Original Article

An evaluation of Ceftriaxone use in the antimicrobial stewardship program for surgical patients at a Hospital in Bandung

Sri Rahayu Evrilia[1*], Ahmad Muhtadi[1], Melisa I. Barliana[2,3], Rina Winarni[4]

[1]Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Jl. Bandung Sumedang, KM. 21, Jatinangor, Sumedang, Indonesia, 45363. [2]Department of Biological Pharmacy, Universitas Padjadjaran, Sumedang, Indonesia. [3] Center of Excellence in Higher Education for Pharmaceutical Care Innovation, Universitas Padjadjaran, Indonesia.[4]Dr. Hasan Sadikin Hospital, Bandung, Indonesia.

Correspondence: Sri Rahayu Evrilia. Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Jl. Bandung Sumedang, KM. 21, Jatinangor, Sumedang, Indonesia, 45363. E-mail: evrilia27@gmail.com

ABSTRACT

The use of rational antibiotic Ceftriaxone in surgery requires paying attention to factors such as antimi-crobial activity at the wound location and the duration of administration because Ceftriaxone includes broad-spectrum antibiotics. An antimicrobial stewardship program aimed to measure the use of antibiotics in hospitals using the average daily dose calculations (DDD). This research aimed to know the differences of DDD values of antibiotic Ceftriaxone before and after the program in surgical patients. This study was an observational analytic study using retrospective analysis of surgical inpatients from December 2015-July 2016. The study involved 197 subjects consisting of 98 subjects before the program, and 99 subjects after the program. The value of DDD /100 patient-day Ceftriaxone antibiotics after the antimicrobial stewardship program was lower than before the program (consecutively 71,194 and 72,692 DDD/100 patient-day, p= 0,001). The use of antibiotics Ceftriaxone was decreased in neurosurgery in digestive patients after an antimicrobial stewardship program.

Keywords: Antimicrobial stewardship program, Ceftriaxone, DDD, surgery.

Introduction

The increased prevalence of infection caused by antibiotic-resistant pathogenic bacteria has been observed in the surgical department. The bacteria mentioned included *extended-spectrum beta-lactamase (ESBL)* bacteria *Escherichia coli* and *Klebsiella spp., Enterococcus species, Pseudomonas aeruginosa* and *Acinetobacter baumannii resistant carbapenems*, and *Klebsiella pneumoniae carbapenemase* producers. [1]

The results of *Antimicrobial Resistance in Indonesia* (AMRIN Study) between the years of 2000-2005 showed that 43% of *Escherichia coli* were resistant to various types of antibiotics including ampicillin (34%), cotrimoxazole (29%), and chloramphenicol (25%). Out of 781 patients currently hospitalized, 81% had *Escherichia coli* resistance to various antibiotics including ampicillin (73%), cotrimoxazole (56%), and chloramphenicol (43%), ciprofloxacin (22%), and gentamicin (18%). The results of this study proved that the problem of antimicrobial resistance also occurred in Indonesia. [2]

Antimicrobial Stewardship Program has been an essential program in hospitals. One of its objectives is to prevent the emergence of antimicrobial resistance. Another aim is to reduce the incidence of drugs' side effects including secondary infections (e.g., *Clostridium difficile* infection) by optimizing the selection of optimal antibiotic regimens such as the dosage, duration of therapy, and the mode of administration of antibiotics in each patient. [3] To control the antimicrobial resistance in hospitals, in April 2016 Dr. Hasan Sadikin implemented the Antimicrobial Stewardship Program (ASP). It

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complied with the decree from the president director of Dr. Hasan Sadikin Bandung Number HK.03.05/C011/15167/IX/2015 which assigned the members of the Antimicrobial Resistance Control Team (PPRA) for its implementation in the surgical patientward. [4]

The assessment of the quantity of antibiotic use in the hospitals was measured using the *defined daily dose* (DDD). It was relatively easy to do, and was recommended by the World Health Organization (WHO). [5]

This study intended to evaluate the implementation of an antimicrobial stewardship program on the quantity of antibiotic Ceftriaxone by calculating the average daily dose in surgical patients at RSUP Dr. Hasan Sadikin Bandung before and after the intervention.

Methods

The study employed Analytical observations with a cross-sectional design and retrospective data retrieval in surgical treatment room before and after ASP intervention from December 2015 to July 2016. The subjects of the study were selected based on a set of criteria. The first criterion was the age group, namely the adult group (18-65 years old) and the geriatric group (above 65 years old), irrespective of their gender. The next criterion was whether the patients were administered with Ceftriaxone antibiotics for, Ceftriaxone empirical, definitive or prophylactic therapy. The next was the duration of its use (long-term therapy for > 14 days, and short-term one for <14 days)). The rest of the criteria were ASA I-II classification, net operating patients, clean-contaminated operations, blood samples, and complete medical records.

