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Evaluation of Antibiotic Prescription Pattern in Special Newborn Care Unit (SNCU) of Tertiary Care Teaching Hospital

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Abstract

Antibiotic prescription pattern analysis in a hospital setting is critical to the sensible use of drugs. To reduce overall mortality and morbidity, rational antibiotic usage necessitates effective clinical and laboratory teamwork. In light of this, the pharmacology department undertook a two-year prospective observational study in collaboration with the Special Newborn Care Unit (SNCU) of a tertiary care hospital in Cuttack, Odisha. 239 prescriptions were examined for the rationale and duration of antibiotic treatment. Poor feeding was the most prevalent reason (137) for starting antibiotics in neonates. Ampicillin (91.4%) and Cefotaxime (61.8%) were the most widely utilized antibiotics for both early and late-onset sepsis. The average number of antibiotics used per prescription was 2.5; on quantification, the use of Ampicillin (251.9) was highest in days of therapy. The majority (77.9%) of the patients recovered without sequela. The most common adverse drug reaction (ADR) was increased serum creatinine (2.09%).

Keywords: Antibiotic, EOS, LOS, Neonates Sepsis, Prescription Pattern, WHO-UMC.

Introduction

The fragile physiologic system, greater bacterial exposure, and insufficient immunity in neonates make them susceptible to a higher risk of bacterial infections (1). Septicemia is the main cause of neonatal mortality worldwide (23.4%), and in India, two-thirds of neonatal deaths occur during the first month of life (2, 3). Neonatal sepsis can be classified into two categories based on presentation time: early-onset sepsis (EOS) and late-onset sepsis (LOS). Sepsis is classified as early if it occurs within 72 hours of life and late if it occurs after 72 hours (4). Newborns admitted to a Special Newborn Care Unit (SNCU) receive antibiotics for infections or suspected infections (2). However, recent studies from India and abroad highlight concerns about non-adherence to approved antibiotics, leading to indiscriminate and irrational use of antibiotics among neonates. This has in turn led to increased physical, mental and financial burdens for patients and their families. For the global and Indian community looms a larger threat in the form of rising antibiotic resistance due to this irrational use of antibiotics (3, 5, 6). In the majority of investigations on newborn sepsis, antibiotics were the most commonly recommended medicine. The drug consumption trend was comparable across most areas and nations, with antibiotics being the most commonly utilized in all reports (7). Since newborn sepsis, including meningitis, accounted for 16% of neonatal mortality worldwide in 2015, the widespread use of antibiotics was not surprising (8). Empirical antibiotic use in preterm infants was based on sensitive but nonspecific clinical diagnosis of possible infections to avoid a high risk of death and poor outcomes, and antibiotics were given to clinically healthy infants who were born with risk factors for early-onset sepsis. The selection pressure exerted by widespread antibiotic use is unfortunately driving antimicrobial drug resistance (8). Though the problem is global but unevenly distributed, data from high-income countries such as the United Kingdom show that 95% of pathogens are susceptible to the most commonly used empirical antibiotic regimen, whereas up to 70% of pathogen isolated in neonatal sepsis may be resistant to the recommended first-line regimen in low- and

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middle-income countries (9). Many newborns in South Asian hospitals received carbapenems as first-line treatment for sepsis or suspected sepsis (10). Our findings also reflect the increased usage of antibiotics such as third-generation cephalosporins, meropenem, and tazobactam, which is consistent with studies from Asia and Latin America. A South Asia study analysis found that 50–88% of frequent isolates from health facilities for neonatal sepsis were resistant to first-line antibiotics such as ampicillin, gentamicin and cefotaxime. However, susceptibility to antibiotics on the WHO "watch list," such as meropenem and vancomycin was observed (11). All of these suggest that antibiotic resistance is a complicating factor in neonatal sepsis due to broad availability and antibiotic usage in neonates, and our awareness of this becomes critical. Rather than increasing the use of antibiotics, infection control strategies such as hand cleanliness, surveillance cultures, contact precautions, and antibiotic stewardship should be implemented (12). So we carried out a study to analyze the current prescribing pattern of antibiotics for neonates admitted to SNCU of our setup.

