

EVALUATION OF ANTIBIOTIC PRESCRIPTION PATTERN IN NEONATAL INTENSIVE CARE UNIT OF A RURAL MEDICAL COLLEGE HOSPITAL.**¹Dr. Prashant Wadagbalkar, Dr. Swati Raipurkar, ³Dohare Nagesh, ⁴Saurabh Singh, ⁵Amritesh Ranjan**¹Professor and Head, Department of Pharmacology, RKDF Medical College Hospital & Research Center, Bhopal, MP, India.²Professor and Head, Department of Paediatrics, Index Medical College Hospital & Research Centre, Indore, MP, India.^{3,4}PG Resident, IMCHRC, Indore, MP, India.⁵PG Resident Department of Paediatrics, IMCHRC, Indore, MP, India.**Corresponding Author: Dr. Prashant Wadagbalkar**

Professor and Head, Department of Pharmacology, RKDF Medical College Hospital & Research Center, Bhopal, MP, India.

Article Received on 10/07/2016

Article Revised on 30/07/2016

Article Accepted on 20/08/2016

ABSTRACT

Neonates are most vulnerable to infections, due to which there is high mortality and morbidity. Antibiotics are the commonest drugs used in NICU, empirically, rationally or irrationally. This is a retrospective study over the period of 6 months from May 2015 to November 2015. Clinical, haematological, microbiological, biochemical, radiological & therapeutic data was collected, analyzed and evaluated from case papers from NICU. Drugs (antibiotics, dose, duration) was noted. **Result:** out of 200 patients 127(63.5%) were treated rationally. Amikacin and Cefotaxime were commonest AMAs used. **Conclusion:** Antibiotic prescription policy be formulated and displayed in NICU, to promote rational prescription, to reduce the emergence of resistant strains and cost of treatment.

KEYWORDS: Clinical, haematological, microbiological, biochemical, radiological & therapeutic.**INTRODUCTION**

Antibiotics are the greatest contribution of the 20th century to therapeutics. Their advent changed the outlook of physicians about the power, drugs can have on diseases. As a class, they are one of the most frequently used as well as misused drugs(1). They are like double edged sword, i.e. if misused will lead to emergence of microbial resistance and increase in the cost of treatment.. In NICU, antibiotics are the most commonly prescribed medicines, since sepsis is the main cause of neonatal mortality accounting to many neonatal deaths worldwide(2). Sepsis in newborn has varied presentations ranging from dullness, not accepting feeds, to seizures and sclerema. There are many other conditions mimicking sepsis e.g. congenital adrenal hyperplasia and Inborn errors of metabolism, both of which are uncommon. In fear of sepsis, very frequently, the neonatologists start antibiotics prophylactically and empirically, in spite of the culture being negative. Use of third generation cephalosporins or third line antibiotics as per the protocol given in the table 1 as well as improper doses for prolonged duration lead to emergence of resistant strains like MRSA and fungal infections etc. This made the paediatricians and pharmacologists think about reviewing the protocols and see for the antibiotics being used, growth resistant strains causing late onset septicemia leading to Neonatal deaths.

AIM of the study

The aim was to record the antibiotic prescribing patterns and to compare them with current antibiotic policy. table 1(14).

The objective was to know antibiotics commonly used and antibiotics used out of the protocol, for what duration, and outcome of patients receiving multiple antibiotics.

MATERIAL AND METHODS*Inclusion criteria:*

Patients admitted in our nursery were included in our study.

Exclusion criteria :

Those patients who did not receive antibiotics were excluded,

Study design:

Retrospective study

Duration of study:

6 months

Following the increased incidence of late onset septicemia, sclerema, thrombocytopenia and use of higher antibiotics, a retrospective study was planned & conducted by paediatricians and pharmacologists. The study was conducted in the NICU of Index Medical College Hospital and Research Centre, a rural medical

college near, Indore MP India. The NICU is a 20 bedded unit which includes the out born nursery, Inborn nursery, septic newborn nursery and stepdown nursery.

An ethical committee approval was obtained from institutional ethical committee.

Sample size

Total of 200 newborns were admitted to NICU during the 6 months study period from 1st May 2015 to 30th November 2015. The case sheets of these patients were

retrospectively reviewed to determine the antibiotic prescribing patterns.