The measurement of the amount of an antibiotic used followed the ATC/DDD standard, recommended by WHO, 2011. The formula for the calculation DDD was:

DDD/100 day treatment = [use of antibiotics annually (g) × 100]/[DDD (g/d) × LOS all patients]

Statistical analysis was performed using Student's *t-test* for the paired data. A level of p=0,001 was considered significant.

Results

The patients who received antibiotics in an antimicrobial stewardship program, were treated in a surgical treatment room during December 2015- May 2016, and met the inclusion criteria amounted to 197 people. The study subjects consisted of 98 subjects before the antimicrobial stewardship program, and 99 subjects after the antimicrobial stewardship program that began in April 2016.

The essential characteristics of study subjects such as age, sex, outpatient room, length of stay have been represented in Table 1.

Table 1: The Basic Characteristics of Study Subjects

Characteristics		Before ASP (n= 98)	After ASP (n= 99)
Age	<20 years	29 (29.5)	33 (33.3)
	20-35 years	48 (48.9)	46 (46.4)
	>35 years	21 (21.4)	20 (20.2)
Sex	Female	36 (36.7)	31 (31.3)
	Male	62 (63.3)	68 (68.7)
Outpatient room	Kana	47 (47.9)	39 (39.4)
	Kemuning	51 (52.0)	60 (60.6)
Length of stay	3 days	16 (16.3)	19 (19.2)
	4 days	23 (23.5)	25 (25.2)
	5 days	28 (28.6)	32 (32.3)
	>5 days	31 (31.6)	23 (23.2)

Description: data presented in (%)

Patients receiving antibiotic therapy should be cultured to receive appropriate antibiotic therapy for therapeutic purposes. Most of the blood culture results in both groups found no bacterial growth of 87.5% in the study subjects before ASP, and 79.2% in subjects after ASP. In the subjects before ASP, 14 positive cultures were found to contain bacteria, 3 gram-negative superbug germs (1 *Pseudomonas aeroginosa (MDR)*, 2 *Escherichia coli (ESBL)*, 1 *Citrobacter freundii*, 4 *Acinobacter baumannii,* 1 *actinobacter* gram positive (*Kocuria kristiae (MDR*), 2 *Klebsiella pneumonia*, 2 *Enterobacter cloacae* and 1 gram-positive coccus (*Staphylococcus epidermidis*).

On the post-ASP subjects, 20 positive cultures were found to be bacteria, 2 germs of super gram-positive coccus (1 germ of *Enterococcus faecalis*, 1 germ *Staphylococcus haemolyticus*, 14 super gram-negative bugs, 3 *Acinetobacter baumannii*, 5 *Escherichia coli*, 6 germs *Pseudomonas aeroginosa*, 1 *Candida tropicalis*, 1 *Klebsiella pneumoniae*, 1 *Citrobacter freundii*, and 1 *Proteus mirabilis.*

The results of blood cultures and susceptibility tests of antibiotic Ceftriaxone can be seen in Table 2.

Table 2. Results of blood cultures and susceptibility test of antibiotic Ceftriaxone

Type of bacteria	Amount of bacteria	Susceptibility test of antibiotic Ceftriaxone
Escherichia coli (ESBL)	7	S
Staphylococcus haemolyticus (MRCOS)	1	R
Pseudomonas aeruginosa (MDR)	7	R
Acinetobacter baumannii (MDR)	7	R
Citrobacter freundii	2	S
Kocuria kristiae	1	R
Klebsiella pneumonia	3	R
Enterococcus faecalis (wild type)	1	R
Enterobacter cloacae	2	R
Candida tropicalis	1	R
Staphylococcus epidermidis (MRCONS)	1	R
Proteus mirabilis	1	S

Information : S = Susceptible, R = Resistant

Most positive blood cultures were resistant to Ceftriaxoneantibiotics.

Table 3 shows the characteristics of Ceftriaxone antibiotic use Ceftriaxonein the study subjectsn.

Table 3. Characteristics of antibiotic use Ceftriaxonein the study subjects

Use of Antibiotics		Before ASP	After ASP
Duration of use	≤ 72 hours	21 (21.4)	97 (97.9)
	≥ 72 hours	77 (78.6)	2 (2.02)
Culture Retrieval	Before use of antibiotics	46 (46.9)	51 (51.5)
	After use of antibiotics	52 (53.0)	48 (48.5)

Description: data presented in (%)

Less than 72 hour-long antibiotic administration before ASP was 21.4%, and more than 72-hours duration of antibiotic Ceftriaxones was 78.6% (p=0.001). While less than 72-hour duration of administration after ASP of Ceftriaxones was as much as 97.9%, and the duration of Ceftriaxone for more than 72 hours was 2.02% (p=0.001). Before ASP, the culture taken showed 46.9% and 53.0% before and after antibiotic administration; respectively. After ASP, the culture retrieval performed before and after antibiotic administration showed 51.5% and 48.5%; respectively.

