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Patterns of Antibiotic Use in The One Hour Bundle Treatment of Sepsis

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ABSTRACT

Introduction: Sepsis and septic shock are major health problems, affecting millions of people worldwide and a leading cause of death. Administration of broad-spectrum empiric antibiotics as a one hour sepsis bundle treatment is associated with antimicrobial resistance which has various adverse effects and reduces the quality of health services. The aim of this research was to determine the pattern of empiric antibiotic use in the management of one hour bundle of sepsis at Haji Adam Malik General Hospital Medan.
Method: This study used a descriptive method from November 2022 to December 2022 in the Emergency Room (ER), Medical Inpatient Room, Surgical Inpatient Room, and Adult Intensive Care Unit (ICU) of Haji Adam Malik General Hospital Medan. This study used a consecutive sampling technique to recruit 42 sepsis patients who were given a one hour bundle of sepsis according to the inclusion and exclusion criteria. This descriptive analysis was used to determine the characteristics of the sample, namely age, sex, culture results, and antibiotic sensitivity test results.
Results: The most common use of antibiotics in the one hour bundle sepsis strategy was ceftriaxone 1 gram in 20 patients (47.6%), Ampicillin-Sulbactam 1.5 grams in 10 patients (23.8%), Levofloxacin 750 mg in 6 patients (14.3%), Meropenem 1 gram in 4 patients (9.5%), and Ciprofloxacin 200 mg in 2 patients (4.8%).
Conclusion: Antibiotic administration time is less than 1 hour in the one hour bundle strategy carried out in the ER. Most of the antibiotics given are in accordance with the antibiotic sensitivity test results, but there are still some patients who still experience resistance to the antibiotics.given so it is important to always or immediately carry out culture and sensitivity tests on patients so that the antibiotics given can be more optimal.

Keywords: Sepsis, One Hour Sepsis Bundle, Antibiotic, Resistant

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INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Sepsis and septic shock are major health problems, affecting millions of people worldwide each year and are the leading cause of death, accounting for one in three and one in six respectively. Early identification and appropriate management in the early hours after the development of sepsis, will improve good outcomes.[1,2]

Since 2016, sepsis criteria have been assessed through the Sequential Organ Failure Assessment (SOFA) score, while for emergency room patients using quick SOFA (qSOFA) which consists of three variables, namely: changes in consciousness (GCS <15), tachypnea (respiratory rate > 22 x/minute) and hypotension (systolic pressure ≤100 mmHg).[3,4] In the latest guidelines from the Society of Critical Care Medicine (SCCM) in 2021, it is no longer recommended to use the qSOFA score as the sole tool for screening against

sepsis, but rather to use Systemic Inflammatory Response Syndrome (SIRS), and National Early Warning Score (NEWS), or Modified Early Warning Score (MEWS).[1]

Data from Germ Patterns and Their Sensitivity to Antibiotics at Adam Malik Haji Center General Hospital (RSUP HAM) Medan for the January-December 2020 period showed >80% sensitivity to the antibiotics Meropenem, Amikacin, Tigecyclin (for Gram negative bacteria), and Minocycline, Doxycycline, Linezolid, Tigecyclin (for Gram-positive bacteria) in several treatment rooms, namely intensive care rooms, surgical inpatients, medical inpatients, pediatric inpatients. IV of 2018 concerning Guidelines for the Use of Antibiotics, such as administering Amikacin, Meropenem, Gentamicin,and the combination of Sefoperazone and Sulbactam can be given after being approved by the Antibiotic Resistance Control Program Team (PPRA) in inpatient rooms and the Intensive Care Unit (ICU).

METHOD

This study used a descriptive method to determine the empirical use of antibiotics as a one-hour bundle treatment with an observational design. Where each subject was only observed once and the measurement of subject variables was carried out at the time of the examination. This study was also conducted to determine the description of antibiotic resistance and to evaluate the suitability of broad-spectrum antibiotics in septic patients.