Data collection

Patient demographics (gestational age, sex, birth weight), maternal factors like leaking, hypertension, Diabetes mellitus & septic screen were recorded. The following was recorded to evaluate the antimicrobial prescribing patterns, name of the drugs used, duration of drugs, evidence of sepsis, duration of stay in hospital, antimicrobials prescribed according to/against the NICU protocol.

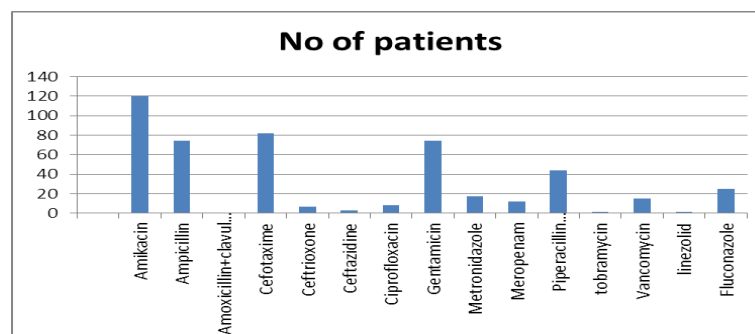
Table 1(15) Antibiotic policy

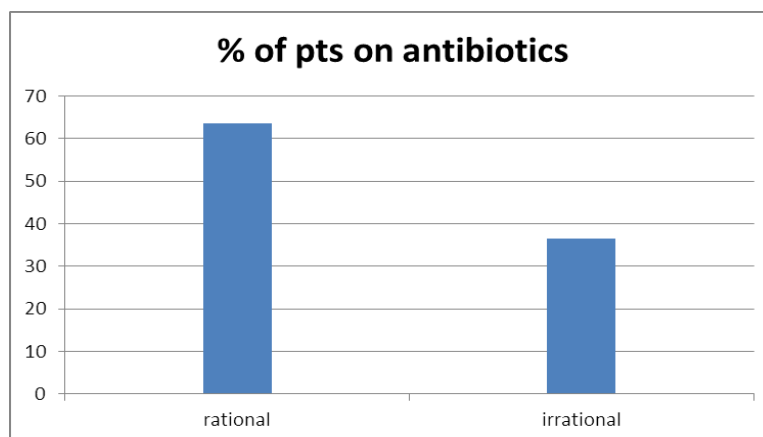
Description	Antibiotic (dose & duration)
Duration of empiric antibiotic therapy	Treat for 7 days (stop antibiotics if cultures are reported negative, exception in meningitis)
First line therapy	Amikacin, 15- 20 mg/kg daily IV/Gentamicin 4mg/kg IV
	Ampicillin 50-100mg/kg per day IV/cefotaxime 50 -100 mg/kg IV/Amoxi clav 30-50 mg/kg IV
Second line therapy	Piperacillin/tazobactam 125mg/kg per dose IV
Third line therapy	Meropenam 20-40 mg/kg per day in divided doses
Fourth line therapy	To be discussed with consultant
	Ciprofloxacin 10-20mg/kg per day in 12 hourly
Necrotising enterocolitis	Metronidazole 10mg/kg per day
Fungal infections suspected in cases not responding to antibiotics, thrombocytopenia, urine for fungus positive	Fluconazole

Table 2 (antibiotic prescribed, number of patients and duration of antibiotics)

S no	Antibiotic agent	In antibiotic policy	No of patients	Duration of use		
				minimum	maximum	Average
1	Amikacin	Yes	120	5	10	
2	Ampicillin	Yes	74	3	10	
3	Amoxicillin+clavulonic	Yes	01	5		
4	Cefotaxime	Yes	82	3	10	
5	Ceftriaxone	Yes	07	3	14	
6	Ceftazidime	No	03	7	15	
7	Ciprofloxacin	Yes	08	3	14	
8	Gentamicin	Yes	74	3	10	
9	Metronidazole	Yes	17	10	10	
10	Meropenam	Yes	12	5	14	
11	Piperacillin +tazobactum	Yes	44	3	12	
12	Tobramycin	No	01		05	
13	Vancomycin	Yes	15	5	10	
14	Linezolid	No	01		07	
15	Fluconazole	No	25		10	

RESULTS





Out of 230 patients admitted to NICU, 200 patients were prescribed antibiotics, 30 patients did not receive antibiotics and were, therefore excluded from the study.

