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Research Article

Qualitative Evaluation of Antibiotics Use for Ventilator Associated Pneummonia (VAP) Patient in ICU Dharmais Cancer Hospital Using Gyssens Method

Shahyawidya Ramadhanti, Maksum Radji, Rizka Andalusia
Fakultas Farmasi Universitas Indonesia, Depok, Indonesia

Abstract
Ventilator-associated pneumonia (VAP) is a pulmonary infection that occurs after more than 48 hours of mechanical ventilation or endotracheal intubation. VAP is the most common nosocomial infection in Intensive Care Unit (ICU), and the use of antibiotics will affect the treatment of the infection. This study aims to evaluate the quality of antibiotic use for VAP treatment in ICU Dharmais Cancer Hospital using Gyssens method, evaluating the different outcomes of antibiotic therapy that are rational and irrational according to the Gyssens method, and evaluating the distribution of rational (category 0) and irrational (category 1-5) antibiotic use. This prospective study was carried out from February to May 2017 with descriptive analyses. Antibiotic uses were documented prospectively by a pharmacist and analyzed using Gyssens method. Pharmacist used total sampling method, which included all adult VAP patients in ICU. A total of 29 patients (18.24%) were reviewed from 159 patients. The most dominant antibiotic use for VAP empiric treatment was meropenem and the most dominant antibiotic use for VAP definitive treatment was levofloxacin. Factors affecting the quality of antibiotic use include type of therapy, number of antibiotics used by patient and length of stay (P>0.05). Factors affecting the therapy outcome of a VAP patient was time of antibiotic use (P<0.05). The relationship between outcome therapy and quality of antibiotic use based on Gyssens method shows on category 0, which died 64.3%, category 2 died 66.7% and the category 4 died 75%. The relationship between outcome and quality of antibiotic use based on Gyssens method shows more irrational use of antibiotics, then the therapy outcome is not getting better.

Keywords: antibiotic, Gyssens-method, ICU, pneumonia, VAP, ventilator

Evaluasi Kualitatif Penggunaan Antibiotik pada Pasien *Ventilated Associated Pneumonia* (VAP) di Ruang ICU RS Kanker Dharmais Menggunakan Metode Gyssens

Abstrak
Ventilator-associated pneumonia (VAP) adalah infeksi paru yang terjadi setelah lebih dari 48 jam penggunaan ventilasi mekanik atau intubasi endotrakeal. VAP adalah infeksi nosokomial yang paling umum di Intensive Care Unit (ICU) dan penggunaan antibiotik akan berpengaruh terhadap terapi infeksi tersebut. Penelitian ini bertujuan untuk mengevaluasi kualitas penggunaan antibiotik untuk pengobatan VAP di ICU Rumah Sakit Kanker Dharmais menggunakan metode Gyssens, mengevaluasi perbedaan hasil terapi antibiotik yang rasional dan irasional menurut metode Gyssens, dan mengevaluasi distribusi penggunaan antibiotik secara rasional (kategori 0) dan tidak rasional (kategori 1-5). Penelitian prosprektif ini dilaksanakan pada bulan Februari sampai Mei 2017 dengan analisis deskriptif. Penggunaan antibiotik didokumentasikan secara prospektif oleh apoteker dan dianalisis menggunakan metode Gyssens. Apoteker menggunakan metode total sampling yaitu seluruh pasien dewasa VAP di ICU. Sebanyak 29 pasien (18,24%) dianalisis dari 159 pasien. Penggunaan antibiotik yang paling dominan untuk pengobatan empiris VAP adalah meropenem dan penggunaan antibiotik yang paling dominan untuk pengobatan definitif VAP adalah levofloxacin. Faktor-faktor yang mempengaruhi kualitas penggunaan antibiotik antara lain jenis terapi, jumlah antibiotik yang digunakan pasien, dan lama rawat inap (P>0,05). Faktor yang mempengaruhi hasil terapi pasien VAP adalah waktu penggunaan antibiotik (P>0,05). Hubungan antara outcome terapi dengan kualitas penggunaan antibiotik berdasarkan metode Gyssens menunjukkan pada kategori 0 meninggal 64,3% kategori 2 meninggal 66,7% dan kategori 4 meninggal 75%. Hubungan antara outcome terapi dengan kualitas penggunaan antibiotik berdasarkan metode Gyssens menunjukkan semakin tidak rasional penggunaan antibiotik maka hasil terapi tidak semakin baik.

