sale of “top” products’.²

DUS generates data that can be further evaluated by various means like comparing the current guidelines/recommendations to the patterns observed in the hospital during the study to further improve the drug utilization. This data can also be used to compare the pattern and cost of drugs used in different regions over the time³.

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The main aim of drug utilization study is to increase rational use of the drugs in population.⁴With advancement in the medical technology, there are variety of treatment modality available but there is difference in cost of treatment and treatment related complications of these modalities. So, we need to find most efficacious, cost effective treatment modality.⁵ In current scenario, DUS plays vital role in mostvulnerable patients to issue an evidence-based prescription and helps us to evaluate risk-benefit profile of drugs, so that we can prescribe effective drugs without creating additional economic load on the society.⁶

DUS can be conducted on any population type but some populations are more vulnerable than others like neonates. So rational use and appropriate prescribing is crucial in neonates, elderly etc.⁷Neonates, term and preterm are most venerable especially preterm because of organ immaturity and consequently difficulties adapting to extra-maternal life. Prematurity due to above reason itself cause high mortality and risk further increase after their exposure to the high number of drugs⁸.

Table 1

Characters	Group An= 67		Group Bn=32		Group Cn=1	
	M	F	M	F	M	F
1. Gender	46	21	24	8	1	0
2. Gestational weight at hospitalization (Average± SD)	1792 g± 752.07	1358 g±768.58	2780 g± 758.02	2467 g± 748.81	1820 g	0
3. Average duration of hospitalization (days)	11.5		7		7	
4. Disease						
a. RDS (%)	63		22		1	
b. GIT associated	2		2		-	
c. CNS associated	0		2		-	
d. others	2		6		-	
5. Number of drugs						
a. less than 5	60		31		1	
b. 5 to 10	6		1		0	
c. more than 10	1		0		0	
6. average drugs prescribed per patient	2.7		2.01		2	
7. Pharmacoeconomics analysis of antibiotics use in RDS						
a. most commonly prescribed	Amikacin		Amikacin		Amikacin and cefotaxime	
c. cheapest combination prescribed	Amikacin + cefotaxime		Amikacin + cefotaxime		-----	
d. average cost for cheapest combination prescribed	120.77 ± 64.57		120.77 ± 64.57		120.77	
e. costliest combination prescribed	Cefotaxime + gentamycin + piperacillin with tazobactam + Cefoperazone + meropenem		Amikacin + Cefoperazone + meropenem		-----	
f. average cost per patient	263.149 ± 295.971		232.84 ± 296.54		120.77	

Table 2

Sr. No.	Group	Drug name (Exposure)	Group A n-67	%	Group B n-31	%	Group C n-1
1. Antibiotics	Aminoglycosides	Amikacin	45	67.2	21	67.7	1
		Tobramycin	5	7.5	0	0	0
		Gentamycin	2	2.9	0	0	0
		Netilmicin	2	2.9	0	0	0
	cephalosporins	Cefotaxime	27	40.3	7	22.6	1
		Cefoperazone	18	26.8	11	35.5	0
	Glycopeptideantibiotics	Vancomycin	7	10.4	3	9.6	0
		Meropenem	5	7.5	2	6.4	0
	β- lactamases	Piperacillin and tazobactam	5	7.5	1	3.2	0
		Quinolone					
2. Coagulants		ciprofloxacin	3	4.5	0	0	0
3. Respiratory stimulants		Vitamin K	31	46.3	17	54.8	0
4. anti-epileptics	Methyl xanthine	Caffeine citrate	17	25.3	0	0	0
5. ant-acids	Barbiturates	Phenobarbitone	8	11.9	3	9.7	0
6. anti-emetics	H ₂ blockers	Ranitidine	6	8.9	2	6.4	0
		Domperidone	3	4.4	0	0	0
7. steroids	Prokinetics	Metoclopramide	3	4.4	0	0	0
		Dexamethasone	3	4.4	0	0	0
		Multivitamin syrup	10	14.9	2	6.4	0
		NS solution (Bolus)	10	14.9	5	16.1	1
8. health supplements	Loop diuretic	Human milk fortifiers	8	11.9	0	0	0
		Aminoven	2	2.9	0	0	0
		Vitamin D ₃	5	7.4	2	6.4	0
		Multivitamin infusion	3	4.4	0	0	0
9. diuretics	Loop diuretic	Iron	3	4.4	0	0	0
		Furosemide	1	1.5	0	0	0
		Dobutamine	1	1.5	0	0	0
10. others	Loop diuretic	Dopamine	0	0	1	3.2	0
		PCM	2	2.9	0	0	0

The general problem in Neonatal Intensive care unit (NICU) is that the efficacy and safety of drugs evaluated in adults usually applied to the neonates, such practices cause problems like off-label use of drugs, in-effective drug therapy, increase in mortality and morbidity, wastage of resources, with increase in cost treatment. Hence, drug utilization studies provide evidence-based data to be applied for improving their odds of survival even in premature infants.⁹

Results shown by some studies that, the anti-microbial agents are the most commonly used in NICU which are even not required and have inappropriate use up to 50% of times. Hence, rational drug use studies are most important part of pharmacological evaluation.^{10,11}

Due to above stated reasons; we have planned DUS in NICU its prescription pattern and pharmaco-economic evaluation of drugs.

