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A Pilot Study of the Evaluation of Using Antibiotics in Sepsis Patients in Palu, Indonesia

Alwiyah Mukaddas, Tatat Rahmita Utami, Amelia Rumi*

Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Tadulako University, Palu, Indonesia

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***Correspondence:** Amelia Rumi, Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Tadulako University, Palu, Indonesia.
E-mail: ameliarumiuntad20@gmail.com
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Abstract

BACKGROUND: Treatment therapy with antibiotics is one of the factors supporting success in the treatment of sepsis.

AIM: This study aims to evaluate the use of antibiotics in patients with sepsis using parameters of the day of decline in body temperature, heart rate, respiration rate, changes in consciousness status, and comorbid factors.

MATERIALS AND METHODS: The design of this study is pilot study with a retrospective approach on sample of 14 sepsis patients who met the inclusion criteria. Descriptive analysis using the univariate method for see changes in levels of body temperature, length of stay, respiration rate, heart rate, comorbid factors, and changes in the consciousness status.

RESULTS: The results showed an average value for decline of body temperature after using antibiotics with a baseline of 38.47°C–37.87°C, heart rate shows the average value from baseline heart rate after using antibiotics from baseline of 110.8 bpm to 88.4 bpm, the respiration rate shows the average value for the respiration rate after using antibiotics from baseline of 30.8 x/min to 22.1 x/min, Glasgow Coma Scale (GCS) score showed an average value after using antibiotics from baseline 9 to 7, on comorbid factors showing six patients with one comorbid and eight patients with more than 1 comorbid factor.

CONCLUSION: The study concluded that body temperature is still in the category of fever, heart rate, and respiration rate which are the normal category, patient consciousness is still at the level of somnolence even though patient's GCS score has decreased, and patients with one factor of comorbidities are faster in death because they have a fatal type of comorbid such as acute of hepatitis, coma hepaticum, and acute kidney injury.

Introduction

Sepsis is the condition in which the patient goes through periods of bacteremia, systemic inflammatory response syndrome, sepsis, severe sepsis, shock septic, or multiple organ dysfunction syndrome which has gone into overlap and suggests a progressive deterioration physiology [1]. Clinically, sepsis is differentiated based on sepsis, severe sepsis, and sepsis shock. Severe sepsis can be seen from the dysfunction of one organ or organ system while septic shock can be seen from the presence of organ or organ system dysfunction and hypotension that does not improve with fluid resuscitation [2].

Therapy with antibiotics appropriately and adequately is still one of the factors supporting success in the treatment of sepsis which is proven to reduce mortality in sepsis and sepsis cycles [3]. Antibiotics are antimicrobial product obtained from substances derived from the microorganism or a synthetic substance which can kill or inhibit the work of another microorganism [4]. Antibiotics are given immediately during the 1st h after being diagnosed with severe sepsis and septic shock. Where every hour, the administration of antibiotics is delayed because delays in administering antibiotics can cause death, where every hour the delay antibiotic administration is associated with 6% increase in mortality [5].

According to Dewi (2014), sepsis has caused most of the deaths in hospital Dr. Cipto Mangunkusumo Jakarta in 2010. Number of patients with sepsis also increased at hospital Dr. M. Djamil Padang, from 2010 to 2013, 351 patients, 512 patients, 757 patients, and 734 patients [6], [7].

The purpose of this study was to look at the pattern of antibiotic use in sepsis patients and evaluate of antibiotic use in patients with sepsis in terms of days of decreased body temperature, length of stay, respiration rate, heart rate, comorbid factors, and changes in consciousness status.

Ethics approval

This research has been approved by the Research Ethics Committee of the Faculty of Medicine and Health, Tadulako University, with a letter number 3869/UN28.1.30/KL/2019.

Materials and Methods

The subjects of this study were septic patients who were hospitalized and received antibiotic therapy fulfilling the inclusion criteria: Patients aged >18 years who had data in their medical record on: Levels of body temperature, length of stay, respiration rate, heart rate, comorbid factors, and changes in the consciousness status. The exclusion criteria: Patient's medical records are incomplete or missing and patients who are suffering shock septic.

Methods and analysis

The study was a pilot study in which data were collected retrospectively on medical record data from sepsis patients in a private hospital in Palu City, Central Sulawesi, Indonesia. The sample retrieval technique is a total sampling by gathering all medical records of sepsis patients that meet the criteria of inclusion and exclusion because of a very small number of samples. The baseline score when patients were first diagnosed sepsis and the value of evaluation was seeing the effectiveness of the antibiotic usage being made from the 1st day of dropping body temperature and then measuring other parameters such as heart rate, respiration rate, and Glasgow Coma Scale (GCS). Descriptive analysis using the univariate method for see changes in heart rate, respiration rate, changes in the patient's consciousness status, before and after using antibiotics.