Kata kunci: antibiotik, ICU, metode Gyssens, pneumonia, VAP, ventilator

Correspondence: Shahyawidya Ramadhanti, Fakultas Farmasi Universitas Indonesia, Depok, Indonesia, email: shahyawidya@gmail.com

Introduction

Ventilator-associated pneumonia (VAP) is a pulmonary infection that occurs after more than 48 hours of mechanical ventilation or endotracheal intubation.[4] VAP is the most common nosocomial infection in the ICU. The use of mechanical ventilators is an important aspect of critical patient care in the ICU. The incidence of VAP varies between 8% and 28% and has a mortality rate of 50%.[1-3] This is related to the increased risk of other infections, increased hospitalization costs, and increased duration of care in the ICU.

One important component of VAP patient management is empirical antibiotic preparation before antibiotics are given by cultures and antibiotics according to cultures, which called definitive therapy. According to Kollef et al., nearly 50% of the antibiotics used in ICU chambers are used for VAP treatment.[5] Administration of antibiotics for VAP must be balanced which involves providing appropriate broad-spectrum antibiotics timely and avoiding unnecessary antibiotic use by narrowing the spectrum or discontinuing antibiotics after 48–72 hours based on culture results and their sensitivity.[6]

Gyssens et al. develop an evaluation of the use of antibiotics to assess the accuracy of the use of antibiotics: the accuracy of indications, the accuracy of selection based on effectiveness, toxicity, price and spectrum, duration of administration, dose, interval, route, and time of administration.[7] This study aims to evaluate the quality of antibiotic use for VAP treatment in ICU Dharmais Cancer Hospital using Gyssens method, evaluate the different outcomes of antibiotic therapy that are rational and irrational according to the Gyssens method, and evaluate the distribution of rational (category 0) and irrational (category 1–5) antibiotic use.

Method

This analytical descriptive study with a prospective approach was carried out from February to May 2017 at the ICU room of Dharmais Cancer Hospital with ethical clearance number 014/KEPK/II/2017. All adult patients (17–60 years old) with ventilators who were diagnosed with VAP and given antibiotics were included in this study.

Patients on ventilator are monitored for developments and their ventilator use is analyzed after 48–72 hours by assessing laboratory results and the patient's clinical condition. Laboratory findings such as complete blood tests and pulmonary examination results assist in determining whether the patient may be diagnosed with VAP. Diagnosis of VAP utilizes the Clinical Pulmonary Infection Score (CPIS), where a score above 6 indicates VAP.

Once a patient was diagnosed with VAP, their progress was closely monitored, including the rational use of antibiotics both before bacterial culture results were available and afterwards. To evaluate the rational use of antibiotics is using the Gyssens method. The Gyssens method is a framework used by healthcare professionals, particularly pharmacists and infectious disease specialists, to assess the rationality of antibiotic use. Key components of the Gyssens method typically include: (1) indication, (2) selection, (3) dosing, (4) duration, (5) review, and (5) monitoring.

By applying the Gyssens method, healthcare providers aim to promote the judicious use of antibiotics, improve patient outcomes, and reduce the overall burden of antibiotic resistance in healthcare settings.
Throughout the data collection and observation process, pharmacist play a crucial role. This approach aims to enable

Table 1. Characteristic of Patients Diagnosed with VAP in the ICU Dharmais Cancer Hospital for the Period February–May 2017

Characteristic	Category	Total	(%)
Age (years old)	17–30	4	13.8
	>30–59	20	69.0
	>59	5	17.2
Gender	Male	18	62.1
	Female	11	37.9
VAP Onset	Late	15	51.7
	Fast	14	48.3
Use of Antibiotic	Single	14	48.3
	Combination	15	48.3
Type of Therapy	Empiric	29	100.0
	Definitive	9	31.0
Length of Stay (days)	13–16	4	7.5
	9–12	15	28.3
	5–8	34	64.2
Outcome	Dead	20	69.0
	Not Dead	9	31.0
Total		29	100.0

pharmacists to monitor ventilator use and infection management in VAP-susceptible patients, ensuring appropriate antibiotic use based on Gyssens method evaluation.

The data were analyzed using SPSS version 23. Chi-square ($p<0.05$) is used to analyzed categorically whether the type of the therapy, number of antibiotics used by a patient, and length of stay are related to the quality of antibiotic use and therapy outcomes. Meanwhile, Spearmann correlation is used to analyze numerically the outcomes identified by Chi-square that most influence the quality of antibiotic use and therapy outcomes.

