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NEONATAL CARE UNIT ANTIBIOTIC THERAPY IN THE CHILDREN WELFARE TEACHING HOSPITAL

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ABSTRACT

Background: Antibiotics are commonly used medication in neonatal care units (NCU) as sepsis regard the main cause of neonatal morbidity and mortality, especially in preterm infants. Consequently, practitioners in NCU have to use empirical antibiotics. Frequently prescribe empirical antibiotics while awaiting culture results. Unfortunately, use of broad-spectrum antibiotics or prolonged treatment of empirical antibiotics may result in adverse effects including the emergence of antibiotic resistance microorganisms, prolonged hospitalization and increased cost. Narrow-spectrum antibiotics are effective in common neonatal pathogens. The aim of this study is to evaluate the implementing strategies for wise and scientific use of antibiotics. A cross-sectional method was performed to during the period from 1st of April 2017 to 28th of February 2018 in neonatal care (NCU) ward in Child Welfare Teaching Hospital. Results revealed that the most admitted neonates were male 66%, age of neonates at admission time mostly ≥7 days(67.5%) and around 64% with CRP positive, regard duration of treatment mostly more than 14 days(42.5%). Pathogens isolated 51.2% *Staphylococcus aureus*, *streptococcus spp.* 17.5% and *acinatobacter boumania* 15% respectively. Antimicrobial prescribed *Carbapenems(Meropenem)* 40%, *Glycopeptides(Vancomycin)* 37.5% and *Aminoglycosides (Amikacin)* 17.5%. Antibiotics are commonly prescribed in NICU and are lifesaving in most of a serious infection, in the other hand overuse of antibiotics has potential risk of negative effects to neonates. **Conclusions:** Most neonatal pathogens isolated by cultures are susceptible to narrow-spectrum antibiotics and common. There is high consumption of broad spectrum antibiotics in the NCU.

KEYWORDS: Antibiotic; Empirical; Neonatal care unit; microorganisms; Infection; culture.

INTRODUCTION

Antibiotic prescriptions in Neonatal Care Unit (NCU) is about 10 times that on other general hospital wards and, while this use is dictated by the seriously illnesses of patients in ICU, research suggests that mise/overuse contributes substantially.[1]

In developing countries, unwise use of antibiotics has become a common practice and rational where the prevalence of infectious disease burden is aggravated by uncontrolled access to antibiotics. In those countries, antibiotics are prescribed to 44-97% of patients in hospital, and are often unnecessary.[2] Use of antibiotics is fundamental but there over/misuse may result in serious adverse effect, development of wide range antibiotics resistance microorganisms, this set new threats to public health.[3] Once resistance has been established it will be difficult to treat and can't be reversible.[4] The challenging risk factor of clinically important now day is development of multi resistant antibiotic bacteria not only single resistant one.[5] High rate of empirical antibiotic exposure (75-95%) have been reported; as neonates with risk factors for developing infectious diseases or sick neonates frequently antibiotics prescribed as common practice, till culture and sensitivity results.[6] Analysis of antibiotic consumption in inpatients is basic data for assessment of therapy costs, assessment of bacterial resistance in hospital environments and innovation of drug policy.[6]

Strategies most be implemented for reducing the unwise use of antibiotics to prevent the possibility of development and spreading of resistant micro organisms. Neonatal sepsis presents during three periods:

Early onset sepsis (birth to 7 days) often begins in utero and usually is as result of infection caused by the bacteria in the mother`s genitourinary tract. Organisms related to this sepsis (*group B streptococci, E.Coli, Klebsiella, L,monocytogenes, and non typeable H. influenza.*

Late onset sepsis (8 to 28 days) *group B streptococci, staphylococcus aureus, gonococcus, candida albicans,*

E.coli, S.pneumoniae, Neisseria meningitides, H. influenza).

