Performance of Antibiotic Used in Stroke Patients at Dr Soetomo Academic Hospital Surabaya

Nur Shofwan Zahroni[a], Paulus Sugianto[b,d], Ni Made Mertaniasih[c,e], Devi Ariani Sudibyo[b,d]

[a]Medical Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[b]Department of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[c]Department of Medical Microbiology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[d]Department of Neurology, Dr Soetomo Academic Hospital, Surabaya, Indonesia
[e]Department of Clinical Microbiology, Dr Soetomo Academic Hospital, Surabaya, Indonesia

*Corresponding Author: Paulus Sugianto, E-mail: paulus.sugianto@fk.unair.ac.id

Abstract

Background: The prevalence of stroke in 2018 in Indonesia is 10.9 per mil. Decreased immunity in stroke complications can occur due to bacterial infections. Antibiotics are a treatment modality for bacterial infections that are regulated and monitored for their use to inhibit bacteria that are resistant to antibiotics.

Objective: To find out the pattern of antibiotic use in stroke patients at Dr Soetomo Academic Hospital Surabaya.

Methods: This is a retrospective study of medical records to determine patterns of antibiotic used based on DDD and DDD/100 patient-days in stroke patients in Seruni room at Dr Soetomo Academic Hospital Surabaya with sampling method is purposive sampling. The sample population is all stroke patients in the Seruni room at Dr Soetomo Academic Hospital Surabaya Indonesia for the period of July – December 2021.

Result: The total sample in this study was 166 stroke patients, which were 33.13% taking antibiotics. Pneumonia had the highest frequency of infectious cases affecting stroke patients, accounting for 44 cases (25.6%). The most route of administration was parenteral (92.7%). The most widely used antibiotic was Ceftriaxone with 27.4% (95.5 DDD or 6.04 DDD/100 patient-days). The total value of antibiotic use was 392.17 DDD or 24.8 DDD/100 patient-days and the highest DDD value was Levofloxacin (138 DDD or 8.73 DDD/100 patient-days).

Conclusion: Pneumonia became the most of infectious cases found, accounting for 44 cases (25,6%). As many as 33.13% of 166 stroke patients received antibiotic treatment. The most route of administration was parenteral (92.7%). The most widely used antibiotic was Ceftriaxone (27.4% used or 95.5 DDD or 6.04 DDD/100 patient-days). The highest DDD value was Levofloxacin (26% used or 138 DDD or 8.73 DDD/100 patient-days).

Keywords: antibiotics; stroke; DDD; DDD/100; infection

1. Introduction

Stroke is a functional disorder of the brain that lasts for at least 24 hours or until it causes death, this is due to a blockage of the brain blood vessels or a ruptured brain blood vessel. Based on the cause, stroke is divided

into ischemic stroke and hemorrhagic stroke (Wittenauer, 2012). The prevalence of stroke in Indonesia based on a doctor's diagnosis in the age group over 15 years in 2018 was 10.9 per mil (Indonesia MoH, 2018). Complications that often occur in stroke patients are Urinary Tract Infection (UTI) and Pneumonia. This complication can occur due to deteriorating neurological status of the patient which has an impact on decreasing the body's immunity so that it becomes susceptible to infection. The presence of this infection worsens the patient's condition and increases the risk of death (Shim, 2016).

Ampicillin/sulbactam, cefuroxime, ceftriaxone, levofloxacin, and moxifloxacin can be used as therapy for Stroke Associated Pneumonia (SAP) without risk factors; and ceftazidime can be used in combination with gentamicin in SAP with risk factors (Indonesia MoH, 2019). Antibiotics commonly used in UTI cases are trimethoprim sulfamethoxazole, ciprofloxacin, and ampicillin (Flores-Mireles et al., 2015). The increasing frequency of antibiotic-resistant bacteria in the last few decades is a dangerous thing. Antibiotic resistance can lead to increased health costs, lengthening the duration of hospitalization, and mortality rates. The unwise use of antibiotics can lead us to the post-antibiotic era, where even the slightest wound or an ordinary infection can cause death (WHO, 2020).

Wise use of antibiotics can be done by paying attention to indications, dosage, frequency, and duration of administration, as well as using first-line antibiotics first. Restrictions on the use of antibiotics are carried out in accordance with the applicable guidelines for the use of antibiotics (Hadi et al., 2006). The purpose of this study was to determine the pattern of antibiotic use in stroke patients in the Seruni Room at Dr Soetomo Academic Hospital Surabaya. The method used in this study was to calculate the Defined Daily Dose (DDD) value for each type of antibiotic. DDD is an estimation of the average dose of drug used per day for main indications in adults (WHO, 2021).