Results

Demographic characteristics

Table 1 shows that of the 14 patients with sepsis, 7 patients were male (50%), comparable to the number of female patients also 7 people (50%). The age range patients were 46–55, 56–65, and more than 65 years all categories by 4 patients (28.6%).

Table 1: Demographic characteristics of sepsis patients in Palu, Indonesia

Characteristics	Number of sepsis patients (n=14)	Percentage
Gender		
Male	7	50
Female	7	50
Age		
26–35	1	7.1
36–45	1	7.1
46–55	4	28.6
56–65	4	28.6
>65	4	28.6

Clinical manifestations

Table 2 shows that the dominant clinical manifestations in 14 sepsis patients were fever, leukocytosis, tachycardia, decreased consciousness with a percentage of 85.8%, tachypnea with a percentage of 71.4%, and leukopenia with two patients.

Table 2: Clinical manifestations in sepsis patients in Palu, Indonesia

Symptoms	Number of sepsis patients	Percentage
Fever	12	85.8
Leukocytosis	12	85.8
Leukopenia	2	14.2
Tachypnea	10	71.4
Tachycardia	12	85.8
Loss of consciousness	12	85.8

Diagnosis

Table 3 shows the diagnosis of sepsis patients dominated by diabetes mellitus (DM) (28.6%), CKD (21.4%), pneumonia (14.2%), and AKI (14.2%).

Table 3: Diagnosis of sepsis patients in Palu, Indonesia

Diagnosis	Number of sepsis patients	Percentage
Type 2 diabetes	4	28.6
CKD	3	21.4
Pneumonia	2	14.2
AKI	2	14.2

CKD: Chronic kidney disease, AKI: Acute kidney injury.

Comedication

Table 4 shows that other therapies combined with antibiotics were ranitidine (71.4%), paracetamol (64.2%), and dexamethasone (57.1%).

Table 4: Medication profile of sepsis patients in Palu, Indonesia

Other therapies used	Number of sepsis patients	Percentage
Ranitidine	10	71.4
Omeprazole	6	42.9
Sucralfate	3	21.4
Lansoprazole	1	7.1
Ketorolac	4	28.5
Natrium Diclofenac	1	7.1
Metamizole sodium	1	7.1
Mefenamic acid	1	7.1
Paracetamol	9	64.2
Amino acid	2	14.2
Curcuma xanthorrhiza	1	7.1
PotassiumChloride	1	7.1
Vitamin B1	4	28.5
Vitamin B6	4	28.5
Vitamin B12	4	28.5
Novorapid	3	21.4
Levemir	2	14.2
Metformin	1	7.1
Domperidone	2	14.2
Ondansetron	2	14.2
Loperamide	1	7.1
Furosemide	1	7.1
Metilprednisolone	1	7.1
Dexamethasone	8	57.1
Norepinephrine	1	7.1
Dopamine	1	7.1
Allopurinol	1	7.1
Alprazolam	1	7.1
Citicoline	4	28.5
Propranolol	1	7.1
Loratadine	1	7.1
Ambroxol	2	14.2
Phenytoin	1	7.1
Infuse NaCl 0,9 %	14	100
Infuse ringer lactate	14	100

Antibiotic therapy evaluation heart rate

Table 5 shows that there was a change from the baseline heart rate from 110.8 bpm to 88.4 bpm

where the evaluations show the average heart rate of patients become normal after using antibiotics.

Table 5: Heart rate of sepsis patients in Palu, Indonesia

	Mean value			Percentage
	Baseline	Evaluation	Deviation	
Heart rate	110.8	88.4	22.4	20.21

Respiration rate

Table 6 shows that there has been a change from the baseline respiration rate which was valued at 30.8 x/min–22.1 x/min and evaluations show the average of patients respiration rate to normal after using antibiotics.

Table 6: Respiration rate of sepsis patients in Palu, Indonesia

	Mean value			Percentage
	Baseline	Evaluation	Deviation	
Respiration rate	30.8	22.1	8.7	28.2

Day of decreasing body temperature

Table 7 shows that there was a change from the previous baseline body temperature of 38.47°C–37.87°C where the initial body temperature was diagnosed with a decline during antibiotics but is still in category fever.

Table 7: Body temperature of sepsis patients in Palu, Indonesia

Baseline (°C) (n = 14)	Evaluation (°C)
38.47	37.87

GCS

Table 8 shows that there were changes from the previous baseline GCS 9–7. However, the evaluation results showed that patients remained in somnolence state, but the GCS scores decreased. It suggests that the patient's conscious status has not improved or has not increased the GCS score after antibiotic therapy.