Nosocomially acquired sepsis (8 days to discharge) (coagulase –negative staphylococcal, fungi, enteric bacteria.[13]

MATERIALS AND METHODS

A cross-sectional study concentrated on the use of antibiotics in NCU. A data collected over period from 1st of April 2017 to 28th of February 2018 in neonatal care (NCU) ward in Children Welfare Teaching Hospital. Data collected from case sheets of all the neonates admitted to NCU and results of blood culture obtain during their residue and were positive (positively blood culture results), the data collected includes the acute phase reactant as C-reactant protein (CRP) results and cause of presentation, sex, age at time of presentation gestational age, antibiotic used and the duration of their using, and the type of antibiotics. Excluding those with incomplete data (no results of blood culture as it lasting around ten days) or those discharge on responsibility or incomplete treatment and results of culture and sensitivity are contaminated despite complete duration of treatment. In this study not all antibiotics resistance results are included, only those antibiotics are available and practically used in addition there's limitation in antibiotics disc for culture and sensitivity available in lab.

RESULTS

This study started from 1st of April 2017 to 28th of February 2018. The data included (80) neonates who admitted to NCU ward in Children Welfare Teaching Hospital. The results of blood cultured obtain positive, other data collected included gender, age, duration and type of antibiotic, and other lab. results CRP.

Most admitted neonates were males (66%), age of neonates at admission time mostly ≥7 days(67.5%) and around 64% were CRP positive, regard duration of treatment more than 14 days(42.5%). Blood cultures results of these neonates are (51.2%) *Staphylococcus aureus, streptococcus spp*. (17.5%) and *acinatobacter boumania* (15%) respectively.

Most of these pathogens obtain by culture response to narrow usual antibiotics that are available in NCU.

Table 1: Prevalence of *microbial according to cultured blood results.*

Isolate	Prevalence (%)
Staphylococcus aureus	41(51.2)
Escherichia coli	2(2.5)
Klebsiella pnemonia	7(8.8)
Acinatobacter boumania	12(15)
Strepto. spp	14(17.5)
Pseudomonas aregenosa	1(1.25)
Salmonella spp	1(1.25)
Serratia mrcesena	1(1.25)
Serratia plymathics	1(1.25)
Total	80(100)

Table 2: Univariable index, sex, age, CRP results, and the duration of treatments.

Variable		Frequency%
sex	Male	53(66)
	Female	27(34)
Age	< 7 days	26(32.5)
	≥7 days	54(67.5)
C R P	+ positive	64(80)
	-negative	16(20)
Duration of treatment		
< 7 days		18(22.5)
7-14 days		28(35)
> 14		34(42.5)

CRP C-reactive protein.

Table 3: Age at presentation, causative organisms according to culture and sensitivity, final cause of admission (according to case sheets).

Age at Presentation(n=80)	*Cause of Admission	Causative Organisms
< 7 days 26(32.5)	Septicemia 18	*Staphylococcus Spp 8*
		Streptococcus Spp 4
		Escherichia coli 2
		Klebsiella pneumonia 2
		Acinatobacter boumania 2
	Meningitis 8	*Staphylococcus Spp 1*
		Streptococcus Spp 7
≥7 days 54(67.5)	Septicemia 32	*Staphylococcus Spp 16*
		Streptococcus Spp 1
		Klebsiella pneumonia 3
		Acinatobacter boumania 8
		**Others 4*
	Pneumonia 13	*Staphylococcus Spp 9*
		Klebsiella pneumonia 2
		Acinatobacter boumania 2
	Meningitis 9	*Staphylococcus Spp 7*
		Streptococcus Spp 2

*Cause of admission according to final diagnosis in case sheet
*Others (*Salmonella spp, Serratia mrcesena, Pseudomonas aregenosa, Serratia plymathics)*

Table 4: Antimicrobial resistance according to culture and sensitivity, disc availability, suspected organisms and antimicrobial availability.

Antibiotic group	Antibiotic	Staph. resist	Strepto. resist	Acinatobacter resist	*Klebsiella resist*
Aminoglycosides	Gentamicin	3	4	-	-
	Amikacin	4	5	7	2
Cephalosporins	Cefotaxime	3	1	8	-
	Ceftriaxone	2	1	9	6
	Ceftazidime	-	-	5	3
Penicillins	Amoxicillin	7	-	-	-
	Ampicillin	50	11	1	3
Macrolides	Erythromcin	28	13	-	-
Fluoroguirolones	Ciprofloxacin	4	3	1	-
Carbapenems	Meropenem	1	-	8	-
	Imipenem	-	-	-	-
Glycopeptides	Vancomycin	1	-	-	-

- Not tested, not all antibiotic sensitivity result mention only available drugs.

