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Evaluating the Appropriate Use of Piperacillin /Tazobactam in Pediatric Intensive Care Unit of a Major Tertiary Care Hospital

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Abstract

Background: Piperacillin/Tazobactam(Pip/Taz) is a broad-spectrum antibacterial covering aerobic, and anaerobic microorganisms. Pip/Taz plays a major role in treating sepsis, respiratory infection, and intraabdominal infection. Many studies showed inappropriate use of Pip/Taz might increase the risk of resistance. This study aimed to evaluate the appropriateness use of Pip/Taz prescribing in pediatric patients in Peidatric Intensive Care Unit (PICU) at a major tertiary hospital. *Method:* A retrospective and observational study was conducted to evaluate the appropriateness use of Pip/Taz in PICU. The study included all neonates and pediatrics less than 14 years old in the PICU setting who had received at least dose of Pip/Taz during their admission for the period between Jan 2020 and Jan 2021. Assessment of antimicrobial appropriateness was evaluated according to Infectious Diseases Society of America (IDSA) guidelines. Data were retrieved from the hospital's Electronic Medical Records (EMRs) and exported to Excel spreadsheet. *Results:* Of 124 Pip/Taz prescriptions, 34% were inappropriate. The common indications for using Pip/Taz empirically were with sepsis and suspecting of pneumonia. The reasons for inappropriate use of Pip/Taz were due to continue using the drug based on clinical condition even the results of cultures had no growth of organisms 71%, then starting the drug without taking culture 14%, then the drug continued without justification despite culture resulted with no growth 10%, and finally continued without following sensitivity 5%. *Conclusion:* This study showed that there was inappropriate use of Pip/Taz at PICU. The inappropriate use was attributed to not following the lab results, culture sensitivity and not requesting microbiology culture.

Key words: Piperacillin-tazobactam Pip/Taz, Appropriateness use, antimicrobial stewardship program, PICU.

INTRODUCTION

In the last years, the bacterial organisms became more powerful than before, they became more resistant to multi antimicrobial drugs including broad-spectrum antimicrobial. Nowadays, the World Health Organization (WHO) is cautious about developing antimicrobial-resistant (AMR) and it has been dealing with it as a major global public health issue [1]. AMR organisms are difficult to treat, increase the cost of patient care, increase the length of stay at the hospital and increase the rate of mortality [2, 3]. Abusing antimicrobial drugs can lead to worse patient condition like superinfection with other organisms, increase the incidence of side effects, or appearing of complications related to antimicrobial drugs [4, 5] O'Neill's study estimated that by 2050, more than 10 million people

would die due to AMR infection [6]. Many studies showed a correlation between the inappropriateness use of antimicrobial drugs by the health care providers (HCPs) and the emergence of AMR organisms in the hospitals [7, 9].

Pseudomonas aeruginosa and extended-spectrum beta-lactamases (ESBL) producing gram-negative bacteria are at the top organisms which resist to multiple antimicrobials. HCPs are facing limited therapeutic options for treating these types of bacteria [10]. Pip/Taz plays a major role in treating patients with suspecting sepsis, pneumonia, febrile neutropenia and intra-abdominal infections. Pip/Taz considered as one of the most powerful broad-spectrum antibacterial which covers gram-positive, gram-negative aerobic, and anaerobic. It also can be used in multi-resistant

organisms such as Pseudomonas aeruginosa and Enterobacteriaceae [11, 13]. Many studies showed inappropriate use of Pip/Taz might increases the risk of resistance, especially with Pseudomonas aeruginosa organism [14-16]. Some studies found that more than 50 % of prescribed antimicrobials by HCPs were inappropriate [17, 18].

Approaching some strategies to reduce inappropriate utilization of broad- spectrum antimicrobials can minimize the emergence of AMR [19]. The IDSA has published stewardship guidelines to optimize antibiotic use by using cost-effective interventions, minimize or avoiding AMR, decreasing the rate of side effects, and growth of clostridium difficile infections [20-22]. Implementation of antimicrobial stewardship programs (ASPs) is one of strategies that might minimize developing AMR by enhancing the staff education, restrict broad spectrum antibiotics like meropenem, early deescalating antibiotic, and early converting from intravenous to the oral formula [23-26]. Limited information is currently available in the literature about pip/Taz prescribing in Saudi Arabia specifically in assessing its use in PICU. This study aimed to evaluate the appropriateness use of Pip/Taz prescribing in pediatric patients in PICU at a major tertiary hospital in Saudi Arabia. The objectives of this study were to evaluate the appropriateness of using Pip/Taz in PICU, and to estimate effects of using it inappropriately.