2. Methods

2.1. Study design and site

This is a descriptive observational study with a retrospective study of medical records to determine the pattern of antibiotic use using DDD and DDD/100 patient-days in stroke patients in the Seruni Room at Dr Soetomo Academic Hospital Surabaya.

2.2. Sampling and material

The sampling technique used was purposive sampling. The sample of this study were medical records of all stroke patients in the Seruni Room at Dr Soetomo Academic Hospital Surabaya for the period of July 1st until December 31st 2021. The total sample are 166 stroke patients. This study has received ethical approval in the form of a research protocol from the Health Research Ethics Commission Dr. Soetomo Academic Hospital Surabaya-Faculty of Medicine, Universitas Airlangga, Surabaya with protocol number 1588/121/4/VIII/2022.

2.3. Data collection

Medical record was included age, sex, length of stay, diagnosis of stroke, diagnosis of infection, type of antibiotic and number of doses in grams, and route of administration of antibiotics. The data obtained and recorded is then processed using the Excel 2019 program from Microsoft.

3. Result

3.1. Diagnosis of infection

Table 1. Diagnosis of infection

Infection	Frequency	Percentage (%)
Pneumonia	44	25.6
Urinary Tract Infection (UTI)	4	2.3
Others		
Lower Respiration Tract Infection	1	0.6
Bronchitis	1	0.6
Septicemia	9	5.2
Cellulitis	1	0.6
TB Vasculitis	1	0.6
No Diagnonis	111	64.5
Total	172	100

The majority of stroke patients had no or undiagnosed cases of infection (64.5%). The frequency of infections as the complications found was 61 (35.5%) of 172 total cases with nine different types of infections. Pneumonia had the highest frequency of infections affecting stroke patients, accounting for 44 cases (25.6%), second is sepsis in 9 cases (5.2%), and the other infections showed on Table 1.

3.2. Use of antibiotic

Table 2. Use of antibiotic

Antibiotic	Frequency	Percentage (%)
Amikacin	3	4.1
Ampicillin-Sulbactam	2	2.7
Azithromycin	1	1.4
Cefixime	1	1.4
Cefoperazone	2	2.7
Cefoperazone-Sulbactam	8	11
Ceftriaxone	20	27.4
Ciprofloxacin	4	5.5
Levofloxacin	19	26
Meropenem	1	1.4
Metronidazole	5	6.8
Moxifloxacin	7	9.6
Total	73	100

As many as 55 of 166 patients used antibiotic treatment. A total of 12 types of antibiotics were used. The highest percentage of antibiotic use was ceftriaxone (27.4%) and followed by levofloxacin (26%). The rest showed on Table 2.

3.3. Route of administration

Table 3. Route of administration

Route of administration		Frequency	Percentage (%)
Oral		4	25.3
Parenteral		51	92.7
	Total	55	100

Based on Table 3, the choice of the parenteral route as the route of administration of antibiotics in this study was very large (92.7%) while the oral route was only a few (7.3%).

3.4. DDD/100 patient-days value

Table 4. DDD/100 patient-days value

Type of Antibiotic		DDD	DDD/100
Amikacin		22	1.39
Ampicillin-Sulbactam		10	0.63
Azithromycin		5	0.32
Cefixime		0.5	0.03
Cefoperazone		2.25	0.14
Cefoperazone-Sulbactam		24.25	1.53
Ceftriaxone		95.5	6.04
Ciprofloxacin		20	1.27
Levofloxacin		138	8.73
Meropenem		6.67	0.42
Metronidazole		33	2.09
Moxifloxacin		35	2.21
	Total	392.17	24.8

The total values of DDD and DDD/100 patient-days of inpatient stroke patients with antibiotics in the July – December 2021 period were 392.17 DDD and 24.8 DDD/100 patient-days. The highest values is levofloxacin, namely 138 DDD and 8.73 DDD/100 patient-days, followed by ceftriaxone with 95.5 DDD and 6.04 DDD/100 patient-days. The rest showed on Table 4.