Table 5: Antimicrobial used according to availability and suspected organisms.

Antibiotic group	Antibiotics	Frequencies (%)
Aminoglycosides	Gentamicin	2.5
	Amikacin	17.5
Cephalosporins	Cefotaxime	12.5
	Ceftriaxone	
Glycopeptides	Vancomycin	37.5
Fluoroguirolones	Ciprofloxacin	12.5
Carbapenems	Meropenem	40
	Imipenem	

Most antibiotics are used in combination so percentage more than 100%.

DISCUSSION

This study is an attempt on clarification the risk of mise/over use of antibiotics hence to prevent the emergence of antibiotic resistance microorganisms, prolonged hospitalization and decreased cost.[7]

The practice of antibiotic prescription in NCU appears to be based on how the practitioner in NCU, interpret, and response to neonatal clinical presentations ultimately considered and treat unproven infection. Thus these fact

lead to unwarranted use of antibiotics and some time overused.[8]

Antibacterial therapy in infants presents many challenges. Antibiotics are usually prescribed in NCU and are lifesaving in most of a serious infection, in the other hand overuse of antibiotics has potential risk of negative effects to neonates and the population as a whole. Misuse of antibiotic may lead to resistant infections, which may result in prolong patients hospitalized and are costly and difficult to treat.[10]

As the clinical features for neonatal sepsis are nonspecific and subtle, misuse of antibiotics is much more probable.[11]

The decision of empirical use of antibacterial agents in infants influenced by several key considerations. It is essential to know the differential diagnosis of likely pathogens to age appropriate. Clark reported that culture negative preterm infants who received empiric antibiotics about 98%.[12]

In this cross-sectional study, we found that, as most of patients' ages are more than 7 days (67.5%) (LOS) so they susceptible to certain microorganisms which are mostly isolated, by culture and sensitivity these microorganisms are Staphylococcus *aureus 51.2%, Strepto. Spp 17.5% and Acinatobacter boumania 15%* respectively (table1), these microorganisms are expected according to ages of patients and are not differ from organisms that universally mentioned in the textbooks.[13] In addition to that These microorganisms do not elicit any gross resistance to usual antibiotics, as appear in results of culture and sensitivity (table 4), therefore this study result in:

(1) mise/overuse exists from inappropriate choice of the empirical antimicrobials as response to neonatal situations this evidenced by the susceptibility test.[14] The empirical antimicrobials for EOS, it usually consist of ampicillin and gentamicin this empirical regimen covers the most commonly encountered microorganisms but in our study show aggressive used of third generation Cephalosporin, (Cefotaxime), and usually used with Glycopeptides(Vancomycin); however, *staphylococcal* coverage with *vancomycin* plus an *aminoglycoside.*[15] In this study found the empirical broad spectrum antibiotic used mainly is *Carbapenems* 40%, then *Glycopeptides(Vancomcin)* 37.5% then *Cephalosporin(Cefotaxime*) 12.5% and used in combination mostly, with limitation used of *Cefotriaxone* may be due to shortage or practitioner strategy, or it may be due to a paucity of pediatrics data regarding pharmacodynamics and optimal dosages; as consequences, pediatric recommendations are commonly extrapolated from studies in adults.[9] This inappropriate use of such antibiotics (broad spectrum) may result in serious adverse effects; alteration of gut colonization (cause persist diarrhea); emergency of resistant strains(cost and prolong hospitalization), and increasing susceptibility of fungal infection(invasive candidiasis).[16] Short course of *Carbapanems* and third generation *cephalosporins* cover most of bacteria therefore there are no need to over used such broad antibiotics especially when in combination and for long period, as resistant bacteria may results from prolonged use. Third-generation *cephalosporins* overuse may result in the emergence of ESBL-producing strains of GNB (Extended-Spectrum Beta Lactamase producing *E.coli* strain) in NCUs.[17,18]

