

The Use of Antibiotics in the Pediatric Cardiology Unit, Assiut University

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Abstract

Introduction: Inappropriate prescription of antibiotics, dosage, and administration can lead to an increase in morbidity and mortality among pediatric patients. There are different indications for the use of antibiotics in the management of congenital and acquired heart diseases, such as rheumatic fever (RF), infective endocarditis (IE), pericarditis, and pneumonia in patients with congenital heart disease (CHD).

Aim and Objectives: To audit the use of antibiotics in the Pediatric Cardiology Unit, Assiut University Children's Hospital, and to evaluate their adherence to the guidelines of their use in patients with rheumatic fever, infective endocarditis, pericarditis, and pneumonia in patients with CHD.

Patients and Methods: This retrospective observational study included 200 patients admitted to the Pediatric Cardiology Unit at Assiut University Children's Hospital. They received antibiotics as a part of their management plan for rheumatic fever, infective endocarditis, pericarditis, or pneumonia with CHD for one year, from October 2019 to September 2020.

Results: Our study included 200 patients, 118 male and 82 female, with an age range of 31 days to 15 years with a median age of 8 months. **Antibiotic use was adherent to guidelines** in 100% of patients when used as a prophylaxis against rheumatic fever, 50% of patients for eradication of streptococcal infection, 68.5% of the patients prepared to cardiac catheterization as a prophylaxis against infective endocarditis, 100% of the patients with infective endocarditis, 75% of patients with pericarditis and 68.8% of patients with pneumonia and CHD.

Conclusion: The antibiotic therapy used adhered to the guidelines in 69% of patients.

Keywords: Antibiotics, Pediatrics, Cardiology.

Introduction

Antibiotics are agents that can prevent and destroy the proliferation of microorganisms. The treatment of infectious diseases depends mainly on antibiotics [1].

The use of antibiotics should be based on the correct diagnosis, the

location of the infection, the patient's condition,

sensitivities to antibiotics, the severity of the microbial cause, and the pharmacokinetics and pharmacodynamics of antimicrobials. In

every antibiotic decision, you must consider the side effects and cost [2].

Inappropriate prescription of antibiotics, dosage, and administration can lead to an increase in morbidity and mortality among pediatric patients. Therefore, improper and excessive use of antibiotics must be reduced by limiting their use to certain circumstances [3].

Bacteria enter the bloodstream from the mouth and can cause an infection anywhere in the body. Most people's immune system kills these bacteria, but some patients need antibiotic prophylaxis to decrease the chance of infection [4].

Aim of the Study

The purpose of this research was to audit the use of antibiotics in the Pediatric Cardiology Unit at Assiut University Children's Hospital and to evaluate their adherence to the guidelines of their use in rheumatic fever, infective endocarditis, pericarditis, and pneumonia in patients with CHD.

Patients and Methods

This retrospective observational study included 200 patients admitted to the Pediatric Cardiology Unit at Assiut University Children's Hospital. They received antibiotics as a part of their management plan for rheumatic fever, infective endocarditis, pericarditis, or pneumonia with CHD for one year from October 2019 to September 2020.

Inclusion Criteria

All patients fulfilled the following criteria: Patients aged from 1 month up to 18 years and patients who received antibiotic therapy because of either rheumatic fever, infective endocarditis, pericarditis, or pneumonia in patients with CHD.

Exclusion Criteria: patients under one month of age.

Recommended antibiotics for children with cardiac diseases according to guidelines: rheumatic fever, infective endocarditis, pericarditis, and pneumonia in patients with CHD.

Ethical Committee

The Faculty of Medicine, Assiut University's ethical committee, approved this study.

IRB number:17100518.

Sample Size

The sample size was calculated using EpiInfo 7. Based on prevalence, adherence to guidelines is 82.6%, according to the National Antimicrobial Prescribing Survey (NAPS), Melbourne, Australia [5], with confidence limits of 5% and a confidence level of 90%. The minimum number of patients required for this study is 160. The sample was increased to 200 to cover dropouts.