METHODS

Study design and data collection

A descriptive, retrospective, and observational study was conducted at prince sultan military medical city (PSMMC) to evaluate the appropriateness use of Pip/Taz in PICU. The study included all neonates and pediatrics less than 14 years old that were admitted in PICU setting and had received at least one dose of Pip/Taz during their admission for the period between Jan 2020 and Jan 2021. Data were retrieved from the hospital's electronic medical records (EMRs) and exported to Excel Spreadsheet. The retrieved data included patient demographics, indications for Pip/Taz use, duration of antimicrobial therapy, culture, and sensitivity results if available.

Assessment of antimicrobial appropriateness was evaluated according to IDSA guidelines as follows: (27)
1. If the indication of antimicrobial use was empiric therapy, all cases were reviewed to identify if a microbiology culture had been requested.
2. If a microbiology culture had been requested, each case was reviewed for the follow-up of antimicrobial therapy (continuation, discontinuation, escalation or de-escalation) based on reported results.
3. If the indication for treatment was targeted therapy and the antimicrobial was not used initially as

empiric therapy, culture and susceptibility results were reviewed to check whether the targeted therapy was in accord with the susceptibility data and the organism was not susceptible to a narrow-spectrum antimicrobial.

The inappropriateness of antimicrobial therapy was evaluated as follows:
1. If the spectrum of activity was too broad
2. If Antimicrobial used without culture request
3. Failure of suitable antimicrobial de-escalation
4. Allergy to the prescribed antimicrobial
5. Antimicrobial prescription despite the microbiology result indicating resistance.

STATISTICAL ANALYSIS

Data included patient demographic and characteristics were analyzed using Microsoft Excel 2013 software (Microsoft Corporation, Redmond, WA, USA). Data were analyzed using simple descriptive statistics using mean and median for continuous data.

RESULTS

During the period of study, total of 124 prescriptions of pip/Taz who were collected and received at least one dose. Male gender represents with 70 (56.4%). Mean age was 5 years old. Baseline characteristics, indications and co-morbidities are illustrated in table 1. The main reasons for starting pip/Taz was empirical therapy based on either presence of fever, chest x ray finding, increased white blood cell count and deterioration of patient condition. Number of cases were prescribed for suspecting either pneumonia or sepsis were 55 (44.4%) respectively, for wound infection by 8 (6.5%), for Gastrointestinal(GI) infection by 3(2.4%), urine infection by 2 (1.6%) and 1 (0.8%) for blood infection. Out of 124 of prescriptions of Pip/Taz , 82 (66%) of uses were appropriate while 42 (34%) were inappropriate. The most frequent conditions for which Pip/Taz was either appropriate or inappropriate prescribed empirically with sepsis and pneumonia Table 2.

The reasons for inappropriate use of Pip/Taz were due to continue using the drug based on clinical condition even the results of cultures had no growth of organisms 30 (71%) then starting the drug without taking culture 6 (14%), then continued without justification despite culture resulted with no growth 4 (10%), and finally continued without following sensitivity 2(5%) Table 3.

Sepsis and pneumonia were the most causes of indications among the cases that continued based on clinical condition, there were no cultures have been requested or Pip/Taz was continued without following sensitivity. Urine infection and sepsis were the most inappropriate reasons which Pip/Taz was continued

without justification. Multi drugs resistance including Pip/Taz were seen in 5 cases.