Methodology

A prospective observational study was conducted at the pharmacology department in collaboration with the SNCU of the pediatrics department at a tertiary care institution in Cuttack, Odisha. The study period was 24 months (1st November 2018 to 30th October 2020). Before including any neonates in the study, ethical approval was obtained from IEC/IRB (IEC application no.26/07.02.2020) S.C.B MCH, Cuttack, and from parents written informed consent was taken. In case the parent was illiterate, a witness was present to ensure that they understood the details of the study. For inclusion, neonates of either gender, aged 0-28 days, who were admitted to the SNCU and had at least one antibiotic prescribed by the treating physician were considered. Neonates receiving antiviral, antifungal, with neonatal jaundice receiving phototherapy, any congenital anomaly, surgical disorder, cancer or post-operative neonates admitted to SNCU on oxygen therapy were excluded from the study.

1200 neonates were screened and 403 neonates were found to be eligible according to our inclusion criteria (Figure 1). Sampling was purposive, and 1-2 days a week were fixed by the paediatrician according to their fixed admission days for maximum recruitment and inclusion of eligible neonates admitted to SNCU on those days. Once recruited, neonates were followed up either till discharge, leave against medical advice (LAMA), or death. The researcher visited the SNCU as often as required to keep complete track of the medications being used by every recruited subject. After the initial visit, baseline demographics such as patient age, sex, weight, mode of birth, presenting clinical symptoms, period of hospital stay, indications for antibiotic received, culture and sensitivity report, and if any suspected ADRs developed were recorded and analyzed for 24 months. Frequencies of prescribing of antibiotics belonging to different classes were recorded and drug utilization was measured in DOT/1000 patient days (13). Data were captured in a structured case report form.

Suspected ADR reporting forms by the Indian Pharmacopeia Commission –National Coordinating Centre (IPC-NCC) were used to note down if any adverse drug reaction occurred. ADRs were assessed for causality and severity using the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) Scale and Hartwig's severity scale, respectively. Safety analysis was done for all participants. Microsoft Office Excel 2016 was used to analyze data using the Statistical Package for Social Sciences software (SPSS version 20.0, IBM SPSS Inc., Chicago, IL). Numbers & percentages were used to express qualitative data and mean was used to express quantitative data.

Results

Out of the total 239 neonates, male neonates (120;50.2%) were higher than females (119;49.7%). The most common age group for SNCU admissions were pre-term (170;71.1%) than term (69;28.8%) neonate. Out of 119 female neonates, 63.8% belong to LBW as compared to 120 male neonates 58.3% belong to LBW. The proportion of neonates admitted into SNCU mostly belongs to inborn (219;91.6%) as compared to outborn (20;8.3%). Out of the total 239 neonates admitted more cases were of early-onset sepsis (163;68.2%) as compared to late-onset sepsis (76;31.7%). The most common diagnoses that necessitated admission of neonates to SNCU were low birth weight (195; 81.5%) and prematurity (177; 74%). Poor feeding/sucking (137 nos) in neonates and leaking per vagina (31 nos) in mothers were the most common clinical signs for

using antibiotics in SNCU. Among the total patients (239) the most common indication for antibiotic usage was necrotizing enterocolitis(NEC) (110;46%) followed by bloodstream infection(BSI) (51;21%). The most commonly used antibiotics were penicillin (83.6%), aminoglycosides (77.4%), and cephalosporin (32.6%). Ampicillin was used in the maximum number of patients (175;73.2%), followed by gentamicin (165;69%) and cefotaxime (78;32.6%). In patients with NEC & BSI most commonly used antibiotics were ampicillin, amikacin, gentamicin & cefotaxime. Piperacillin-Tazobactam was the most commonly used fixed-dose combination (25; 10.4%), given frequently based on empirical therapy as well as in conditions where Klebsiella, Enterobacter and Pseudomonas were isolated from culture. Blood culture reporting takes 72 hrs & was done in 36 (15.06%) patients.