The study population was new patients who were diagnosed with sepsis or septic shock during the sampling period at the IGD Haji Adam Malik General Hospital, Medan, with a total of 42 samples. The sample of this study were sepsis patients who were given the one hour bundle of sepsis at the Haji Adam Malik General Hospital in Medan. The data obtained will be processed with the help of the Statistical Package for Social Science (SPSS) program. This descriptive analysis was used to determine the characteristics of the sample, namely age, sex, culture results, and antibiotic sensitivity test results.

RESULTS

After conducting a descriptive study on 42 sepsis patients who received a one-hour sepsis bundle that met the inclusion and exclusion criteria at Haji Adam Malik General Hospital Medan from November 2022 to December 2022, the results of the study sample characteristics were obtained as follows.

Table 1 Characteristics of the Research Sample

Characteristics	n (%)
Gender n (%)	
Man	25 (59.5)
Woman	17 (40.5)
Age n (%)	
18 – 35 Years	3 (7,2)
36 – 45 Years	3 (7,2)
46 – 55 Years	8 (19)
56 – 65 Years	19 (45.2)
> 65 years	9(21,4)

Based on gender, 25 patients (59.5%) were male and 17 patients (40.5%) were female. For age, the majority of patients were 19 people (45.2%) aged 56-65 years, followed by 9 patients (21.4%) aged > 65 years, 8 patients (19%) aged 46-55 years, and each 3 patients (7.2%) were aged 18-35 years and 36-45 years respectively.

The most common use of antibiotics in the one hour bundle sepsis strategy was Ceftriaxone 1 gram in 20 patients (47.6%), Ampicillin-Sulbactam 1.5 grams in 10 patients (23.8%), Levofloxacin 750 mg in 6 people (14, 3 %), Meropenem 1 gram in 4 patients (9.5%), and Ciprofloxacin 200 mg in patients (4.8%).

Table 2 Antibiotics used in the One – Hour Bundle

Types of Antibiotics	n (%)
Ceftriaxone 1 gr	20 (47.6)
Ampicillin Sulbactam 1.5 gr	10(23,8)
Ciprofloxacin 200 mg	2(4,8)
Levofloxacin 750 mg	6 (14,3)
Meropenem 1gr	4 (9.5)
Total	42 (100)

Table 3 The timeliness of giving antibiotics according to the one hour bundle

No	Diagnosis Time	Time of Administration of Antibiotics	Time Difference
1	15:13	15:45	00:32:00
2	15:55	16:10	00:15:00
3	4:45 p.m	17:05	00:20:00
4	09:30	09:55	00:25:00
5	09:56	10:36	00:40:00
6	07:45	08:13	00:28:00
7	06:15	06:37	00:22:00
8	10:10	10:42	00:32:00
9	10:15	10:46	00:31:00
10	14:15	14:41	00:26:00
11	4:47 p.m	17:11	00:24:00
12	13:24	13:54	00:30:00
13	12:32	12:52	00:20:00
14	06:40	07:10	00:30:00
15	12:00	12:36	00:36:00
16	13:05	13:42	00:37:00
17	13:22	13:41	00:19:00
18	14:44	15:11	00:27:00
19	16:22	16:54	00:32:00
20	16:11	16:42	00:31:00
21	12:55	13:25	00:30:00
22	07:26	07:59	00:33:00
23	12:43	13:12	00:29:00
24	11:34	11:54	00:20:00
25	09:54	10:17	00:23:00
26	18:02	18:47	00:45:00
27	15:23	15:53	00:30:00
28	12:12	12:42	00:30:00
29	06:22	06:22	00:00:00
30	12:00	12:35	00:35:00
31	12:22	12:48	00:26:00
32	14:14	14:53	00:39:00
33	14:54	15:43	00:49:00
34	09:23	09:54	00:31:00
35	09:30	09:59	00:29:00
36	13:02	13:43	00:41:00
37	15:45	16:27	00:42:00
38	12:22	12:42	00:20:00
39	2:45 p.m	15:25	00:40:00
40	18:06	18:56	00:50:00
41	17:00	17:43	00:43:00
42	18:22	18:47	00:25:00

After documenting the time of diagnosis and the time of administration of antibiotics, it was found that the time difference between the two did not reach 1 hour, with the shortest span being 15 minutes and the longest being 49 minutes.

