DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 10, Number 3, May 2021

EVALUATION OF ANTIBIOTIC USAGE IN ISCHEMIC STROKE PATIENTS WITH INFECTIONS AT RSUP DR. KARIADI SEMARANG IN 2018

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ABSTRACT

Background: According to WHO, stroke is the second leading cause of death in the world with isschemic stroke as the most common type of stroke with 80% population. Data at RSUP Dr. Kariadi in 2015 showed that the most common complication in stroke was infection (37.9%). The most common cause of infection was bacteria with antibiotics as the main therapy. It is necessary to monitor the use of antibiotics due to increased cases of antibiotic resistance. **Objective:** To determine the rationality of antibiotic use in ischemic stroke patients with infections at RSUP Dr. Kariadi Semarang in2018. **Method:** This is a descriptive observational study. The sample consisted of 41 medical records of inpatient male ischemic stroke patients at RSUP Dr. Kariadi Semarang in 2018. The use of antibiotics was evaluated using the Gyssens method. **Results:** The results of evaluation of antibiotics by the Gyssens method showed that antibiotic rationality is 53%. The most widely used antibiotics are ampicillin sulbactam (30.4%) and levofloxacin (27.5%). Giving empirical therapy (57.5%), and diagnosis of infection in patients including pneumonia (50,8%), sepsis (19.3%), UTI (17.5%), pressure sores (5.3%), abscesses mandible (3.5%), ulcerative colitis (1.7%), cellulitis (1.7%), gasteroeneritis (1.75%). **Conclusion:** The use of antibiotics in ischemic stroke patients hospitalized at RSUP. Dr. Kariadi Semarang in 2018 is rational. Its users have the right antibiotics, indications, dosage, administration, route, time, interval and patient.
Keywords: antibiotics, infection, ischemic stroke, drug resistant

INTRODUCTION

According to WHO, stroke is the second leading cause of death around the world. Based on the research conducted by Basic Health Research in 2018, the incidence of stroke increased 3.6% in 5 years period.[1] The type of stroke having the highest incidence in population is non-hemorrhagic stroke (80%).[2] Stroke sufferers are easily infected while being treated in hospital. Based on research held at RSUP Dr. Kariadi in 2015, the most common complication found on stroke patients is infection (37.9%).[3] Several factors are suspected having contribution to cause infection in stroke patients. These factors include age factor, swallowing disfunction, and urinary disorders.[4]

Antibiotic usage is an effective treatment to reduce worsed conditions for strokes patients with infections. Based on research held at Bethesda Hospital Yogyakarta in 2018, the appropriate use of antibiotics in stroke patients showed the number of 36.0% while the other 64.0% was found inappropriate.[5] Therefore, the risk of antibiotic resistance caused by inappropriate use of antibiotics was increased. Based on WHO data, in 2013 there were 700,000 deaths due to antibiotic resistance and this figure will continue to increase if it is not controlled for its use. The death rate due to antibiotic resistance has increased and was predicted to keep increasing until 2050.

This study was conducted at RSUP dr. Kariadi Semarang. The place selection was done purposively due to the reason of RSUP dr. Kariadi being the largest hospital in Semarang, therefore the large number of patients using antibiotic is expected. The purpose of this study is to determine the rationality of antibiotic usage as a therapy in hospitalized ischemic stroke patients with infections in RSUP dr. Kariadi Semarang during the period of 2018.

METHOD

This is an observational descriptive study, conducted at Dr. Kariadi Semarang after receiving permission to conduct the research from the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University. The subjects were based on the medical records of male ischemic stroke patients, with clinical indication of antibiotic prescription, and ages 59-89 years old, with completed and readable medical records (Table 1).

The collecting data were categorizing antibiotic prescriptions according to the Gyssens method. Category 0 (classified as rational antibiotic usage), category I (inappropriate timing of antibiotic usage), category II (inappropriate dosage and route of antibiotic administration), category III (inappropriate

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duration of antibiotics), category IV (inappropriate antibiotic usage due to availability of other more effective antibiotics in terms of toxic effects, price, and spectrum), category V (no indication of infection), category VI (medical record data is not complete).

RESULT

The forty-one subjects collected which range of age 59 to 69 years old is the highest (73.2%), age 70 to 79 years old was 19.5%, and age 79 to 89 years is 7.3%. This finding is in accordance to the previous studies that discover stroke patients in the age range of 60s have a higher risk of infection.[3] The common infections diagnosis out of 41 medical records were pneumonia (50,8%), sepsis (19.3%), and UTI (17.5%).[6] Twelve types of antibiotics were found prescribed to the patients in 41 medical records of this study. The most common types of antibiotics being prescribed were Ampicillin sulbactam (30.4%) and Levofloxacin (27.5%).