In Table 1 DOT (Days of therapy) metric of the study confirmed that the use of ampicillin (251.9) was the highest, followed by amikacin (185.6), gentamicin (181.9) and cefotaxime (136.7) in DOT/1000 patient days. In 50% of cases the frequency of antibiotic usage was once daily with the mean duration of antibiotic usage among patients was 9.72 days

Table 2 shows that while doing outcome analysis, the frequency of recovery without sequel and referral was the highest with EOS i.e. (127;77.9%) and (15;9.2%), respectively. Death in neonates was mostly associated with EOS (4;2.4%).

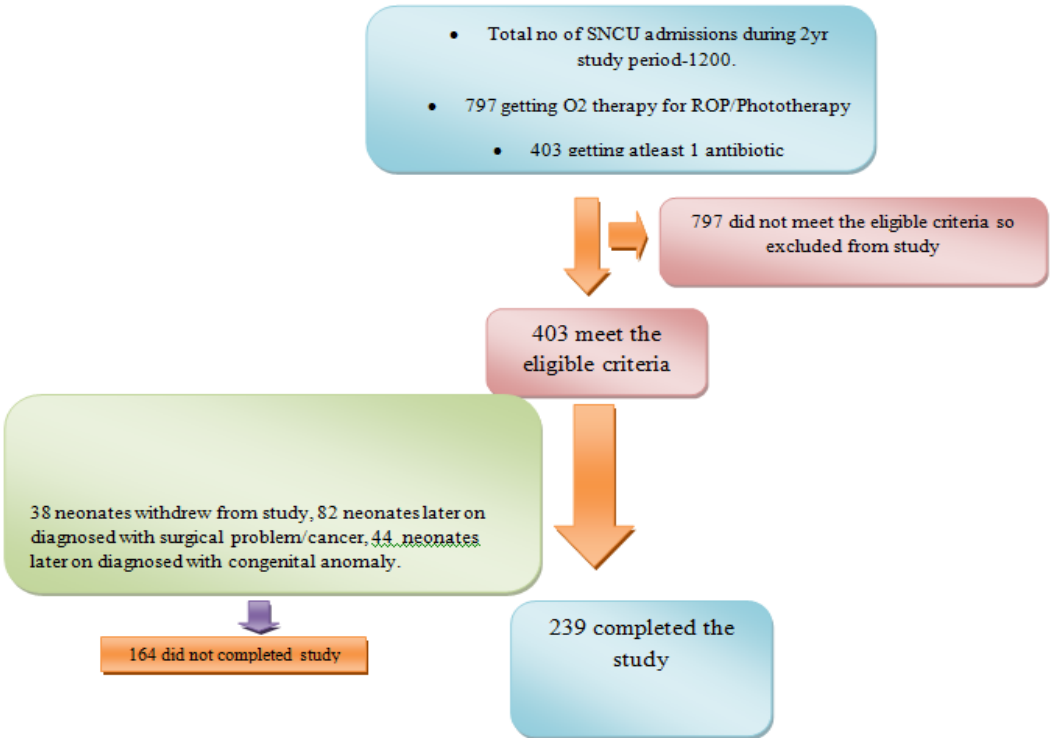

Figure 1: Study Plan

Table 1: Quantification of Antibiotics Used in SNCU in Days of Therapy (DOT*)

Antibiotic used	DOT*	DOT/1000 Patient days	Percentage use
Ampicillin	954	251.9	23.1%
Amikacin	703	185.6	17%
Gentamicin	689	181.9	16.7%
Cefotaxime	518	136.7	12.5%
Vancomycin	305	80.5	7.4%
Meropenem	301	79.4	7.3%
Linezolid	178	47	4.3%
Piperacillin+Tazobactam	169	44.6	4.1%
Colistin	112	29.5	2.7%