Statistical Analysis:

When describing categorical variables, we used the notation "number and percent" (N, %), while when describing continuous variables, we used the notation "mean and standard deviation" (Mean, SD). The Chi-square test is used to compare categorical data, whereas the t-test (independent-samples T test) is used to compare continuous variables. We used the Pearson and Spearman correlation coefficients to analyze the correlation. It was determined to be statistically significant if the two-tailed p-value was less than 0.05. The IBM SPSS 20.0 program was utilized for each carried-out analysis.

The Chi-square test for categorical data allows for a comparison to be made between all of the groups.

* Statistically substantial distinction (p <0.05); ** statistically significant difference (p < 0.01).

Results

About 82 (41.0%) of the studied cases were females, while 118 (59.0%) were males. The age range of the studied

cases was 31 days to 15 years, with a median age of 8 months, as shown in Table (1).

Table 1: Sociodemographic data of the studied patients

Variable	No. (n=200)	Percent %
Age		
Range	31-day - 15 year	
Median	8 months	
Sex		
Male	118	59.0
Female	82	41.0

Antibiotic therapy used to eradicate GAS (Group a streptococcal infection) adhered to guidelines in only 4 (50%) patients, with a statistically insignificant difference. However, prophylaxis of rheumatic fever was adherent to guidelines in 2(100%) of patients, as shown in Table (2) and Table (3).

Table 2: Adherence of antibiotic therapy for eradication of GAS to the guideline:

	Diagnosis (eradication of GAS) (n=8)		
	No.	%	P. value
Adherence to guideline			
Yes	4	50	1.000
No	4	50	

Table 3: Adherence of Antibiotic therapy used as a prophylaxis of rheumatic fever to guideline:

	Prophylaxis of rheumatic fever (n=2)		
	No.	%	P. value
Adherence to guideline			
Yes	2	100	-
No	0	0.0	

Antibiotic therapy was adherent to guidelines in 13 (68.5%) of the patients prepared for cardiac catheterization as a prophylaxis against infective endocarditis, while antibiotic therapy

was not adherent to guidelines in 6 (31.5%) of the patients due to inappropriate use of amikacin and cefotaxime with ampicillin as shown in Table (4).

Table 4: Adherence of antibiotic therapy used as a prophylaxis against infective endocarditis to guidelines:

	Prophylaxis against "infective endocarditis" (n=19)		
	No.	%	P. value
Adherence to guideline			
Yes	13	68.5	0.480
No	6	31.5.0	

Antibiotic therapy used in treating patients with infective endocarditis adhered to guidelines in 6 (100%) patients, as shown in Table (5).

Table 5: Adherence of Antibiotic therapy used in patients with infective endocarditis to guidelines:

	Diagnosis "infective endocarditis" (n=6)		
	No.	%	P. value
Adherence to guideline			
Yes	6	100.0	-
No	0	0.0	

Antibiotic therapy used in patients with pericarditis adhered to guidelines in 6 (75%) of patients. In comparison, antibiotic therapy was not adherent to guidelines in 2 (25%) of the patients due to the inappropriate use of metronidazole as an empirical therapy for pericarditis, as shown in Table (6).

Table 6: Adherence of antibiotic therapy used in patients with pericarditis to guidelines:

	Diagnosis "pericarditis" (n=8)		
	No.	%	P. value
Adherence to guideline			
Adherent	6	75	0.157
Not adherent	2	25	

Antibiotic therapy used in patients with pneumonia with CHD adhered to guidelines in 108 (68.8%) patients. In comparison, antibiotic therapy was not adherent to guidelines in 49 (31.2 %) of

the patients due to inappropriate use of metronidazole, ceftazidime, and amikacin as empirical therapy to patients admitted for pneumonia with CHD. as shown in Table (7).