Table 1. Subject characteristics

	Characteristics	**Percentage (%)**
Age	59-69	73,2
	70-79	19,5
	79-89	7,3
Infection	Pneumonia	50,8
	Sepsis	19,3
	UTI	17,5
	Infection DecubitusUlcer	5,3
	Cellulitis	3,5
	Gasteroenteritis	1,7
	Abses Mandibula	3,5
Type of antibiotic	Amoxicilin	1,4
	Ampicilin sulbactam	30,4
	Azitromicin	1,4
	Cefixime	4,3
	Cefoperazone sulbactam	1,4
	Cefotaxime	1,4
	Ceftriaxon	1,4
	Ciprofloxacin	11,6
	Gentamicin	11,6
	Levofloxacin	27,5
	Metronidazole	2,9
	Moxifloxacin	4,3
Type of therapy	ADE *(Antimicrobial Drug Empiric)*	57,5
	ADET*(Antimicrobial Drug Extend Empiric)*	27,2
	ADD *(Antimicrobial Drug Documented)*	15,1
	ADP *(Antimicrobial Drug Prophylaxis)*	0
	ADU*(Antimicrobial Drug Unknown)*	0

The most common types of antibiotic therapy in this study were empirical therapy (57.5%), followed by extend empiric therapy (27,2%) and definitive antibiotic administration (15.1%).

Table 2 shows the evaluation results of 12 antibiotic types in 41 medical records. The evaluation based on the Gyssens method resulted in 53.0% of category 0 (rational antibiotic use), 15.1% of category I (inappropriate antibiotic use), 3.9 % of category IIA (inappropriate antibiotic dose), 0% of category IIB-IIC (inaccurate intervals and routes), 3.0% of category IIIA (duration of administration too

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long), 19.6% of category IIIB (duration of administration too short), 4.5% of category IVA-D (giving ineffective, high toxic effect, too expensive, too broad spectrum of administration), 0% of category V (no indication of antibiotic administration), and 0% of category VI (incomplete medical record data) 0%.

Table 2 Evaluation result of antibiotic prescribing based on the Gyssens method

Gyssens Category	Percentage (%)
Category 0	53,0
Category I	15,1
Category IIA	3,0
Category IIB-IIC	0
Category IIIA	4,5
Category IIIB	19,6
Category IVA-IVD	4,5
Category V	0
Category VI	0

DISCUSSION

Based on the research obtained from 41 medical records of hospitalized ischemic stroke patients, the average age of the patients was 59-69 years old. This result is in accordance with the previous study that held at Yogyakarta Hospital in 2018, where the average age of the patients of ischemic strokes with infectious complications were in range of 51-70 years old.[5] This result is associated with decreased immunity, changes in organ function, nutritional deficiencies, comorbidities in old age, and also influenced by unfavorable social environmental factors.[7] The most common type of infection found in this study was pneumonia, which was found in 28 cases (50,8%). This result is in accordance with several studies where the highest prevalence of infection in old age patients is pneumonia with a high mortality rate (30%). Medical comorbid conditions that are suspected to trigger pneumonia in old age patients are swallowing disorders and cough reflex disorders.[8]

The most common types of antibiotics used by the patients in this study were Ampicillin sulbactam (30.9%) and Levofloxacin (27.5%). This result is in accordance with the 2015's Antibiotic Use Guideline by Dr. Kariadi Hospital, which states that Ampicillin sulbactam and Levofloxacin are empirical therapies for hospitalized pneumonia patients.[9] Meanwhile, this result is in contrast to the research that was held at Yogyakarta Hospital in 2018 which mentioned that empirical therapy in hospitalized pneumonia patients is a third generation of cephalosporin class. Because the effectiveness of antibiotics usage in hospitals is influenced by the spread of germs and different types of resistance therefore some hospitals can have different recommendations and guidelines.[11] This regulation is based on the Indonesian Nosocomial Diagnosis and Management Manual.[5,10]