4. Discussion

This study revealed the majority of 166 stroke patients had no infection (64.5%). The frequency of infections as the complications found was 35.5%, which Pneumonia had the highest frequency 44 cases (25.6%), second is sepsis in 9 cases (5.2%). According to research conducted by Westendorp et al. (2011) and Miller & Elkind (2015), pneumonia is a disease with an infection probability of 1% – 33% and closely related to death. This can be caused because a stroke makes the patient's consciousness decrease, causing dysphagia and aspiration, besides that it can be caused by immunosuppression due to stroke (Westendorp et al., 2011). Diabetes mellitus and NIHSS became independent predictors for post-stroke infection, twenty percent from 530 ischaemic stroke patients had a post-stroke infection (Grieten et al, 2022). Severe post-stroke infections are associated with an increase risk of death and poorer functional outcome (Learoyd et al., 2017). From a

study conducted by Fatni Muhafidzah et al., (2021) it was found that 30 people had pneumonia in acute stroke patients (28.30%).

Use of antibiotic, 55 of 166 (33,13%) patients used antibiotic treatment. A total of 12 types of antibiotics were used. The highest percentage of antibiotic use was ceftriaxone (27.4%) and followed by levofloxacin (26%). The same study in the Seruni Room at Dr. Soetomo General Hospital Surabaya in 2018 patients also found that ceftriaxone (43.7%) was the most frequently used antibiotic and levofloxacin was the second most used antibiotic (17.65%) (Sembahulun, 2020). Antibiotics are given according to indications and if necessary, test for bacterial resistance. Antibiotic therapy for pneumonia using ampicillin/sulbactam, cefuroxime, ceftriaxone, levofloxacin, and moxifloxacin for SAP without risk factors; and using ceftazidime in combination with gentamicin in SAP with risk factors (Indonesia MoH, 2019). The once-daily levofloxacin regimen 750 mg provided a satisfactory PK/PD profile against the major pathogens of pneumonia, implying promising clinical and bacteriological efficacy for patients with pneumonia (Cao et al., 2013). Ceftriaxone is a broad-spectrum antibiotic that has antimicrobial activity on both gram negative and gram positive, it can be used as a single therapy or in combination with other antibiotics (Shirin & Shahidul Islam, 2020). According to Ringger et al. (1998) and Lamb et al. (2002), ceftriaxone effective to penetration in body fluids such as brain, spinal, pleural, and peritoneal. However, ceftriaxone only used by parenterally because is not absorbed after oral administration (Campos et al., 2017) (Albin et al., 1986).

In this study reported the route of administration, the parenteral route as the route of administration of antibiotics in this study was very large (92.7%) while the oral route was only a few (7.3%). The parenteral route is more frequently administered in hospitalized patients, recommended for severe, life-threatening infections, and infections that are inside the body because of concerns about not achieving adequate antibiotic concentrations at the site of infection. In addition, parenteral administration can also be given to patients who cannot take the drug orally, for example due to vomiting, and patients with impaired immune systems due to reduced ability to fight infection, this route is recommended (McCarthy & Avent, 2020). In the study by Carolina & Widayati (2014) it was found that 76.4% used the parenteral route as the route of administration of antibiotics.

The total values of DDD and DDD/100 patient-days of inpatient stroke patients with antibiotics in the July – December 2021 period were 392.17 DDD and 24.8 DDD/100 patient-days. The highest value is levofloxacin, namely 138 DDD and 8.73 DDD/100 patient-days, followed by ceftriaxone with 95.5 DDD and 6.04 DDD/100 patient-days. The results of the DDD and DDD/100 patient-days values were lower than another study conducted by Sembahulun (2020), where the total DDD and DDD/100 patient-days values were 1090.28 DDD and 46.85 DDD/100 patient-days. Based on the type of antibiotic, different results were obtained for DDD and DDD/100 patient-days per antibiotic, the highest being ceftriaxone 525.5 DDD and 22.58 DDD/100 patient-days, the second being levofloxacin with 313 DDD and 13.45 DDD/100 patient days. From study by Khoir (2019), The highest DDD value approximately 26,53 DDD / 100 patient-days was ceftriaxone. The second highest DDD value was levofloxacin at 21,08 DDD / 100 patient-days.

5. Conclusion

As many as 33.13% of 166 stroke patients in Dr Soetomo Academic Hospital received antibiotic treatment. The most route of administration was parenteral (92.7%). The most widely used antibiotic was Ceftriaxone (27.4% use or 95.5 DDD or 6.04 DDD/100 patient-days). The highest DDD value was Levofloxacin (26% use or 138 DDD or 8.73 DDD/100 patient-days). The total value of DDD/100 patient-days in the Seruni room at

Dr Soetomo Academic Hospital Surabaya for the July-December 2021 period was 24.8 DDD/100 patient-days with the largest value being levofloxacin (8.73 DDD/100 patient-days), followed by ceftriaxone (6.04 DDD/100 patient-days).