Table 7: Adherence of Antibiotic therapy used in patients admitted for pneumonia with CHD to guidelines:

	Diagnosis " pneumonia with CHD" (n=157)		
	No.	%	P. value
Adherence to guideline			
adherent	108	68.8	0.002**
Not adherent	49	31.2	

Antibiotic therapy was empirical in about 164 (82%) patients, targeted in about 15 (7.5%) patients, and prophylactic in about 21 (10.5%) patients, as shown in Table (8).

Table 8: Regimen of antibiotic therapy used in our study:

	No. (n=200)	%
Empirical	164	82
Targeted	15	7.5
Prophylaxis	21	10.5

Antibiotic therapy used in all included patients was adherent to guidelines in 138 (69%) of patients, while antibiotic therapy was not adherent to guidelines in 62 (31 %) of the patients, as shown in Table (9).

Table 9: Adherence of antibiotic therapy to guidelines in our study:

	No. (n=200)	%
Adherence to guideline		
Adherent	138	69.0
Not adherent	62	31.0

Discussion

Patients in our study ranged in age from 1 month to 15 years old, with a median age of 8 months. There was a higher prevalence of cardiac diseases among males than females; 118 (59.0%) were males and 82(41.0%) were females. These results were supported by previous studies, which reported that the prevalence rates of congenital heart

diseases are more significant for males than females [6].

Zuhlke LJ Karthikeyan G [7] recommended a single intramuscular injection of benzathine penicillin or 10 days of orally administered ampicillin or amoxicillin to ensure eradication of GAS from the upper respiratory tract.

The World Heart Federation, 2013 recommended long-term antibiotic

prophylaxis for secondary prevention of rheumatic fever by intramuscular injection of benzathine penicillin every 2-3 weeks or oral penicillin twice daily [8].

Antibiotic therapy used as a prophylaxis against rheumatic fever adhered to guidelines in 2 (100%) patients. However, regarding eradicating streptococcal infection, only 4 (50%) of patients adhered to guidelines due to inappropriate use of ampicillin + sulbactam and cefotaxime with benzathine penicillin.

Gasse B. et al. showed that 46% of Lifou, New Caledonia patients receiving antibiotic prophylaxis for rheumatic fever adhered to guidelines [9].

According to Roest AW and de Roos A [10], patients preparing for cardiac catheterization need antibiotic therapy as prophylaxis against infective endocarditis. However, the Endocarditis Committee of the American Heart Association [11] determined which procedures were most likely to cause endocarditis and released new guidelines indicating which patients should receive prophylaxis. Cardiac catheterization was not included in conditions requiring antibiotic therapy as a prophylaxis against infective endocarditis. However, we kept in mind that infection control measurements were not well applied in our community, just as our patients did not follow good dental hygiene. It is recommended that oral Amoxicillin be used as an antibiotic prophylaxis for infective endocarditis. If a patient cannot take oral medication, ampicillin, cefazolin, or ceftriaxone is recommended. Our study showed that antibiotic therapy was used in 19 patients preparing for cardiac catheterization as a prophylaxis against infective endocarditis. Antibiotic therapy adhered

to guidelines in 13 (68.5%) of the patients, while it did not adhere to guidelines in 6 (31.5%) due to inappropriate use of amikacin and cefotaxime with ampicillin.

Baddour et al. recommended that initial empirical therapy for infective endocarditis be started with the following antibiotics while waiting for the results of blood culture: The usual initial regimen is anti-staphylococcal semisynthetic penicillin (nafcillin, oxacillin, or methicillin) and aminoglycoside (gentamicin); sometimes penicillin is added. If methicillin-resistant *S. aureus* (MRSA) is suspected, vancomycin should be substituted for semisynthetic penicillin. Vancomycin should be used instead of penicillin or semisynthetic penicillin in penicillin-allergic patients [12].

Our study showed that antibiotic therapy was empirical in about 6 (24%) patients with infective endocarditis. Vancomycin was used in about six (100%) of the patients. Gentamicin was used in about six (100%) patients. Ceftriaxone was used in about 1 (16.6%) of the patients. Antibiotic therapy used in treating patients with infective endocarditis adhered to guidelines in six (100%) patients.