Empiric therapy is the most common type of therapy, which is 57.5%. This result is in accordance with the antibiotic guidelines of Dr. Kariadi Hospital which mentioned that empirical therapy is recommended as initial therapy for hospitalized patients with clinical symptoms of infection, before getting culture results.[9] This result is in line with the research that was held at Fatmawati Hospital in 2011 which mentioned that the empirical antibiotics was given mainly to hospitalized patients.[12] Some of other articles states that broad-spectrum antibiotics in stroke cases are considered more appropriate to use if no specific clinical symptoms was found and no diagnostic support was made and their usage was effective in reducing the incidence of mortality.[5, 12]

Quality of Antibiotic Usage

The evaluation results in this study obtained 57.6% of category 0, indicating the usage of antibiotics in RSDK was rational. This awareness of antibiotic usage is allegedly obtained due to the compilation of the 2015's Antibiotic Use Guideline by Dr. Kariadi Hospital, therefore the antibiotic usage was appropriate.[9] This result is in accordance with the evaluation results of the antibiotic usage at Koja Hospital in 2015 using the same method, where the rational antibiotic use was obtained (79%).[4]

Category I show the inappropriate time of antibiotic administration (15.1%). This inappropriate usage is suspected because there are many drugs given to patients so that the administration is delayed to avoid drug interactions. In accordance with research at Dr. Hospital Sardjito Yogyakarta stated that drug interactions in elderly patients amounted to 69%. Older patients have a risk of diagnosing more than one disease, this will be related to the higher incidence of drug interactions.[15]

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The other problem was found in Category II, where the inappropriate dose usage of antibiotic was 3,0%. This result is not in accordance with the previous research that was held at Dirgahayu Public Health Center in 2017, where the inappropriate dose usage of antibiotic in children patients attained the number of 91.1%, which is much bigger compared to the incidence happened in older patients. This problem is due to the calculated dose based on body weight that was given to children patients is often inappropriate.[16]

The most problem was found in category IIIB, where the usage duration of antibiotics was too short, 19.5%. This problem is allegedly due to the cardiac arrest happened in the patient when receiving the first antibiotic, therefore it implies in the short duration of antibiotic usage. Meanwhile the other problem was found in Category IIIA where 4.5% of usage duration of antibiotic were considered too long. This result is in accordance with the previous research that was held at Koja Hospital, where 5% of the antibiotics administration was considered too long in the usage duration.[4, 16]

The problem that was found in Category IV showed 4.5% of Gentamycin usage without specific bacterial causes. Gentamycin is an antibiotic with a narrow therapeutic index and a serious toxic effect on the kidneys and hearing function, especially in elderly patients.[10] The problem found is in contrast to the other studies, where the problem in category IV reach the bigger number (11.33%). This contrast is allegedly due to the treatment administration regardless of bacterial culture result, interactions of antibiotics with other antibiotics especially in pulmonary tuberculosis, or drug interactions that cause unexpected side effects.[4]

There was found no problem in Category V, because all antibiotics was given based on indication of infection. Same thing happened in Category VI where the patients' history, physical examination, and prescription of the drug were completely written on the medical record, therefore there was no problem found. Meanwhile in Koja Hospital, problems in category VI were found, such as the absence of drugs that doctors prescribed to the patients from the list.[4]

CONCLUSION

The prophylactic antibiotics therapy for the acute phase of ischemic stroke in Dr. Kariadi Hospital Semarang shows a rational pattern around 53.0% of cases during 2018. Our limitations had not analyzed stroke severity by the National Institutes of Health Stroke Scale (NIHSS), comorbid illness, volume, or site of the lesion. Which may affect the condition of infection suffered, or the effectiveness and efficacy of the antibiotics prescribed. The lesion at the middle cerebral artery (MCA) might lead to worsening clinical findings, so will influence the inflammation cascade of stroke.

Ethical Approval

All research procedures received ethical clearance from the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University and licence to conduct research from RSUP Dr. Kariadi Semarang Indonesia before conducting the research. The Ethical Clearance number is 435/EC/KEPK/FK UNDIP/X/2019 from and licence to conduct researh number is DP.0201/I.II/5922/2019.

Conflicts of Interest

The authors declare no conflict of interest.

Funding

No specific funding was provided for this article.

Author Contributions

Authorship contributions as follows: conceptualization, and methodology, SNW, YN and TB; investigation and administration, validation and analysis, ESS, TB and YN; SNW; writing—original draft preparation, SNW; writing—review and editing, YN; supervision, YN and TB.

Acknowledgments

This work was supported by Faculty of Medicine, Diponegoro University and RSUP Dr. Kariadi Semarang, Indonesia.

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