(2) Prolonged use of appropriate antimicrobials therapy course. Complete course of antibiotics is essential for culture-proven sepsis. Conversely, for clinical, not microbiologically demonstrated sepsis the duration of antibiotic therapy which regard optimal still concerns. Recent cohort studies show that, there is an association between development of complications as necrotizing enterocolitis (NEC), late onset sepsis (LOS), and mortality and the duration of empirical antibiotic therapy.[19] In this study duration of treatment varies mostly was > 14 days(42.5%), 7-14 days(22.5%) and < 7 days(22.5%). The course of antibiotics may extended more than three weeks in some cases, this may be true in certain cases were complications as critical infections as meningitis especially with gram negative organisms but this fact collided culture and susceptibility and C-reactive protein as an indicator of treatment response. The accurate and optimal length of the antibiotic therapy is controversy and may difficult to be considered in case of negative cultures with suspicious(clinical) sepsis. There is unexplained reluctance from used CRP(C-reactive protein)(64%), in conjugation with clinical features of patients as guide to stop antibiotics.

The antibiotic therapy should be discontinued as soon as the infection role out by clinical signs, supported by laboratory results (C-reactive protein (CRP) 48 hr apart and white blood cell count return to normal), and blood cultures results are confirmed negative (48–72 hours).[20,21,22] In culture – proven sepsis neonate, duration of therapy is generally 10 days.[23]

Microorganisms during neonatal period are most commonly susceptible to narrow-spectrum antibiotics that elicit by culture and sensitivity (table 5); therefore whenever it possible the clinicians should be treat the patient with short courses of narrow-spectrum antibiotics. The choice of antimicrobials or the length of empirical treatment of antibiotics is often not an indicators of illness severity or associated with risk factors for sepsis but rather with center and thought of practitioner.

Exposure infants to antibiotic could be minimized through accurate monitoring of culture results, antibiotic choice, and duration. Improving adherence guidelines on most frequents microorganisms and appropriate duration of antibiotics. The Medicaid Innovation Accelerator

Program (IAP) provides another opportunity to potentially reduce unnecessary antibiotic exposure to Hospitalized infants.

CONCLUSION

In neonatal care units, sepsis regard the main cause of neonatal mortality and morbidity, so the most common medications prescribed are antibiotics.

There is inappropriate utilization of empirical antibiotics with prolonged unnecessary span of therapy in neonates with suspected sepsis or even culture proven one.

There is unexplained reluctance from used CRP(C-reactive protein) (only 64%), in conjugation with other laboratory parameters and clinical features of patients as indicators to stop antibiotics.

There is unnecessary use of broad spectrum antibiotic in culture-proven sepsis or neonates with suspected sepsis were most of microorganisms during the neonatal period are commonly susceptible to narrow-spectrum antibiotics that elicit by culture and sensitivity.

Author contribution

Dr. Aamer J. Alsudani: Study design, interpretation of data, writing, critical revision
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Author participate in drafting the article, collect and analysis the data; authors give final approval of the version to be submitted