The following data have been collected for the suitability of the empiric antibiotics given with the results of culture and sensitivity tests and the underlying pathological condition.

Table 4 Conformity of empirical antibiotics given with culture results and sensitivity tests.

Given antibiotics	Blood Culture	Resistant Antibiotics	suitability
Ceftriaxone 1 g	Acinobacter Baumani, Klebsiella Pneumoniae	Gentamycin, Tetracycline, Aztreonam, Chloramphenicol	Not Resistance
Ampicillin Sulbactam 1.5 g	Klebsiella pneumoniae	Ampicillin	Not Resistance
Ceftriaxone 1 g	Candida Albicans, Negative MTB, Acinobacter Baumani	Amocixilin, Ampicillin, Ampicillin/Sulbactam	Not resistant
Ampicillin Sulbactam 1.5 g	Corynebacterium striatum	Ampicillin/Sulbactam	resistance
Ampicillin Sulbactam 1.5 g	Acinobacter Baumani, Klebsiella Pneumoniae	Ampicillin/Sulbactam	resistance
Ceftriaxone 1 g	Escherichia coli	Cefazolin	Not Resistance
Ampicillin Sulbactam 1.5 g/6 Hours	Pseudomonas aeruginosa	Ampicillin/Sulbactam	
Ceftriaxone 1 g	Acinobacter Baumani, Klebsiella Pneumoniae	Tetracycline	Not Resistance
Ceftriaxone 1 g	Enterococcus faecium	Tetracycline	Not Resistance
Ceftriaxone 1 g	Acinobacter Baumani, Klebsiella Pneumoniae	Cefazolin, Tigecycline	Not Resistance
Ceftriaxone 1 g	Pseudomonas aeruginosa	Chloramphenicol, Levofloxacin, Ciprofloxacin, Amoxilin/clavulanate, Ampicillin, Ampicillin/sulbactam, Aztreonam, Cefazolin, Cefepime, Cefotaxime	Not Resistance
Levofloxacin 750 mg	Acinobacter Baumani, Klebsiella Pneumoniae	Tetracycline	Not Resistance
Ceftriaxone 1 g	Acinobacter Baumani, Klebsiella Pneumoniae	Chlorampenicol	Not Resistance
Ceftriaxone 1 g	Acinobacter Baumani, Klebsiella Pneumoniae	Chlorampenicol	Not Resistance
Ampicillin Sulbactam 1.5 g	Staphylococcus aureus	Gentamicin, Chlorampenicol, Chlorampenicol, Amocixilin/Clevoanate,	Not Resistance
Ceftriaxone 1 g	Escherichia coli	Ampicillin, Ampicillin/Sulbactam, Cefazolin, Ceftazidime	Not Resistance
Ciprofloxacin	Pseudomonas aeruginosa	Piperacillin/Tazobactam, Cefazolin, Aztreonam, Ciprofloxacin, Tigecycline	resistance
Ciprofloxacin	Pseudomonas aeruginosa, Acinobacter baumani, Candida Ciferii	Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Cefixime, Astreonam. Gentamicin, Tygeciline	Not Resistance
Levofloxacin 750mg	Enterococcus faecium	Gentamicin, Chlorampenicol, Chlorampenicol, Amocixilin/Clevoanate,	Not Resistance
Ceftriaxone 1 g	Escherichia coli	Ampicillin/Sulbactam, Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone, Cefepime, Aztreonam, Meropenem, Amikacin, Gentamicin, Ciprofloxacin	resistance
Ceftriaxone 1g, Azithromycin 500mg	Enterococcus faecium	Ampicillin, Ampicillin/Sulbactam, Cefazolin, Ceftazidime, Ceftriaxone, Aztreonam, Ciprofloxacin, Trimethoprim/Sulfamethoxazole	resistance
Ceftriaxone 1 g	Escherichia coli	Ampicillin, Ampicillin/Sulbactam, Cefazolin, Ceftazidime, Ceftriaxone, Aztreonam, Ciprofloxacin, Trimethoprim/Sulfamethoxazole	resistance