Description: data presented in DDD/100 patient-day

The Ceftriaxone antibiotic value of DDD/100 patient-day Ceftriaxone after ASP was lower than after ASP (successively 71,194 and 72,692) with p=0.001.

Discussion

For administration of antibiotics in surgery, it was needed to take into account some essential things that included: antimicrobial activity should appear on the site of the wound during the wound closure, antibiotics must be active against predicted contaminant microorganisms, and long-term administration of drugs after surgical procedures should not be justified and potentially would result in adverse conditions. Sterility factors and surgical techniques should also receive attention to minimize the risk of infection. [6]

The most commonly found irrationality in the use of antibiotics has been the presence of more effective antibiotics. It is because Ceftriaxone that should be given as a second-line therapy is used as that of a first-line, causing Ceftriaxone to become the most widely used antibiotic. There are other antibiotics that are more effective for use as first-line surgery, namely cephalosporins (such as cefazolin). [7]

There is a need for particular attention to the high use of Ceftriaxone in surgery because Ceftriaxone is a cutting-edge, broad-spectrum antibiotic that acts as a therapeutic drug. In case of infection when Ceftriaxone is used as prophylactic therapy, the choices of antibiotics for therapy become significantly complicated. In addition, Ceftriaxone is also an antibiotic that can induce the onset of the *Extended-Spectrum Beta-Lactamase (ESBL)* strain. [8, 9]

Doctors should be more selective in using Ceftriaxone. A common problem in surgery is prescribing antibiotics more than 24 hours after unconscious surgery. According to Shah *et al.*, the incidence of nosocomial infections in the surgical wards is high enough to cause surgeons to choose antibiotics on the alert for infections despite no clear indications. [10]

According to Slobogean et al.'s research, prophylactic antibiotics given in more significant quantities or the same minimal amount will give surgical wounds infections that do not vary much. Provision of antibiotics in the minimum amount will provide benefits regarding cost, and antibiotics overuse can cause resistance to these antibiotics. [11]

The study showed that there were 48.97% and 46.5% incidences of inpatients who underwent a surgical procedure and were at the age of 20-35. There was a slight difference between men and women regarding incidence due to surgery in both groups; male subjects before ASP showed 63.26% and women subjects showed as much as 36.73%. Meanwhile, after ASP, the numbers shown for male and female subjects were 68.7% and 31.3%; respectively. In addition, male patients had higher incidence rates in neurosurgery and urological surgery.

The result of a positive blood culture before ASP was 12.5%, and after ASP was 20.8%. Patients receiving antibiotic therapy should be cultured to receive appropriate antibiotic therapy for therapeutic purposes. Most of the blood culture results in both groups found no bacterial growth in 87.5% of the study subjects before ASP and 79.2% after ASP. Negative blood culture results may be due to several factors such as the patients' clinical condition, and the duration of antibiotics for seven days before blood culturing. The results showed that some of the most common bacteria found in blood cultures are *Escherichia coli (ESBL), Acinetobacter baumannii*, and *Pseudomonas aeroginosa* which can be sources of infection in surgical wounds.

The results of the characteristics of Ceftriaxone showed a significant difference with the value of p=0.001. Whereas before long ASP, antibiotic value of Ceftriaxone in less than 72 hours, was 21.4%, and during ASP, antibiotic value of Ceftriaxone in more than 72 hours, was 78.6%. While after ASP, antibiotic value of Ceftriaxone in less than 72 hours, was as much as 97.9%, and during using antibiotic value of Ceftriaxone in more than 72 hours, was as much as 2.02% (Tables 3 & 4). This was in accordance with the principle of antibiotic use, where the duration of empirical antibiotics administration was within 48-72 hours. Reducing the duration of antibiotic use has also been one of the ASP interventions to reduce antibiotic use in hospitals.

The DDD/100 patient-day y-level results after ASP were lower than before ASP. The results also showed that the use of Ceftriaxone antibiotics in the surgical wards was lower than the WHO standard, that is 2 DDD daily, which showed that the daily use of Ceftriaxone antibiotics was 0.71 DDD. The results complied with the principle of wise use of antibiotics: the smaller the antibiotic DDD results obtained, the better the use of antibiotics on patients.

DDD/ patient-day antibiotic values for Ceftriaxone before and after ASP can be seen in Table 4.

Table 4. DDD / patient-day antibiotic values Ceftriaxone before and after ASP

DDD	Before ASP	After ASP	Difference (95% CI)
DDD / 100 patient-day	72,692	71,194	1,498

Conclusion

The value of DDD/100 patient-days of Ceftriaxone antibiotic after antimicrobial stewardship program was lower than before the antimicrobial stewardship program in the neurosurgeon and digestive patients.

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