Table 2: Outcome of Neonates in Different Types of Sepsis

Outcome	Frequency in EOS (%age)	Frequency in LOS(%age)
Recover without sequel	127(77.9%)	46(60.5%)
Referal	15(9.2%)	11(14.4%)
LAMA	17(10.42%)	19(25%)
Death	4(2.4%)	0

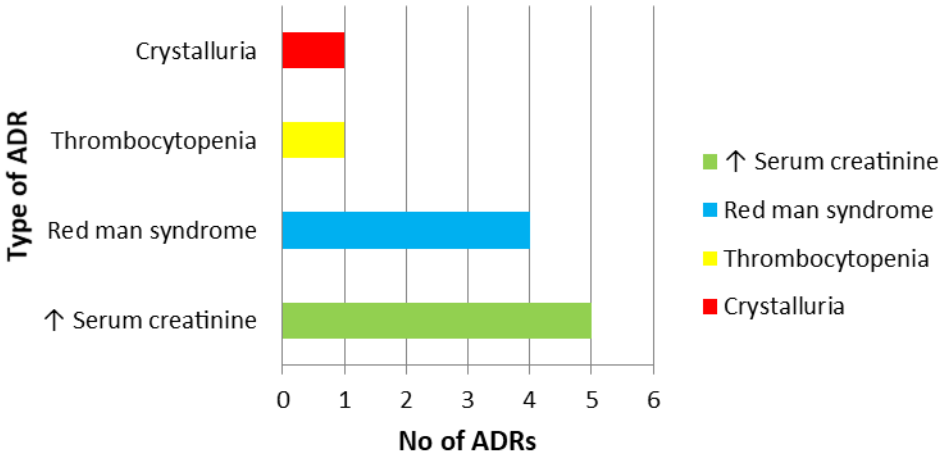

Figure 2: ADR Reports Obtained in the Study

Figure 2 shows out of 239 cases (11; 4.6% of patients) had adverse drug reactions (ADRs). Raised serum creatinine was the most commonly reported ADR (5; 2.09%), followed by Red Man syndrome (2; 0.9%). The class of antibiotics responsible for such ADRs could be the beta-lactam/glycopeptide group. 72.7% of ADRs were possible and 45.4% were probable according to WHO-UMC Scale. ADRs were mostly mild to moderate with death occurring in 4 neonates (2.4%) with Early-Onset Sepsis (EOS).

Discussion

According to Zini *et al.,* the antimicrobial stewardship program reduced antibiotic exposure to culture-negative sepsis and the course of medication soon after birth. Several techniques are being promoted to optimize antibiotic use in LBW newborns with culture-negative sepsis. According to the strategies, the antimicrobial stewardship team was involved in daily decision-making, and staff members had frequent discussions about clinical cases (14). Increased reliance on sterile cultures and cases of culture-negative sepsis were reduced by neonatologists' typical policy of withdrawing antibiotics when cultures proved sterile (48 hours after collection) (15). Without increasing mortality, antibiotic exposure was reduced (14). Zini *et al.,* sought to reduce antibiotic exposure and the potential for antimicrobial resistance in fragile ELBW and VLBW newborns while also offering enhanced and prompt protection in cases of severe sepsis and septic shock. Antibiotic exposure was reduced without increasing mortality, although overall sepsis cases did not decrease between the "intervention" and "maintenance" periods. When antibiotic courses to rule out sepsis were reduced, no sepsis-related deaths occurred during the "maintenance period" (14). In our study, the most common diagnoses and clinical signs that required the start of antibiotic treatment were poor feeding (137 nos), lethargy (112 nos), poor crying (89 nos) and leaking per vagina (31 nos) in mothers. Suryawanshi *et al.,* Galhotra *et al.,* and Shinde *et al.,* were having similar findings (16-18). Our study also found that the most commonly used empirical therapy for early-onset sepsis was ampicillin (91.4%) followed by gentamicin (85.2%). Cefotaxime (61.8%) followed by ampicillin (34.2%) and gentamicin (34.2%) were commonly used for late-onset sepsis, findings are similar in earlier studies by Suryawanshi *et al.,* and Galhotra *et al.,* (16, 17). Our study found that Piperacillin+Tazobactam (10.4%) were the most commonly used antimicrobial agent as a fixed-dose combination. Based on past institutional antibiogram records of culture-proven newborn sepsis, we selected this