Result

During the study period (Table 1), 29 patients met inclusion criteria from 159 patients who used ventilators. Most patients were male (62.1%), the mean age was 49 years, and the length of stay (LOS) was between 5 and 8 days. Most of the patients were diagnosed with VAP late-onset (51.7%), which affected the administration of antibiotics. Because VAP late onset broad-spectrum antibiotics were needed. Outcomes of patients diagnosed with VAP were largely dying (69%).

In the distribution of antibiotic use in the ICU room at Dharmais Cancer Hospital (Table 2), the most empirical antibiotic use was meropenem (37.73%), and the definitive antibiotic use was levofloxacin (22.64%). Meropenem was the first line antibiotic for the ICU room, patients who were transferred to ICU will get this antibiotic and stop the previous antibiotic. Meropenem and levofloxacin were broad-spectrum antibiotics suitable for VAP late-onset. A combination of antibiotics was also used in the ICU room to treat VAP. The most commonly used combination of antibiotics was meropenem and levofloxacin.

The quality of antibiotic use in VAP patients was divided into two groups: use of empiric antibiotics and use of definitive antibiotics. Patients who have received

Table 2. Distribution of Combination Antibiotics for VAP Patients in the ICU Dharmais Cancer Hospital for the period February–May 2017

Use of Antibiotics	Patient	Percentage (%)
Meropenem-Levofloxacin	10	56.0
Tigecycline-Micafungin	1	5.5
Meropenem-Amikasin	2	11.0
Cefoperazone-Metronidazole	1	5.5
Doripenem-Levofloxacin	1	5.5
Cefotaxime-Metronidazole	1	5.5
Meropenem-Micafungin	1	5.5
Levofloxacin-Ceftazidime	1	5.5
Total	18	100.0

appropriate antibiotics (category 0) were 14 of 29 patients who met VAP criteria. There were 3 patients received inappropriate antibiotics because of less precise doses. Besides, 20 patients received inappropriate antibiotics, even though there were other antibiotics that were more effective.

Besides that, other factors affect the quality of antibiotic use, such as type of therapy, outcome of patients, number of antibiotics used by patients, length of antibiotics used, and length of stay. Test results with Chi-square showed that type of therapy (P=0.001), the number of antibiotics used (P=0.008), and length of stay (P=0.002) were related to the quality of antibiotic use. Besides, test results with Spearman Correlation to identify which one was the most dominant factor affecting the quality of antibiotic use showed that length of stay was the most related factor (correlation coefficient = 0.464).

Factors affecting patient outcomes such

Table 3. The Relationship between The Quality of Antibiotic Use and Characteristic (Influencing Factors) n = 53

Characteristic		Rational Use (%)	Irrational Use (%)	Total (%)	P
Use of Antibiotic	Single	18.7	81.3	100	0.006
	Combination	59.5	40.5	100	
Type of Therapy	Empiric	32.4	67.6	100	0.001
	Definitive	81.3	18.7	100	
Outcome	Dead	44.7	55.3	100	0.572
	Not Dead	53.3	46.7	100	
Duration of Antibiotic Use (days)	1–5	61.1	38.9	100	0.075
	6–10	36.4	63.6	100	
	11–15	100	0.0	100	
Length of Stay (days)	5–8	29.4	70.6	100	0.002
	9–12	80.0	20.0	100	
	13–16	75.0	25.0	100	

Table 4. The Relationship between Outcome and Characteristic (Influencing Factors) n = 53

Characteristic		Dead (%)	Not Dead (%)	Total (%)	P
Use of Antibiotic	Single	37.5	62.5	100	0.328
	Combination	24.3	75.7	100	
Type of Therapy	Empiric	32.4	67.6	100	0.31
	Definitive	18.8	81.2	100	
Quality of Antibiotic Use	Irrational	25.0	75.0	100	0.572
	Rational	32.0	68.0	100	
Duration of Antibiotic Use (days)	1 – 5	50.0	50.0	100	0.036
	6 – 10	18.2	81.8	100	
	11 – 15	0.0	100.0	100	
Length of Stay (days)	5 – 8	29.4	70.6	100	0.49
	9 – 12	33.3	66.7	100	
	13 – 16	0.0	100.0	100	

as type of therapy, quality of antibiotic use, number of antibiotics used by patients, length of antibiotic use, and length of stay. Test results with Chi-square showed that only length of antibiotic use (P = 0.036) was related to patient outcome. The relationship between patient outcome and quality of antibiotic use based on the Gyssens method shows that in category 1, the number of dead patients was 64.3%, in category 2, the number of dead patients was 66.7%, and in category 4, the number of dead patients was 75%.