METHODS

A cross-sectional observational study was carried out for six months in NICU in Medical College and Hospital of Punjab after approval by Institutional Ethics Committee. The data regarding patient demographics and drugs administered were collected daily in a structured performa. Patients were enrolled after taking written informed consent after informing the purpose of study. Patients of both gender who gave informed consent were included in the study. An exclusion criterion includes the patients who were discharged/died within 24 hours of admission and patients who did not gave the consent to be enrolled in study.

RESULTS

In this study, 100 patients data was collected during the study period. Out of 100 patients, enrolled in study, 67 patients were preterm (<37 weeks of gestation- Group A), 32 patients were of term age (37-42 weeks of gestation Group-B) and 1 was post term (>42 weeks of gestation Group-C). The characteristics of all the three groups are compared in table 1.

Among all the cases enrolled, the cases in group A showed that males were more frequently admitted than the females and the same trends were seen in group B and Group C. (Table 1)

In comparison of groups, preterm babies had more duration of hospitalization (11.2 days) as compare to other 2 groups which showed (7 days) the similar results. (Table 1)

Preterm had average weight around (1792 g \pm 752.07 in males and 1358 g \pm 768.58 in females) and term pregnancies have (2780 g \pm 758.02 in males and 2467 g \pm 748.81 in females). (Table 1)

The findings also suggest that RDS was major disease prevailing in preterm 63 out of 67 but only 22 from 32 term neonates were suffering from RDS. So, focus of this study DUS was to find drugs utilized for treatment of RDS.

The average number of drugs prescribed in preterm (2.7) were much higher than the term (2.01) infants. In group C, there was one patient who was prescribed 2 drugs. (Table-1)

Amikacin, an antibiotic was the most commonly prescribed drug among all the groups, but the costliest drug prescribed in group A and group B was Cefoperazone. Among the antibiotic combinations most affordable were amikacin + cefotaxime to all the patients which only cost 120.77 \pm 64.57 per patient.

With addition of multi drugs the average treatment cost rose to 263.149 \pm 295.971 in group A and 232.84 \pm 296.54 in group B as seen in table 1.

Table 2 shows the Individual drug prescription in these 100 patients. Antibiotics were the most common prescribed drugs in which aminoglycosides were prescribed to almost every patient after that cephalosporins were second most commonly prescribed drugs.

As coagulants the vitamin k was used most commonly as compared to other drugs, which were used sparingly. A majority of patients were RDS patients so methyl xanthene was widely used as respiratory stimulants along with steroids in some patients.

Patients having CNS disorders were given phenobarbitone as antiepileptic and CNS depressant. Some of the patients were also given supplements along with the breast milk for proper development and growth which also have led to increased cost of treatment along with antibiotics.

DISCUSSION

Our study indicated male predominant pattern (71%), which is also consistent with the various DUS already conducted in India. In study conducted by Parkash J. *et al*¹² in the Neonatal Unit of National Institute of Child Health, Karachi, Pakistan from 1st January 2001 to 31st December 2001 showed 62.1% males. In another study conducted by Vaghela JP. *et al* in NICU of Guru Gobind Singh government Hospital, Gujrat from December 2013 to November 2014 showed 56% of the admissions were male.¹² Almost all DUS studies shows the same results of male predominance in the country mainly due to more access of medical services to male gender.

In our study patient predominance was maximum in preterm (67%) followed by term (32%) and post term (1%). Our results were in resemblance with other studies conducted in India. In a study conducted by Vaghela JP. *et al* in NICU of Guru Gobind Singh government Hospital, Gujrat from December 2013 to November 2014¹³ showed 56% admitted neonates were preterm. In another study conducted by Chaunakar SA. *et al* in NICU of a tertiary care hospital in Mumbai from July 2014 to March 2015 indicated 54.8% of admissions were preterms.⁸ These indicating that preterm are more prone for admission in NICU than the term and post term neonates because preterm neonates require more medical care as compare to term.

