

Study of The Use of Antibiotics in Meningoencephalitis Patients at Dr. Soetomo Hospital in 2019—2020

Muhammad Hasan Al Banna^a, Paulus Sugianto^{b*}, Maftuchah Rochmanti^c

* *paulus.sugianto@fk.unair.ac.id*

^a*Faculty of Medicine Universitas Airlangga, Surabaya*

^b*Departement of Neurology, Faculty of Medicine Universitas Airlangga, RSUD Dr. Soetomo Surabaya*

^c*Departement of Medical Pharmacology, Faculty of Medicine Universitas Airlangga, RSUD Dr. Soetomo Surabaya*

Abstract

Background: Encephalitic meningitis became the 17th ranked disease in Indonesia in 2007, with a mortality proportion of 0.8%. Every patient with suspected encephalitic meningitis needs to be given antibiotics as empiric therapy while waiting for the results of the culture from the lumbar puncture. In fact, the administration of these antibiotics cannot be separated from the risk of resistance, so monitoring and evaluation is needed in administering antibiotics to patients to prevent resistance.

Objective: This study aims to determine patient profiles, patterns, and appropriateness of antibiotic use in meningitis and/or encephalitis patients at RSUD DR. SOETOMO in 2019—2020.

Methods: This is a retrospective observational descriptive study with a total of 82 medical records in patients diagnosed with meningitis and/or encephalitis who were given antibiotics as empiric therapy at RSUD DR. SOETOMO in 2019—2020.

Results: The age of the patients from the 82 data obtained varies quite a bit, but the final elderly aged 56-65 years had the highest number, namely 16 of 82 patients (20%). Then, the sex of the most patients was found in male sex with a total of 49 of 82 with a ratio of men and women was 3:2. Most of the patients' final conditions were found in the final condition of death with a total of 42 of 82 patients (51%). All of the antibiotics used were Ceftriaxone by injection route in 12-hour intervals. The most frequently used dose was 2 grams (89%), and the most frequently used duration was 7 days (21%). The results of the Gyssen method analysis showed that there were 78 (95%) I category, 1 (1%) IIIa, and 3 (4%) IIIb. DDD per 100 days of hospitalization in this study was 66.2 DDD/100 days of hospitalization.

Conclusions: The majority of meningitis and/or encephalitis patients had a final elderly age of 56-65 years, were male, and died in the final condition. Empiric antibiotics were used entirely with Ceftriaxone intravenously at 12 hourly intervals. Most of the antibiotics are given within 7 days and the dose is 2 grams. The results of the analysis found that 95% of the use of antibiotics was already appropriate.

Keywords: antibiotics, meningitis, encephalitis, patient profile, Gyssen method

Introduction

Meningitis is an inflammation of the meninges, the organs that line the brain and spinal cord. Meanwhile, encephalitis is an inflammation that occurs in the brain itself [1,2]. Meningitis and encephalitis can be caused by both infectious and non-infectious factors. Infectious factors that can lead to meningitis and encephalitis are bacteria, viruses, fungi, or parasites. Meanwhile, non-infectious factors that can lead to meningitis and encephalitis are autoimmune processes, cancer/paraneoplastic syndromes, or drug reactions [2].

According to the World Health Organization, more than 1.2 million cases of bacterial meningitis are estimated to occur worldwide each year. The incidence and case-fatality rates of bacterial meningitis vary by

region, country, pathogen, and age group. According to the 2007 Riskerdas report in the 2008 Indonesian Health Profile book, the pattern of causes of death for all ages in 2007 in Indonesia, encephalitic meningitis was ranked 17th with a proportion of deaths of 0.8% [3]

Every patient with suspected encephalitic meningitis needs to be given antibiotics as empiric therapy while waiting for the results of the culture from the lumbar puncture [4]. Research conducted by Karou at 2012, namely CSF analysis with a sample of 533 patients in 2007-2010 at Dapaong General Hospital, found that in the susceptibility test, resistance was found to several antibiotics. So, have a care is needed in the administration of antibiotics in patients with meningitis and/or encephalitis [5].

Methods

This is a retrospective observational descriptive study with a total of 82 medical records in patients diagnosed with meningitis and/or encephalitis who were given antibiotics as empirical therapy at DR. SOETOMO Hospital in 2019—2020. The population of this study were all the patients with meningitis and/or encephalitis who were registered at DR. SOETOMO Hospital in 2019-2020 with a total sampling research sampling technique in which the entire population is sampled and filtered by the inclusion and exclusion criteria.

Variables taken from this study include patient profiles with details of the patient's age, sex, and final condition. In addition, the profile of empiric antibiotic therapy in the form of type of antibiotic, dose, route, interval, duration, and interval of giving antibiotics was also studied.

The research instrument used in carrying out this research was medical record data of patients with meningitis and/or encephalitis who were given empirical antibiotic therapy at DR. SOETOMO Hospital in 2019—2020. No validity and reliability tests are needed because the instruments used are medical records.

Results

The results of processing the data obtained from a total of 82 patients are presented in the form of descriptions, tables, and graphs as follows.