Discussion

Results of this study showed that from 159 patients through February to May 2017, only 29 (18.24%) patients with VAP. This would happen because most of the patients who transfer to the ICU already had pneumonia, so most ICU patients are excluded. Besides, one of the VAP criteria is that patients have to get pneumonia after using a ventilator for 48-72 hours in the ICU room. This is not much different from the study done by Riahdo Saragih in Dr. Ciptomangunkusumo National General Hospital (RSCM), which showed that in 1.693 ICU patients from January 2003 to December 2012, only 201 patients met VAP criteria.8 Another study was done by Othman at King Fahd Hospital from September 2012 to August 2013, and only 48 patients met VAP criteria.[9] Characteristics of VAP patients in the ICU room at Dharmais Cancer Hospital were mean ages of 49 years, the male was the more dominant gender to get VAP, most of the patients met VAP late-onset (51.7%) and length of stay was between 5 days and 8 days. The mean age of 49, is not much different from a study done by Riahdo Saragih in RSCM, whose mean age for those who met VAP criteria was 45 years.[8] Male was the more dominant gender to get VAP, according to a study done by Riahdo Saragih.[8] According to Koenig (2006), males are one of the risk factors for VAP.[3] Patient outcomes: in VAP patients, most of them were dead (69%), according to study done by Riahdo Saragih (57.2%).[8] The distribution of antibiotics used in the ICU room at Dharmais Cancer Hospital, meropenem was the most common antibiotic used to treat VAP in the ICU room. This happened because the

ICU room at Dharmais Cancer Hospital used meropenem as a first-line antibiotic in the ICU which is suitable for the pattern of germs in this hospital. Besides, levofloxacin was the most commonly used definitive antibiotic to treat VAP patients. And both of them, meropenem and levofloxacin, are broad-spectrum antibiotics suitable for VAP late-onset. A combination of antibiotics was also given by the physicians. The most common combination of antibiotics was meropenem and levofloxacin. A study done by Arnold Louie showed that a combination of meropenem and levofloxacin can work synergistically, especially for Pseudomonas aeruginosa, and can suppress resistance.[10] The quality of antibiotics used to treat VAP patients: only 14 patients got appropriate antibiotics; others got inappropriate antibiotics because of a less precise dose; and there was another antibiotic that was more effective. Length of stay was related to the quality of antibiotic use because the longer the patient's treatment, the greater risk of improper use of antibiotics. A study done by Othman showed that the duration of ventilator use and length of stay in the ICU were significantly different in VAP patients.[8] So do nosocomial infections; the longer the patient's treatment, the more use of antibiotics will increase to cure another infection. The length of antibiotic use was related to the patient's outcome because the longer antibiotics are used the less likely they are to heal. According to Gyssens, I.C. (2001), long-term use of antibiotics does not mean it will have a better effect than short-term use.[7] Administration of antibiotics affects three populations of microorganisms: (1) causal microflora, (2) patients' endogenous microflora, and (3) environmental microflora.[10] The table shows that there was no significant relationship between patient outcome and the quality of antibiotic use. The relationship between patient outcome and the quality of antibiotic use showed that the more inappropriate antibiotics used the worse the patient outcome would be. Considering the research was conducted at one of the national referral hospitals for cancer patients, where the ICU is specifically for advanced-stage cancer patients requiring specialized monitoring due to the severity of their condition, this study has several limitations (such as study period, research targets, and researcher capabilities). However, it is hoped to provide an overview of antibiotics usage at one of the hospitals in Jakarta.

Conclusion

In conclusion, in this research, the relationship between patient outcomes and the quality of antibiotic (rational or irrational) use indicates that inappropriate antibiotic use can be a contributing factor to the deterioration of patients' clinical condition (such as prolonged hospital stay or fatal outcomes). The research results show no significant difference in patient outcomes based on the quality of antibiotic use.

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Conflict of interest

The author declared no potential conflicts of interest with respect to the research,

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