Table 4. (Continuous)

Given Antibiotics	Blood Culture	Resistant Antibiotics	Suitability
Levofloxacin 750mg	Acinetobacter baumannii	Ampicillin/Sulbactam, Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone	Not Resistance
Ceftriaxone 1 g	Stenotrophomonas maltophilia	Cefazolin, Tigecycline	Not Resistance
Levofloxacin 750 mg	Enterococcus faecalis	Ampicillin/Sulbactam	Not Resistance
Ceftriaxone 1 g	Acinetobacter baumannii	Ampicillin/Sulbactam, Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone	resistance
Ceftriaxone 1 g	Candida albicans	Cefazolin, Tigecycline	Not Resistance
Ampicillin Sulbactam 1.5g	Corynebacterium striatum	Tetracycline, Ciprofloxacin, Clindamicin, Levofloxacin	Not Resistance
Levofloxacin 750mg	Acinetobacter baumannii	Gentamycin, Tetracycline, Aztreonam, Chloramphenicol	Not Resistance
Ceftriaxone 1 g	Enterococcus faecium	Benzylpenicillin, Ampicillin, Gentamicin, Ciprofloxacin	Not Resistance
Meropenem 1 g	Acinetobacter baumannii	Ampicillin/Sulbactam, Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone	Not Resistance
Ampicillin Sulbactam 1.5g	Pseudomonas aeruginosA	Cefazolin	Not Resistance
Ceftriaxone 1 g	Stenotrophomonas maltophilia	Tigecycline	Not Resistance
Levofloxacin 750mg	Acinetobacter baumannii	Ampicillin, Ampicillin/Sulbactam, Cefazolin, Ceftazidime, Ceftriaxone, Aztreonam, Ciprofloxacin, Trimethoprim/Sulfamethoxazole	Not Resistance
Ceftriaxone 1 g	Acinetobacter baumannii	Cefazolin	Not Resistance
Meropenem 1 g	Acinetobacter baumannii	Ampicillin/Sulbactam, Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone	Not Resistance
Ceftriaxone 1 g	Escherichia coli	Ampicillin	Not Resistance
Meropenem 1g	Acinetobacter baumannii	Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone	Not Resistance
Meropenem 1 g	Enterococcus faecium	Benzylpenicillin, Ampicillin, Gentamicin, Streptomycin, Ciprofloxacin	Not Resistance
Levofloxacin 750mg	Staphylococcus aureus	Benzylpenicillin, Oxacillin, Gentamicin, Ciprofloxacin, Levofloxacin, Moxifloxacin, Erythromycin, Clindamycin, Amoxicillin, Cefadroxil, Cefradine	Not Resistance
Ampicillin Sulbactam 1.5 g	Acinetobacter baumannii	Cefazolin	Not Resistance
Ceftriaxone 1 g	Candida albicans	Piperacillin/Tazobactam, Cefazolin, Ceftazidime, Ceftriaxone	resistance

After documenting data on antibiotic resistance in sepsis patients at H. Adam Malik General Hospital Medan, the results showed that the most resistance was to Cefazolin, Ampicillin and Ceftazidime with a total of 21, 19 and 12 patients, respectively. In addition, 10 patients were found to be resistant to Ceftriaxone, 9 patients to be resistant to Gentamicin and Piperacillin-Tazobactam, respectively; 8 patients were resistant to Aztreonam and Ciprofloxacin, respectively; 5 patients were resistant to Tigecycline and Tetracycline, respectively; 3 patients were resistant to Amoxicillin, Chloramphenicol, Levofloxacin, Benzylpenicillin and Trimethoprim-Sulfamethoxazole, respectively; 2 patients were resistant to Clavulanate and Cefepime, respectively and 1 patient was resistant to Cefotaxime and Streptomycin, respectively.