REFERENCES

1. Kollef MH, Fraser VJ. Antibiotic resistance in the intensive care unit. *Ann Intern Med*, 2001; 134: 298–314.) (Roder BL, Nielsen SL, Magnussen P, et al. Antibiotic usage in an intensive care unit in a D anish university hospital. *J Antimicrob Chemother*, 1993; 32: 633–642.)
2. Orrett FA (2001) Antimicrobial prescribing patterns at a rural hospital in Trinidad: evidence for intervention measures. Afr J Med Med Sci., 2001; 30: 161-164). (4. Arya SC (2004) Antibiotics prescription in hospitalized patients at a Chinese university hospital. J Infect, 2004; 48: 117-118).
3. Carson J (1968) Misuse of Antibiotics. Br Med J., 1968; 1: 512.
4. Wolff MJ (1993) Use and misuse of antibiotics in Latin America. Clin Infect Dis., 1993; 17 Suppl 2: S346-351.
5. Naveed S, Qamar F, Maqsood A, Ayub A, Kauser H, Malik H, Fatima K and Hameed A. Prevalence and Consequences of Misuse of Antibiotics, Survey Based Study in Karachi. Bioequivalence & Bioavailability. Naveed et al., J Bioequiv Availab, 2015; 7(5): 202-204 (2015) – 202. http://dx.doi.org/10.4172/jbb.1000240
6. Warrier I, Du W, Natarajan G. Patterns of drug utilization in a neonatal intensive care unit *J Clin Pharmacol*, 2006; 46: 449–455.
7. Naveed S, Qamar F, Maqsood A, Ayub A, Kauser H, et al. (2015) Prevalence and Consequences of Misuse of Antibiotics, Survey Based Study in Karachi. J Bioequiv Availab, 2015; 7: 202-204. doi:10.4172/jbb.1000240
8. Joseph Schulman, MD, MS, Robert J. Dimand, MD, Henry C. Lee, MD, Grace V. Duenas, MPH, Mihoko V. Bennett, PhD, Jeffrey B. Gould, MD, MPH. Neonatal Intensive Care Unit Antibiotic Use. PEDIATRICS, May 2015; 135: 5.
9. Mark R. Scholeiss. Principles of antibacterial Therapy. Nelson textbook of pediatrics. Behrman RE, Kliegman RM, 20 edition. WB Saunders, Philadelphia, 2016: 1298-1313.
10. Rachel Sooter. Minimizing Antibiotic Exposure In Infants At Risk For Early Onset Sepsis. University of Vermont Scholar Works @ UVM. Page 4-6 2016 http://scholarworks.uvm.edu/graddis
11. Toltzis P, Blumer JL: Antibiotic resistant Gram negative bacteria in the critical care setting. Pediatr Clin North Am, 1995; 42: 687–702., Hart CA: Klebsiella and neonates. J Hosp Infect, 1993; 23: 83–86).
12. Clark RH, Bloom BT, Spitzer AR, et al. Empiric use of ampicillin and cefotaxime, compared with ampicillin and gentamicin, for neonates at risk for sepsis is associated with an increased risk of neonatal death. *Pediatrics*, 2006; 177: 67–72).
13. Clarence W. Gowen, Jr. Fetal and Neonatal Medicine. Nelson Essentials of Pediatrics. 6th Edision. Saunders Elsevier., 2015; 213-263.
14. Rima M.Z. Al-Sawan Amrit L. Soni Qusai Al-Saleh, Abla A. Al-Alfyb Mazin Al-Essa, Usha Rajaramu, Lekshminarayanapuram V. Deverajan, Misuse of Antimicrobial Agents in Survey in Kuwait, Medical Principles and Practice, Med Principles Pract, 1999; 8: 119–125.
15. Tricia Lacy Gomeella. Sepsis. Neonatology anagement, procedures, On-call problems, Diseases, and Drugs. Mc Graw Hill Education. 17th Edition, 865-874.
16. Tripathi N, Cotton CM, Smith PB. Antibiotic use and misuse in the neonatal intensive care unit. Clin Perinatol., 2012; 39(1): 61–8.
17. Christian Nordqvist. Antibiotic Resistant ESBL-Producing E.coli Strain Spreading In UK. medical news Today. https://www.medicalnewstoday.com/articles/83453.php
18. Gray JW, Ubhi H, Milner P. Antimicrobial treatments of serious Gram-negative infections in newborns. Curr Infect Dis Rep., 2014; 16(2): 400–8.
19. Cotten CM, Taylor S, Stoll B, Goldberg RN, Hansen NI, Sánchez PJ, et al. Prolonged duration of initial empirical antibiotic treatment is associated with increased rates of necrotizing enterocolitis and death for extremely low birth weight infants. Pediatrics, 2009; 123: 58–66.
20. Cotten CM, McDonald S, Stoll B, Goldberg RN, Poole K, Benjamin Jr DK. National Institute for

Child Health and Human Development Neonatal Research Network. The use of antibiotic (third-generation cephalosporin) were association with invasive candidiasis in extremely low birth-weight infants. Pediatrics, 2006; 118(2): 717–22.

21. Sivanandan S, Soraisham AS, Swarnam K. Choice and duration of antimicrobial therapy for neonatal sepsis and meningitis. Int J Pediatr., 2011; 2011(712150): 1–9. 9
22. Kaiser JR, Cassat JE, Lewno MJ. Should antibiotics be discontinued after 48 hours for negative late-onset sepsis evaluation in neonatal intensive care unit? J Perinatol., 2002; 22: 445–7.
23. Valdana Milisavljevic, Sepsis Neonatorum. Neonatology clinical practice and procedures. Mc Graw Hill Education. 15Th Edition., 2015; 751-757.