Out of the 200 patients who were prescribed antibiotics, 197 patients,(98%) received antibiotics according to the protocol, while 5 of the 200 patients(2.5%) were prescribed antibiotics which were not in the antibiotic policy.

Out of 200 neonates 108 were males 92 were females.

Mean age was 5.6 days.

Mean gestational age was 36 weeks.

Mean birth weight was 2.2 kg.

Average duration of stay in hospital was 8.5 days.

Number of AMAs per neonate 2.125

Among 200 patients, 49 patients(29.5 %) received antibiotics for 10 days or more, while 19(9.5%) patients received 5 or more than 5 antibiotics during the stay who were having fulminant sepsis.

The most commonly prescribed antibiotics was Amikacin in 120 patients (60%), Cefotaxime in 82 patients(41%), Ampicillin and gentamicin in 74 patients(37%). In similar studies these AMAs were used in 44, 87,17 patients respectively.^[15]

These all were considered as first line antibiotics.

Second line antibiotics, piperacillin plus tazobactam were given to 44 patients (22%). similarly in the other study done it was used in 30 patients.^[15]

They were given according to antibiotic protocol to those patients, who had pneumonia and other signs of sepsis, (CRP positive, neutropenia, thrombocytopenia, blood culture positive).

Third line antibiotics eg, Meropenam were prescribed in 12 patients (8%) whose blood culture showed resistant strains or had signs of fulminant sepsis eg. Sclerema, necrotizing enterocolitis & meningitis while Vancomycin and Metrogyl was given to 15 and 17 patients respectively, in cases of MRSA infections and NEC. While study done at Punjabrao Deshmukh medical

hospital Amravati showed use of Meropenam and Vancomycin in 19 and 11 out of 118 patients, which is similar with our findings.^[15]

60% of patients showed signs of sepsis,(CRP positive, necrotizing enterocolitis, pneumonia meningitis, sclerema, thrombocytopenia, neutropenia) while 40% did not show any signs of sepsis but were given antibiotics prophylactically or empirically .

Out of 200 patients 21 had sclerema, 32 had pneumonia, 3 patients had meningitis,13 patients had NEC, while 58 patients had CRP + but without any complications, All these patients received rational antimicrobial therapy. remaining 73 patients received prophylactical and empirical antibiotics

DISCUSSION

The main aim of this study was to evaluate prescribing pattern of antibiotics against the existing protocol so as to know the use of irrational antibiotics and their effect on the emergence of resistant bacterial strains and Candidiasis^[4].

WHO defines rational drug therapy as “Patients receive medication appropriate to their clinical need, in doses that meet their individual requirement, for an appropriate period of time, and at the lowest cost to them and their community “(WHO 1985)(12). But it does not include laboratory investigations. Ideally it is considered rational if clinical diagnosis is supported by hematological and microbiological data.^[12]

In our study we focused on the rational drugs accordingly to the protocol, duration of drugs, doses and empirical drugs used in certain circumstances.

Out of 200 patients only 5 patients were administered antibiotics, which were not included in the protocol. Ceftazidime was given to 3 patients whose blood culture revealed Pseudomonas growth showing sensitivity for ceftazidime. While only one patient was given tobramycin with multidrug resistant E.coli.

Linezolid was given to 1 patient who had fulminant sepsis not responding to any antibiotics.

Maximum duration of antibiotics was 15 days. While out of 14 antibiotics 11 antibiotics were used for maximum of 10-14 days.

Antibiotic policy is used in NICU and deviation from policy is indicated in special clinical conditions. These deviations should be guided by cultures, clinical presentations and other parameters of sepsis^[5,6,7]

Use of third line antibiotics should have a reason to start them in special conditions eg., signs of severe septicemia (sclerema, pneumonia, meningitis, NEC), blood culture indicating the use of such higher antibiotics and in septicemic patients on first and second line antibiotics not responding to them.

Before starting the antibiotics, many preventive aspects of (key points) can be taken into consideration to reduce the sepsis & restrict antibiotics.