Table 5 Description of antibiotic resistance in HAM Hospital

Types of Antibiotics	Number of Patients
Gentamycin	9 samples
Ceftriaxone	10 samples
Ampicillin	19 samples
Amoxicillin	3 samples
Cefazolin	21 samples
Tigecycline	5 samples
Chloramphenicol	3 samples
Levofloxacin	3 samples
Aztreonam	8 samples
Tetracycline	5 samples
Cefepime	2 samples
Cefotaxime	1 sample
Clavulanate	2 samples
Ceftazidime	12 samples
Piperacillin/Tazobactam	9 samples
Benzylpenicillin	3 samples
Trimethoprim/sulfamethoxazole	3 samples
Ciprofloxacin	8 samples
Streptomycin	1 patient

DISCUSSION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Sepsis and septic shock are major health problems, affecting millions of people worldwide each year and are the leading cause of death, accounting for one in three and one in six respectively. Early identification and appropriate management in the early hours after the development of sepsis, will improve good outcomes.[1]

Improved recognition of sepsis, consistent with the overall one-hour bundle, and with three main components: fluid resuscitation, blood cultures, and administration of antibiotics. The risk of death before implementing the protocol was four times greater, and the absolute risk reduction was 9%. Data from Germ Patterns and Their Sensitivity to Antibiotics at Haji Adam Malik General Hospital Medan for the January-December 2020 period showed >80% sensitivity to the antibiotics Meropenem, Amikacin, Tigecyclin (for Gram negative bacteria), and Minocycline, Doxycycline , Linezolid, Tigecyclin (for Gram-positive bacteria) in several treatment rooms, namely intensive care rooms, surgical inpatients, medical inpatients, pediatric inpatients. IV of 2018 concerning Guidelines for the Use of Antibiotics, such as administering Amikacin, Meropenem, Gentamicin,and the combination of Sefoperazone and Sulbactam can be given after being approved by the Antibiotic Resistance Control Program Team (PPRA) in inpatient rooms and the Intensive Care Unit (ICU).[2-3]

Kumar et al reported that delay in administration of antibiotics was common: 79% of patients did not receive antibiotics until hypotension developed, and of those patients, only 14.5% received them within the first hour of hypotension. Only 32.5% received antibiotics within 3 hours and only 51.4% within 6 hours. Kumar et al demonstrated that each additional hour without antibiotics increased the risk of death in septic shock patients by 7.6% during the first 6 hours. 62 However, Bloss et al demonstrated that delay in administration of antimicrobial therapy was more than 1 hour after the onset of organ dysfunction (OR (95). % CI): 0.96 (0.69 to 1.33) not associated with an increase in 28-day mortality.[3-5]

This study has a major limitation, namely not following up on outcomes such as morbidity and mortality rates from one hour bundle sepsis applied to patients. This is an observational study of the one-hour bundle of sepsis treatment, especially broad-spectrum empiric antibiotics and the results of their resistance cultures.

CONCLUSION

The antibiotics given in the study were not in accordance with sepsis regulations at Haji Adam Malik General Hospital Medan. The time for administering antibiotics was less than 1 hour in the one hour bundle strategy. Most of the antibiotics given are in accordance with the antibiotic sensitivity test results, but there are still some patients who still experience resistance to the antibiotics given so it is important to always or immediately carry out culture tests and sensitivity tests on patients so that the antibiotics given can be more optimal. The description of antibiotic resistance in Haji Adam Malik General Hospital Medan has the most resistance results to Cefazolin, Ampicillin and Ceftazidime with a total of 21, 19 and 12 patients, so that it can be considered to select other types of drugs for empiric drug administration in patients.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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AUTHORS' CONTRIBUTIONS

MHRS collects the data and writes the initial manuscript. ERD provided contribution and revision regarding the data analysis and imaging aspect of the discussion. RH provided contribution and revision regarding the data analysis and clinical aspect of the discussion. All authors read and approved the final manuscript.

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