Table 8: GCS of sepsis patients in Palu, Indonesia

	Mean value			Percentage
	Baseline	Evaluation	Deviation	
GCS	9	7	2	24.8

GCS: Glasgow Coma Scale.

Comorbidities factor

Table 9 shows that sepsis patients were dominated by patients with more than 1 comorbidity (57.1%) compared to those who only had one comorbidity (42.9%).

Table 9: Comorbidities factors of sepsis patients in Palu, Indonesia

Comorbid of factors	Number of sepsis patients (n=14)	Percentage
One comorbid	6	42.9
More than 1 comorbid	8	57.1

The evaluation of antibiotics therapy

Table 10 shows the total number of antibiotic use. Use of single antibiotic therapy as ceftriaxone, meropenem, cefuroxime, and cefobactam was with a percentage of 14.2% and combination of antibiotic therapy ceftriaxone + metronidazole was 28.6%.

Table 10: Medications antibiotics profile of sepsis patients in Palu, Indonesia

Therapy	Antibiotics therapy	Number of sepsis patients (n=14)	Percentage (%)
Single	Ceftriaxone	2	14.2
	Meropenem	2	14.2
	Cefobactam	2	14.2
	Cefotaxime	1	7.1
	Cefuroxime	2	14.2
Combination	Ceftriaxone + metronidazole	4	28.6
	Ceftriaxone + ciprofloxacin	1	7.1
	Metronidazole + meropenem	1	7.1
	Metronidazole + cefadroxil	1	7.1
	Metronidazole + cefixime	1	7.1
	Metronidazole + cefuroxime	1	7.1
	Metronidazole + gentamicin	1	7.1
	Meropenem + ceftazidime	1	7.1
	Meropenem + cefuroxime	1	7.1

Length of stay

Table 11 shows that half of the patients with a diagnosis of sepsis in this study (85.8%) were treated for 2–10 days, 7.1% of patients were treated for more than 10 days, and 7.1% of patients were treated for more than 20 days.

Table 11: Length of stay of sepsis patients in Palu, Indonesia

Length of stay	Number of sepsis patients (n=14)	Percentage	Note
0–10 days	12	85.8	Death cases
10–20 days	1	7.1	Death case
>20 days	1	7.1	Death case

Discussion

In this study, the age of most sepsis patients was between the ages of 46–55, 56–65, and more than 65 years as many as 4 patients (28.6%). This result is consistent with the research conducted by Nurul that the proportion of elderly patients died of more sepsis. This is confirmed in the Bhattacharjee study that elderly people have the greatest risk of developing sepsis with its various complications, including higher mortality. The risk of sepsis in the elderly increases due to various causes such as comorbidities, decreased kidney and liver function, and low body response to overcome sepsis [8], [9].

Sepsis is not influenced by gender but is influenced by age and the type of underlying disease. Other studies have found mixed results, namely, that women only 10% of developing sepsis and dying [10].

Most clinical manifestations are fever, leukocytosis, tachycardia, and changed level of consciousness. The fever is the most common symptom. In this study, 12 patients entered the hospital with body temperature starting from 38°C to 40°C in the category of fever and generally indicated an infection, but two patients were admitted to the hospital with a normal body temperature of 36°C–6.2°C which generally indicated

no presence of infection. Leukocytosis is a common symptom in patients diagnosed with sepsis. Mild disorientation or confusion usually occurred in the elderly. Other manifestations include anxiety and agitation.

The diagnosis of sepsis is dominated by DM. Patients with DM are at risk of infection and sepsis. Sources of bacterial infections that cause sepsis, one of which is a bacterial infection in wounds with long periods (chronic wounds). Chronic injuries often occur in people with DM where there is damage to blood vessels, innervation, and decreased endurance which causes bacteria to thrive and wounds are difficult to heal. Bacteria can enter the bloodstream and spread throughout the body, resulting in sepsis reactions to so why DM is a deteriorating factor of comorbidity in sepsis.

Most of the seriously ill patients admitted to the hospital's intensive care unit showed signs of gastric mucosa damage. Patients with sepsis who were treated received prophylactic stress ulcer therapy, namely, H2 blocker/PPI/combination (ranitidine and omeprazole). In adult sepsis, patient corticosteroids were not given if fluid resuscitation is adequate and the use of vasopressor drugs achieves stable hemodynamics. If the target is not achieved, then corticosteroids need to be given [2]. Corticosteroids that are recommended by the guidelines for SMF Internal Medicine Clinical Guidelines from 2013 for Dr. Moewardi Surakarta (PPK) were methylprednisolone and dexamethasone.