The highest age distribution was found in the late elderly category, namely ages 56-65 years with a total of 16 out of 82 patients and a percentage of 20%. If it is associated with the patient's final condition, the results also show that the elderly category has the highest number of patients with the final condition of death.

Table 1. Distribution of age

Age Distribution	N	%
Toddlers (0-5 years)	0	0%
Children (6-11 years)	0	0%
Early adolescents (12-16 years)	1	1%
Late adolescents (17-25 years)	14	17%
Early adults (26-35 years)	14	17%
Late adults (36-45 years)	15	18%
Early elderly (46-55 years)	11	13%
Late elderly (56-65 years)	16	20%
Seniors (>65 years)	11	13%
TOTAL	82	100%

Table 2. Distribution of age and final condition

Age Distribution	Final Condition	
	Died	Lived
Toddlers (0-5 years)	0	0
Children (6-11 years)	0	0
Early adolescents (12-16 years)	0	1
Late adolescents (17-25 years)	7	7
Early adults (26-35 years)	5	9
Late adults (36-45 years)	7	8
Early elderly (46-55 years)	7	4
Late elderly (56-65 years)	9	7
Seniors (>65 years)	7	4
TOTAL	42	40

The sex distribution of meningoenephalitis patients who were given antibiotics at DR SOETOMO Hospital in 2019-2020 was mostly male, namely 49 out of 82 patients with a percentage of 60%, 16 more than female patients.

Table 3. Distribution of sex

Sex Distribution	N	%
Male	49	60%
Female	33	40%
TOTAL	82	100%

Distribution of the final condition of meningoenephalitis patients who were given antibiotics at DR SOETOMO Hospital in 2019-2020 found that more patients died compared to living patients. The difference was found in a number of 2 patients, namely 42 of 82 patients died and 40 of 82 patients lived.

Table 4. Distribution of final condition

Final Condition Distribution	N	%
Lived	40	49%
Died	42	51%
TOTAL	82	100%

A total of 82 meningoenephalitis patients at DR SOETOMO Hospital in 2019-2020 were all given empiric antibiotic therapy with *Ceftriaxone*, with parenteral administration, and in 12-hour intervals. The dose and the duration given were varied. The highest dose of antibiotics given was found at 2 grams, which was 73 of 82 patients with a percentage of 89%. The dose is the amount of drug given to the patient in one administration. There was one patient who received two different doses of antibiotics, namely 2 grams on the first seven days and 1 gram on the following seven days.

Table 5. Distribution of Ceftriaxone dose

Antibiotic Dose (gram)	N	%
2	73	89%
1	8	10%
2 & 1	1	1%
TOTAL	82	100%

The most frequent dose of antibiotics given to meningoenephalitis patients at DR SOETOMO Hospital in 2019-2020 was obtained at a duration of 7 days, namely 17 out of 82 patients with a percentage of 21%.

Table 6. Distribution of administration duration

Duration	N	%
0	1	1%
1	8	10%
2	7	9%
3	7	9%
4	4	5%
5	7	9%
6	3	4%
7	17	21%
8	6	7%
9	2	2%
10	5	6%
11	3	4%
12	1	1%
14	5	6%
16	1	1%
18	2	2%
19	1	1%
20	1	1%
29	1	1%
TOTAL	82	100%

Discussion

The late elderly or 56-65 years old is the most age that has the final condition of death. This is in line with what Wang (2014) wrote in his article that elderly patients have a higher likelihood of comorbidities, neurological and laboratory findings, abnormalities on CT and MRI of the head, and adverse clinical outcomes (ACO) findings [6]. The highest sex distribution was found in the male sex, namely 49 out of 82 patients with a percentage of 60%. This is line with a state that the X chromosome has an important role in immunological functions, especially in its role in synthesizing immunoglobulins either directly or indirectly. This can increase the chances of men getting an infection compared to women considering that men only have one X chromosome [7].

Empirical antibiotic therapy was analyzed both qualitatively and quantitatively. Qualitative studies can be carried out using the Gyssen method. Meanwhile, for quantitative studies can be done with the DDD system on ATC/DDD. The analysis using the Gyssen method shows the results as below.

Table 7. Gyssen method analysis

Category	Results	N
VI	The data obtained is not complete enough to be categorized	-
V	Drug administration is inappropriate or not according to indications	-
IV	A Medication is not appropriate because:	-
	There are drugs that more effective	-
	B Medication is not appropriate because:	-
	There are drugs that less toxic	-
III	C Medication is not appropriate because:	-
	There are drugs that cheaper	-
	D Medication is not appropriate because:	-
II	There are drugs that have narrower spectrum	-
	A Medication is not appropriate because:	1
I	The duration of drug administration is too long	3
	B Medication is not appropriate because:	-
I	The duration of drug administration is too short	-
	A Medication is not appropriate because:	-
	B Medication is not appropriate because:	-
I	Improper dosage of medication	-
	C Medication is not appropriate because:	-
I	Improper drug dosing intervals	-
	Improper drug route administration	-

I	The drug prescription is already correct	78
TOTAL		82

Category I regarding proper drug prescribing, in this study it was found that a total of 78 out of 82 data or 95% of empirical antibiotic therapy given to meningoencephalitis patients at DR SOETOMO Hospital in 2019-2020 were found to be correct.