The European Society of Cardiology (ESC) recommends the urgent use of broad-spectrum parenteral antibiotics when bacterial pericarditis is suspected. Urgent pericardial drainage combined with intravenous antibacterial therapy (e.g., vancomycin, ceftriaxone, and ciprofloxacin) is mandatory in purulent pericarditis. A targeted regimen should be established based on blood and pericardial fluid culture results. [13].

The current study showed that antibiotic therapy used in patients with

pericarditis was empirical in about 5 (62.5%) patients and targeted in about 3 (37.5%). Vancomycin was used in about 8 (100%) of the patients. Ceftriaxone was used in about six (75%) of the patients. Metronidazole was used in about 2% (25%) of the patients. Ceftazidime was used in about 1 (12.5%) of the patients. Cefepime was used in about 1 (12.5%) of the patients. Antibiotic therapy used in patients with pericarditis was adherent to guidelines in 6 (75%) of patients, while it was not adherent to guidelines in 2 (25%) of the patients due to the inappropriate use of metronidazole as empirical therapy.

The Pediatric Infectious Diseases Society and the Infectious Diseases Society of America recommended that the empiric treatment of suspected bacterial pneumonia depends on local epidemiology, the immunization status of the child, and the clinical manifestations at the time of presentation [14].

Children who are adequately inoculated against H. influenzae type b and S. pneumoniae and are not extremely ill should be treated with ampicillin or penicillin G in regions lacking substantial high-level penicillin resistance among S. pneumoniae. Ceftriaxone and cefotaxime may be administered to children who do not fit these criteria. Vancomycin or clindamycin should be added to the first antimicrobial therapy for patients whose symptoms are consistent with staphylococcal pneumonia (pneumatoceles, empyema). In addition, a macrolide antibiotic should be incorporated into the treatment plan if mycoplasma pneumoniae or chlamydia pneumoniae infection is suspected.

Our study showed that antibiotic therapy used for pneumonia in patients with CHD was empirical in about 145 (92.4%) patients and targeted in about 12 (7.6%) patients. Ampicillin-sulbactam was used in about 127 (80.9%) patients. Cefotaxime was used in about 79 (50.4%) of the patients. Amikacin was used in about 26 (16.6%) patients. Ceftazidime was used in about 22 (14%) of the patients. Ceftriaxone was used in about 29 (18.5%) of the patients. Vancomycin was used in about 29 (18.5%) of the patients. Macrolides were used in about 3 (1.9%) of the patients. Metronidazole was used in about 3 (1.9%) of the patients. Meropenem was used in about 1 (0.6%) of the patients.

So, antibiotic therapy used in patients with pneumonia and CHD adhered to guidelines in 108 (68.8%) patients. In comparison, antibiotic therapy was not adherent to guidelines in 49 (31.2%) of the patients due to the inappropriate use of metronidazole, ceftazidime, and amikacin as empirical therapy in patients with pneumonia with CHD.

According to Di Pietro et al., Global adherence to antibiotic use in pneumonia guidelines was fulfilled in 45% of cases. After the intervention, global adherence to guidelines improved (+39%) [15].

Our study showed that antibiotic therapy was empirical in about 164 (82%) of patients, targeted in about 15 (7.5%) of patients, and prophylactic in about 21 (10.5%) of patients.

Antibiotic therapy used in all studied patients adhered to guidelines in 138 (69%) of patients, while antibiotic therapy did not adhere to guidelines in 62 (31 %).

The National Antimicrobial Prescribing Survey (NAPS), Melbourne, Australia, supported that the prevalence

of adherence to antibiotic use guidelines is 82.6% [16].

Conclusion

We concluded that the antibiotic therapy used in all patients was empirical. It was adhered to guidelines by only 69% of patients, as follows: In rheumatic fever, it adhered to guidelines in 100% of patients when used as a prophylaxis against rheumatic fever, but regarding the eradication of streptococcal infection, only 50% of patients adhered to guidelines. In infective endocarditis, it adhered to guidelines in 68.5% of the patients prepared for cardiac catheterization as a prophylaxis against infective endocarditis, while it adhered to guidelines in 100% of the patients with infective endocarditis. In pericarditis, it adhered to guidelines in only 75% of patients, and in pneumonia in patients with CHD, it adhered to guidelines in only 68.8% of patients.