Acknowledgement

References

Albin, H. et al., 1986. "Pharmacokinetics of intravenous and intraperitoneal ceftriaxone in chronic ambulatory peritoneal dialysis," European Journal of Clinical Pharmacology, 31(4), pp. 479–483.

Campos, M.L. et al., 2017. "Ceftriaxone pharmacokinetics by new simple and sensitive ultra-high-performance liquid chromatography method," Diagnostic Microbiology and Infectious Disease, 88(1), pp. 95–99.

Cao, G. et al., 2013. "Pharmacokinetics and pharmacodynamics of levofloxacin injection in healthy Chinese volunteers and dosing regimen optimization," Journal of Clinical Pharmacy and Therapeutics, 38(5), pp. 394–400.

Carolina, M. and Widayati, A., 2014. Evaluasi Penggunaan Antibiotik dengan Metode DDD (Defined Daily Dose) pada Pasien Anak Rawat Inap di Sebuah Rumah Sakit Pemerintah DI Yogyakarta Periode Januari - Juni 2013. thesis. Media Farmasi.

Fatni Muhafidzah, N. et al., 2021. "Faktor Faktor Risiko Terjadinya pneumonia Pada stroke akut di RSUP dr Hasan Sadikin bandung," Jurnal Neuroanestesi Indonesia, 10(3), pp. 151–161.

Flores-Mireles, A., Walker, J., Caparon, M. and Hultgren, S., 2015. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nature Reviews Microbiology, 13(5), pp.269-284.

Grieten, J. et al., 2022. "Hospital-acquired infections after acute ischaemic stroke and its association with healthcare-related costs and functional outcome," Acta Neurologica Belgica, 122(5), pp. 1281–1287.

Hadi, U, Kolopaking, EP, Gardjito, W, Gyssens, IC, & Broek, PVD, 2006. 'Antimicrobial resistance and antibiotic use in low-income and developing countries', Folio Medica Mediana, vol 42, no 3, pp 183-195.

Kementerian Kesehatan Republik Indonesia, 2018. Hasil Utama RISKESDAS 2018.

Kementerian Kesehatan Republik Indonesia, 2019. Pedoman Nasional Pelayanan Kedokteran Tata Laksana Stroke.

Khoir, A.Z., 2019. Evaluasi Penggunaan Antibiotika Secara Kuantitatif pada Pasien Penyakit Dalam (Penelitian di SMF Penyakit Dalam RS Bhayangkara H.S Samsoeri Mertojoso Surabaya). thesis.

Lamb, H.M. et al., 2002. "Ceftriaxone," Drugs, 62(7), pp. 1041–1089.

Learoyd, A.E. et al., 2017. "Infections up to 76 days after stroke increase disability and death," Translational Stroke Research, 8(6), pp. 541–548.

McCarthy, K. and Avent, M., 2020. "Oral or intravenous antibiotics?" Australian Prescriber, 43(2), pp. 45–48.

Miller, E.C. and Elkind, M.S., 2015. "Infection and stroke: An update on recent progress," Current Neurology and Neuroscience Reports, 16(1).

RINGGER, N.C. et al. (1998) "Pharmacokinetics of ceftriaxone in neonatal foals," Equine Veterinary Journal, 30(2), pp. 163–165.

Sembahulun, A.L.N., 2020. Pola Penggunaan Antibiotik pada Pasien Stroke di Ruang Rawat Inap Neurologi RSUD Dr. Soetomo Surabaya (Penelitian Observasional Retrospektif). thesis. Universitas Airlangga Repository.

Shim, R. and Wong, C., 2016. Ischemia, Immunosuppression and Infection—Tackling the Predicaments of Post-Stroke Complications, International Journal of Molecular Sciences, 17(1), p.64.

Shirin, M. and Shahidul Islam, M., 2020, "Ceftriaxone, an empirical goldmine: A systematic review of randomized controlled trials," Mathews Journal of Pharmaceutical Science, 4(1).

Westendorp, W.F. et al., 2011. "Post-stroke infection: A systematic review and meta-analysis," BMC Neurology, 11(1).

Wittenauer, R. and Smith, L., 2012. Background Paper 6.6 ischaemic and Haemorrhagic stroke, Docslib.

World Health Organization, 2020. Antibiotic resistance.

World Health Organization, 2021. Defined Daily Dose (DDD).