combination as the empirical regimen, with pseudomonas, Klebsiella, and enterobacter being the most common isolates. This is in contrast to the study by Das *et al.*, where the most commonly used empirical regimen was Piperacillin+Tazobactam for Escherichia coli and Group B Streptococcus (18, 19). We did not lose any neonates from late-onset sepsis, whereas 2.4% of neonates died in the early-onset sepsis group. According to Kamble and Ovhal (17), the mortality rates for early-onset and late-onset sepsis are 29.6% and 12.06%, respectively. The most commonly used antibiotic agents were ampicillin, followed closely by gentamicin and amikacin similar to the findings of the Scout study (20). Penicillins and aminoglycosides were among the most commonly prescribed antibiotics in hospitalized babies, according to Turkait *et al.,* (7), Allegart *et al.,* 2019 (21), and Rosli *et al.,* 2017 (22). In our setup when there is a suspicion of severe sepsis the physician starts with broad-spectrum antibiotics & waits for culture reports. But if suspicion is less than severe sepsis then the physician starts with antibiotics depending upon clinical condition (empirical therapy), later on, antibiotics are changed depending upon culture sensitivity reports if there is no improvement in clinical condition occurs in the next 48 hours. Also, antibiotics are changed depending on the development of new clinical symptoms. The shift in antibiotics had no statistically significant effect on morbidity and mortality. The most commonly reported adverse drug reaction was a rise in serum creatinine levels (2.09%) in contrast to maculopapular rash (50%) being the most common due to vancomycin injection in Chabhadiya *et al.,* (23). According to the WHO UMC causality evaluation scale, the majority of the adverse medication responses were in the probable (72.7%) group.

Conclusion

Antibiotics were widely used in the SCB Medical College and Hospital's SNCU. It was observed that more than 50% of SNCU patients were given two or more antibiotics. Penicillins, aminoglycosides and cephalosporins were most frequently prescribed as first-line treatment for sepsis. The study also points out that the organisms isolated at SNCU had developed resistance to penicillin & cephalosporins which were managed with piperacillin/tazobactam and meropenem. However, on comparing the total government price versus the market price of these alternatives they were found to be quite expensive. This increased our health care costs & burden on the patients. Therefore it is necessary not only to prepare but also implement and strictly follow an institutional antibiogram report, do a serum drug level measurement, establish a 48 hour rule out sepsis policy and institutional antibiotic stewardship team in our set up to rationalize antibiotic usage.

Abbreviations

SNCU: Special newborn care unit
ADR: Adverse drug reaction
DOT: Days of therapy
EOS: Early onset sepsis
LOS: Late onset sepsis
LAMA: Leave against medical advice
IPC-NCC: Indian pharmacopeia commission-National coordinating centre
WHO-UMC: World Health Organisation-Uppsala Monitoring centre.

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Author Contributions

PP, SP, RU and SM: Conceptualizes the methodology. PP, SP RU: Performs data collection, validation, preparation and analysis. PP, SP RU and SM: supported the scientific discussions. RU and SM: Supported the validation and preparation of the final manuscript. All the authors contribute to the final manuscript.

Conflicts of Interest

Nil.

Ethics Approval

Ethical approval was obtained from IEC/IRB (IEC application no.26/07.02.2020) S.C.B MCH, Cuttack.

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