In pattern of disease, 94% preterm and 68% term patients were admitted with RDS. In a study done by Uppal R *et al*. (study downloaded) in NICU of Kempegowda Institute of Medical Sciences, Bangalore in 2016 indicated most common reason for admission was neonatal sepsis (n=33), and the other common reasons were preterm (n=26), birth asphyxia (n=25) and respiratory distress syndrome (RDS) (n=23).¹⁴ In another study conducted by Choure MK *et al* in year 2014 in in NICU of Government Medical College, Maharashtra elaborated common neonatal factors were preterm low birth weight (LBW) (39%), neonatal sepsis (24%), birth asphyxia (11%), meningitis (6%), and others (20%) and¹⁵. Pattern of results in our study was different from other studies as prevalence of disease in new born population depends on aseptic practices followed during delivery and early child raising.

Average length of stay of patients in our study in NICU is 11.2 days in preterm and 7 days of term patients. These results were comparable to the study conducted by Warriar et al. in Hutzel Women's Hospital (HWH) in Detroit between January 1997 and June 2004, which was 15 days. Similarly, study conducted by Vaghela JP at Guru Gobind Singh Government Hospital, Gujarat showed the results of average stay is 15 days.¹² It was slightly less in our study because of leaving against medical advice (LAMA) and discharge on request (DOR) or death of patients.

In drug prescribing pattern, average number of drugs prescribed to pre-term (2.7) were much higher than the term (2.01) patients. The antibiotics play a major role in this as most of the patients admitted were suffering from RDS and antibiotics play a major role in prophylaxis of infections in NICU. The most commonly used antibiotic was amikacin (aminoglycoside 67%) then followed by cefotaxime (cephalosporin 35%) and the most common combination prescribed among the antibiotics was of amikacin and cefotaxime which is also the cheapest among the antibiotics. These results were almost similar to the study of Amin AJ *et al* in the neonatal intensive care unit (NICU) at Sir Sayajirao Gaekwad Hospital, Vadodara from April 1st to September 31st, 2013.¹²

In European RDS treatment guidelines 2016 recommend the antibiotics are often started in babies with RDS until sepsis has been ruled out, but policies should be in place to narrow the spectrum and minimize unnecessary exposure. A common regimen includes penicillin or ampicillin in combination with an aminoglycoside¹⁶. Antibiotics should be stopped as soon as possible once sepsis has been excluded, which matches our finding of the study. So, this study in our hospital shows that major of the RDS neonates were exposed to combination of two most preferred drugs for the treatment of RDS.

In 2003 the American Academy of Pediatrics recommended that vitamin K1 should be given to all neonates as a single, intramuscular dose of 0.5 to 1 mg, and this recommendation was recently reaffirmed in 2009^{17,18}. In our study second most common drug prescribed other than antibiotics is vitamin K (48%) which acts as predominant pro-coagulant. This is general practice to give vitamin-K as prophylaxis dose in new born. Some patients were also given respiratory stimulants.

This study also showed that only the 46% of patients were provided supportive treatment along with main treatment with anti-emetics, ant-acids, steroids and supplements, which also plays an important role in patient welfare.

A study conducted in Mumbai showed the average cost of hospitalization per neonate was 7383 INR. As preterm (<37 weeks) and low birth weight (<2.5 kg) neonates were exposed to significantly higher number of drugs, had longer hospital stay with overall cost of treatment compared to full term neonates ($P < 0.05$), The average cost of antibiotics prescribed per patient in our hospital was 263.149 ± 295.971 which is lower as per compared to another study⁸. Main reason of this can be included to non-affordability of parents. But our study results⁸ were consistent to other studies that the average treatment cost is higher in preterm than term and then post term individuals.

The strength of our study is that it targets the drug utilization of three comparison groups especially in RDS with relevance

of antibiotics. Our study further explores the cost effectiveness of the treatment. The main limitation of our study was, it was short duration, conducted in 100 patients and in one center. More such studies should be conducted so that we can have drug utilization pattern in more patients which will generate more evidence in rational management of RDS.

CONCLUSION

In this study, we provide detailed and unique overview of drugs which are commonly used in patients admitted in NICU in northern hospitals. The data collected showed various similarities and important differences of drug usage and especially their pattern of usage in the hospital. As majority diseased population is RDS in preterm, so emphasis of our study was on the RDS group of patients and their drug use. Furthermore, as the antibiotic usage is more common and large number of antibiotics were prescribed, so pharmaco-economic analysis of antibiotics was done to find out cheapest and most effective therapy.

To summaries, there is lot of scope available for the further studies on this subject to improve and to rationalize the treatment of patients with special consideration to the cost effectiveness as there is scarcity of resources in our developing country.

Funding/conflict of interests/ethical approval

Our study was not a sponsored study. There were no conflict of interests and the ethical approval was from the institutional ethical committee.

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