Quantitative studies using DDD per 100 of stays, it is found that all of the medication here have 66,2 DDD/100 per 100 of stays score. DDD per 100 of stays shows the quantity of drugs received by 100 inpatients [8]. Then, DDD Ceftriaxone according to WHO standards with units of gram measurement is 2 grams. According to calculations, Ceftriaxone is used as much as 66.2 DDD per 100 of stays, meaning that out of 100 beds in DR SOETOMO Hospital every day there are 66.2 patients receiving Ceftriaxone in the amount of 2 grams. This rate is lower than the DDD per 100 of stays of Ceftriaxone patients in the Intensive Care Unit (ICU) of DR SOEDARSO Hospital Pontianak in the January-June 2019 period which reached 76.15 DDD/100 days of stay [9]. However, this figure is higher than the DDD per 100 of stays of Ceftriaxone patients in surgical patients at the Inpatient Installation of Airlangga University Hospital in November 2016-April 2017 [10]. The use of antibiotics in patients needs to be constantly monitored so that resistance does not occur because there is a specific relationship between the use of Ceftriaxone and resistance [11].

Conclusion

It is found that meningitis and/or encephalitis patients who were given empirical antibiotics at DR SOETOMO Hospital in 2019-2020 were mostly patients with late elderly age, namely 56-65 years (16%), male sex (60%), and had death as a final condition (51%).

The empirical antibiotics given were all with Ceftriaxone, administered intravenously at 12-hour intervals. Besides that, most of the antibiotics were given at a dose of 2 grams (89%), and with a duration of 7 days (21%). The results of qualitative analysis of antibiotics using the Gyssen method obtained 78 data for category I, 1 data for category IIIa, and 3 data for category IIIb. Then, the use of Ceftriaxone in patients with meningitis and/or encephalitis at RSUD DR SOETOMO in 2019-2020 has a value of 66.2 DDD per 100 of stays. And lastly the antibiotics prescription as empirical therapy for meningitis and/or encephalitis patients at DR SOETOMO Hospital in 2019-2020 is already appropriate (95%).

References

- [1] Ellul, M. & Solomon, T. 2018. "Acute Encephalitis – Diagnosis and Management". *Clinical Medicine*. vol 18(2). pp 155—159
- [2] Hersi, K., Gonzales, F., & Kondamudi, N. 2021. "Meningitis". [Online] Available at: <https://www.ncbi.nlm.nih.gov/books/NBK459360/>
- [3] Suseno, U. et al. 2009. *Profil Kesehatan Indonesia 2008*. Jakarta: Departemen Kesehatan Republik Indonesia
- [4] Tunkel, A. et al. 2004. "Practice Guidelines for Management of Bacterial Meningitis". *Clinical Infectious Diseases*. vol 39. pp 1267—1284
- [5] Karou, S. et al. 2012. "Epidemiology and antibiotic resistance of bacterial meningitis in Dapaong, northern Togo". vol 5(11). pp 848-852. doi: 10.1016/S1995-7645(12)60158-8. [Online] Available at: <https://pubmed.ncbi.nlm.nih.gov/23146796/>
- [6] Wang, A. et al. 2014. "Community-acquired meningitis in older adults: Clinical features, etiology, and prognostic factors". *Journal of the American Geriatrics Society*. vol 62(11). pp 2064–2070. [Online] Available at: <https://doi.org/10.1111/jgs.13110>.
- [7] Libert, C., Dejager, L., & Pinheiro, I. 2010. "The X chromosome in immune functions: When a chromosome makes the difference". *Nature Reviews Immunology*. vol 10(8). pp 594–604.
- [8] Yulianti, R. et al. 2017. *Petunjuk Teknis Evaluasi Penggunaan Obat di Fasilitas Kesehatan*. Jakarta: Kementerian Kesehatan Republik Indonesia
- [9] Putri, S., Untari, E., & Yuswar, M. 2019. "Profil Antibiotik pada Pasien Intensive Care Unit (ICU) di Rumah Sakit Dr. Soedarso Pontianak Periode Januari – Juni 2019". *Jurnal UNTAN Farmasi*. [Online] Available at: <https://jurnal.untan.ac.id>.
- [10] Pratama, N. et al. 2019. "Analisis Penggunaan Antibiotik pada Pasien Rawat Inap Bedah dengan Menggunakan Defined Daily Dose dan Drug Utilization 90% di Rumah Sakit Universitas Airlangga". *Indonesian Journal of Clinical Pharmacy*. vol 8(4). pp. 256. [Online] Available at: <https://doi.org/10.15416/ijcp.2019.8.4.256>.

- [11] Muller, A. 2004. "Relationship between ceftriaxone use and resistance to third- generation cephalosporins among clinical strains of *Enterobacter cloacae*," *Journal of Antimicrobial Chemotherapy*. vol 54(1). pp 173–177. [Online] Available at: <https://doi.org/10.1093/jac/dkh282>.