Table-1

Characteristics (N)	124	%
Male	70	56.4
Female	54	43.6
Age (Mean)	4.97 Years	
Co-morbidity		
Asthma	8	6.5
Congenital heart disease	29	23.4
Epilepsy	7	5.6
Global developmental delay	11	9
Gastro esophageal reflux disease	17	14
Oncology diseases	10	8
Congenital anomalies	24	19.4
Medically free	17	14
Diagnosis		
Blood	1	0.8
GI	3	2.4
Pneumonia	55	44.4
Sepsis	55	44.4
Urine	2	1.6
Wound	8	6.5

Table-2

Conditions for which Pip/Taz was prescribed empirically	Appropriate	Inappropriate	Total
Blood	1	0	1
CNS	1	0	1
GI	3	0	3
pneumonia	39	16	55
Sepsis	29	25	54
Urine	1	1	2
Wound	8	0	8

Table-3

Reasons for Inappropriateness	N	%
Continuo based on clinical condition	30	71%
Continuo without justification	4	10%
No culture was requested	6	14%
Not following sensitivity	2	5%

DISCUSSION

This study showed there was inappropriate use of Pip/Taz in PICU. This Study also approved that there is a possibility of developing MDR in pediatric population by 4% which we need to reconsider to avoid abusing antimicrobial.

This study showed a group of patients with either congenital heart diseases or other types of congenital anomalies were the highest group of having recurrent hospital infections which need to start Pip/Taz as empirical antimicrobial. As per PSMMC guideline Pip/Taz considered as one of first line choices to treat hospital acquired infection. Majority of infections that lead to PICU admitted are whether confirmed pneumonia or sepsis. The differentiation in initial diagnosis was based on clinical judgment, chest x-ray, or inflammatory markers.

IDSA set ASP to face challenges of defining the appropriate use of antimicrobial. One criterion is stopping antimicrobial if cultures result no growth after 2-3 days. However, in practice, critically ill patients in PICU mostly do not response quickly within 2-3 days. IDSA defined the duration of antimicrobial course is from 7-10 days and it could extend up to 14 days or more until patient is stable. Therefore, ASP criteria is suitable for patients who are vitally stable and treated in general ward but in PICU is still controversial.

The reasons for not following the microbial sensitivity results could be due to either delaying in posting the lab results, patient was improved with

Pip/Taz, primary nurse or physician didn't review results early, or relaying solely on clinical judgment.

Nada A Alsaleh *et al*. study included only adult hospitalized patients who had received at least one dose of the antimicrobials during their admission. Study found that 43.5% of antimicrobial prescriptions were inappropriate. The two reasons for inappropriate prescriptions were because of ordering the antimicrobial without culture request 32.4%, and also failure of suitable antimicrobial de-escalation 19.9% [28].

Sanaa Saeed Mekdad *et al*. conducted a prospective cohort study included all patients who were admitted to the cardiac surgery unit of a tertiary care center, study showed that among 300 patients who received Pip/Taz , the overall appropriate use of Pip/Taz was seen in 166 patients 55.3% [29].

Fahmi Yousef Khan *et al*. study focused on evaluation of the use of Pip/Taz at Hamad General Hospital in Qatar, They found appropriateness of empirical therapy was about 57%, and most of the inappropriate prescriptions were in cases of aspiration pneumonia and abdominal infections [30].

Balkhy *et al*. study conducted in two centers in Saudi Arabia, aimed to calculate overall and type-specific antimicrobial consumption for pediatric and neonatal ICUs. They found that vancomycin and Pip/Taz were prescribed more frequently in patients at PICU [31].

To the best of our knowledge, this is the first study that has evaluated the appropriateness of Pip/Taz use specifically in PICU mainly in Saudi Arabia. The study had several limitations. The ingrained limitation lies in placing a retrospective study design. The assessment did not occur at the time of prescribing, so, the accuracy of interpretations of information collected from EMR in the assessment of prescriptions relies on quantity of information that had been recorded. A further limitation is that the study was conducted in a single tertiary care hospital, which may limit the generalizability of the study. Finally, study didn't clarify in more details about infection types and taking of considerations of dosing but it was evaluated as appropriate in the assessment.

CONCLUSION

This study sends a message that increasing the awareness between HCPs is needed about importance of the appropriateness use of antimicrobial. Also, to monitor lab results whether previous history or recent. We suggest further prospective studies to confirm our findings and to look for the reasons for Pip/Taz continuation despite negative cultures.

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