KEYPOINTS^[8,9,10,11]

1. hand washing in 6 steps
2. detailed history of Mother regarding leaking, sepsis, or other comorbid conditions.
3. to know vaginal bacterial flora by doing vaginal swab culture and sensitivity
4. do not use prophylactic antibiotics
5. consider carefully whether antibiotics are really needed or not
6. Avoid broad spectrum antibiotics.
7. Always do blood culture, especially in doubt of sepsis.
8. Avoid cefotaxime and other betalactam drugs .
9. Obtain blood culture at 36 to 48 hours and 7 days of life.
10. Shorten duration of treatment.
11. Stop antibiotics when no infection is evident at 36 to 48 hours.
12. Treat late onset septicemia for Gram Negative infections and wherever possible wait for culture reports before treating Gram Positive infection.
13. See whether sepsis is early onset or late onset and then start antibiotics empirically.

CONCLUSION

Antibiotics are very important drugs. They should be administered in neonatal units with great precautions, taking into account gestational age, weight on admission, severity of infection, assessed by haematological data, x-ray, microbiology data.

Judicious use of AMAs and incidence of sepsis can be minimized by forming an antibiotic policy which should be displayed in NICU.

In our case, Antibiotics were used according to the ward Protocol in majority of cases. Although indication for

most of the antibiotics could be justified the prolonged use of some antibiotics was a cause of concern. Also in patients who did not show any signs of septicemia, antibiotics could be stopped earlier. The prolonged use of antibiotics, and use of broad spectrum antibiotics like cefotaxime in unindicated patients may lead to development of sepsis due to resistant strains and candidiasis. There is a need to review the antibiotic policy and do such studies regularly to prevent the patients from receiving prophylactic antibiotics for longer duration.

Funding: Nil

Conflict of interest: Nil

Permission from IRB: Yes

REFERENCES

1. Tripathi KD, Antimicrobial drugs :general considerations, In essentials of Medical Pharmacology, 7th ed. New Delhi, Jaypee publishers, 2013; 688.
2. Depani SJ, Ladhani S, Heath PT, Lamagni TL, Johnson AP, Pebody RG, et al. The contribution of infection to neonatal deaths in England and Wales., *Pediatr Infect Dis J.* 2011; 30(4): 345-7.
3. Stoll BJ, Hansen NI, Sanchez PG, Faix, RG, Poindexter BB, Van Meurs KP, et al. Early onset neonatal sepsis; the burden of group B streptococcal and E. coli disease continues, *Pediatrics.* 2011; 127(5): 817-26.
4. Gould IM. A review of the role of antibiotic policies in control of antibiotic resistance . *J Antimicrob Chemother* 1999; 43: 459-465.
5. Rodriguez D, Almirante B, Park BJ, et al, Candidemia in neonatal intensive care units; Barcelona , Spain, *Paediatr Infect Dis* 2006; 25(3): 224-229.
6. Chapman RL , candida infections in the neonate, *Curr Opin Paediatr*, 2003; 15: 97-102
7. Chapman RL. Prevention and Treatment of Candida infection in neonates. *Semin Perinatol*; 2007; 31(1): 39-46.
8. National Centre for Infectious Diseases CfDC. Prevention of Perinatal Group B Streptococcal Diseases; Revised Guidelines from CDC. *MMWR* 2002; 51(RR11): 1-22.
9. Jardine L, Davies MW, Faogali J. Incubation time required for neonatal blood cultures to become positive. *J Paediatr Child Health* 2006; 42: 797-802.
10. Jardine LA, Sturgess BR, Inglis GD, Davies MW. Neonatal Blood Cultures; effect of delayed entry into blood culture machine and bacterial concentrations on time to positive growth in a stimulated model. *J Paediatr Child Health* 2009; 45: 210-214
11. Karlowicz MG, Buescher ES, Surka AE. Fulminant late onset sepsis in a neonatal intensive care unit, 1988-1997; and the impact of avoiding empiric vancomycin therapy, *Pediatrics*; 2000; 106: 1387-1390

12. Promoting rational use of medicines; core components, WHO Policy perspectives on Medicines, September 2002 WHO Geneva
13. Josiah Olusegun Alamu. Evaluation of antimicrobial use in a neonatal intensive care unit. University of Iowa Research Online 2009, <http://ir.uiowa.edu> assessed on 01-08-2014
14. Borade S, Ghodki S, Bhore, et al. Evaluation of antimicrobial pattern in NICU of tertiary care teaching hospital. *Int J Med Res Rev* 2014; 2(5): 474-479
15. N Schellack, AGS Gous, Antibiotic prescribing pattern in a neonatal intensive care unit, *South Afr J Epidemiol Infect* 2011; 2011, 26(4)(part III) page 267