Recommendations

The present study recommends the following:

- The use of antibiotics in the Pediatric Cardiology Unit must adhere to the guidelines of their use in rheumatic fever, infective endocarditis, pericarditis, and pneumonia in patients with CHD to avoid the emergence and spread of antibacterial-resistant bacteria.
- Auditing and follow-up for the use of antibiotic therapy are recommended to improve practitioners' adherence to the guidelines for antibiotic indication in different diseases.

Limitations of the Study

The retrospective observational study is associated with losing some information in patients, not in the hospital. A prospective study would be more accurate.

List of Abbreviations

Abbreviations	Mean of Abbreviations
CHD	Congenital Heart Disease
ESC	The European Society of Cardiology
GAS	Group A Streptococcal Infection
IE	Infective Endocarditis
MRSA	Methicillin-Resistant Staphylococcus Aureus
NAPS	National Antimicrobial Prescribing Survey
RF	Rheumatic Fever

References

1. Buccellato E, Melis M, Biagi C, Donati M, Motola D, Vaccheri A. Use of antibiotics in pediatrics: 8-year survey in Italian hospitals. *PLoS One*. 2015;10(9).
2. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A*. 2018;115(15).
3. Agarwal S, Yewale VN, Dharmapalan D. Antibiotics use and misuse in children: a knowledge, attitude, and practice survey of parents in India. *J Clin Diagn Res*. 2015;9(11).
4. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance—the need for global solutions. *Lancet Infect Dis*. 2013;13(12):1057-98.
5. McMullan BJ, Hall L, James R, Mostaghim M, Jones CA, Konecny P, et al. Antibiotic appropriateness, and guideline adherence in hospitalized children: results of a nationwide study. *J Antimicrob Chemother*. 2020;75(3):738-46.
6. Otaigbe BE, Tabansi PN. Congenital heart disease in the Niger Delta region of Nigeria: a four-year prospective echocardiographic analysis: cardiovascular topic. *Cardiovasc J Afr*. 2014;25(6):265-8.
7. Zuhlke LJ, Karthikeyan G. Primary prevention for rheumatic fever. *Glob Heart*. 2013; 8:221-6.
8. Remenyi B, et al. Position statement of the World Heart Federation on the prevention and control of rheumatic heart disease. *Nat Rev Cardiol*. 2013; 10:284-92.
9. Gasse B, Baroux N, Rouchon B, Meunier JM, Frémicourt ID, D'Ortenzio E. Determinants of poor adherence to secondary antibiotic prophylaxis for rheumatic fever recurrence on Lifou, New Caledonia: a retrospective cohort study. *BMC Public Health*. 2013; 13:1-9.
10. Roest AA, De Roos A. Imaging of patients with congenital heart disease. *Nat Rev Cardiol*. 2012;9(2):101-15.
11. Gewitz MH, et al. Revision of the Jones Criteria for the diagnosis of acute Rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015; 131:1806-18.
12. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation*. 2015;132(15):1435-86.
13. Asteggiano R, Bueno H, Caforio AL, Carerj S, Ceconi C. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases—Web Addenda. *Eur Heart J*. 2015.
14. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;52(4).

15. Di Pietro P, Della Casa Alberighi O, Silvestri M, Tosca MA, Ruocco A, Conforti G, et al. Monitoring adherence to guidelines of antibiotic use in pediatric pneumonia: the MAREA study. *Ital J Pediatr.* 2017; 43:1-3.
16. McMullan BJ, Hall L, James R, Mostaghim M, Jones CA, Konecny P, et al. Antibiotic appropriateness, and guideline adherence in hospitalized children: results of a nationwide study. *J Antimicrob Chemother.* 2020; 75:738-46.