The patient's heart rate monitoring results showed that there was a change from the baseline heart rate which was previously worth 110.8 bpm–88.4 bpm and the evaluation results showed that the patient's heart rate was normal after using antibiotics. Tachycardia is an early sign of sepsis. In the study, it was reported that the initial heart rate in sepsis patients was 120 x/min. Decrease in heart rate to a 106 x/min in the first 24 h improves life rates [11].

The results of monitoring the patient's respiration rate showed that there was a change from the baseline respiration rate which was previously at 30.8 x/min–22.1 x/min and the evaluation results showed the average respiration rate, the patient becomes normal after using antibiotics. Respiratory rate was one of the assessment parameters which significantly affected mortality in sepsis patients compared to other variables. A study that states that the inaccuracy of the implementation of the surviving sepsis campaign is mainly related to the availability of mechanical ventilation and the adequacy of calories in the first 48 h will increase the risk of mortality [12].

The results of monitoring the patient's body temperature showed that there was a significant difference between body temperature at the initial diagnosis and temperature decreased during antibiotic use. For a decrease in temperature seen from the day, when the patient starts antibiotic therapy, but the body temperature can rise again. In this study, the average decrease in body temperature occurred after 1 day the patient was given antibiotics.

The baseline GCS score is 9 and the evaluation average of 7 is that the patient remains in somnolence state, but the GCS score is decreased. Somnolence is a condition in which the patient is in a deep drowsy condition, but can still be awakened using stimulation. In the study, there has been no improvement in the GCS score after antibiotics were given. This comparably studies made by Alalawi *et al*. that GCS score not only predicts development of sepsis but also has prognostic value. Patients who have low GCS have a high mortality rate [13].

Comorbidity factors are one of the other factors that can increase the mortality of patients with sepsis. The results of this study indicate that patients who die earlier are patients who have one comorbid disease with 1–4 days of hospital stay and have a fairly fatal type of comorbid disease, namely, acute hepatitis, AKI, hepatic encephalopathy, and CKD. Patients who survived for a long time were patients who had more than 1 comorbid disease with a length of stay in hospital 1–24 days later had fatal types of comorbid diseases, namely, DM, diabetic ulcer, bronchitis, pneumonia, CKD and comorbid diseases that were not too fatal namely dyspepsia, pancytopenia, anemia, gout arthritis, obstructive ileus, and peritonitis.

Cephalosporin group of antibiotics, especially ceftriaxone, is widely used as single or combination therapy ceftriaxone is a third-generation broad-spectrum cephalosporin antibiotic for intravenous or intramuscular administration. It is one of the most commonly used antibiotics due to its high antibacterial potential, broad spectrum of activity, and low potential for toxicity. Most widely (commonly) used combination of antibiotics is ceftriaxone and metronidazole with a percentage of 28.6%. Ceftriaxone is a third-generation cephalosporin group. Its activity against Gram-negative germs is stronger and wider. Ceftriaxone cannot overcome infection from anaerobic bacteria so it is combined with metronidazole which can overcome infection from anaerobic bacteria. Anaerobic bacteria that cause pneumonia are *Klebsiella pneumoniae*. The combination of cephalosporins and metronidazole is effective as empirical therapy in due leg infection will increase the complexity of antibacterial activity which can fight Gram-positive and -negative bacteria too anaerobic bacteria [14], [15].

In this study, more than half of patients (85.8%) were treated for 2–10 days, 7.1% of patients were treated for more than 10 days, and 7.1% of patients were treated for more than 20 days. Elderly age, comorbidity, complications, and failure in early diagnosis of sepsis are predictors for the length of stay in septic patients [10].

All patients who suffer from sepsis (100%) leave the hospital in a state of death. This can be caused by several things, namely, patients late for hospital admission, patients diagnosed late sepsis, antibiotics are given are not effective, and the presence of complications or comorbid factors. In this study, antibiotic administration

was not rational because in these patients, no culture tests were carried out, so antibiotic use was carried out empirically, which was said to avoid the use of a combination of antibiotics for therapy for a long time.

Conclusion

Based on the research conducted, it can be concluded that the average value for body temperature after using antibiotics is still in the category of fever, heart rate, and respiration rate which are the normal category, patient consciousness is still at the level of somnolence even though patient's GCS score has decreased, and patients with one factor of comorbidities are faster in death because they have a fatal type of comorbid such as acute of hepatitis, coma hepatikum, and acute kidney injury. Prompt and appropriate early treatment at the time of arrival can indicate a prognosis in which the patient is more likely to accept all the necessary interventions including blood cultures and therefore definitive antibiotic therapy can be administered.

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