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ANALYSIS OF ANTIBIOTIC USE IN VAP (VENTILATOR-ASSOCIATION PNEUMONIA) PATIENTS

ANALYSIS OF ANTIBIOTIC USE IN VAP (VENTILATOR-ASSOCIATION PNEUMONIA) PATIENTS

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Abstract

VAP is a nosocomial infection that most often occurs in the ICU. VAP increases morbidity, mortality, treatment costs and hospitalization time in the ICU. Antibiotic is primary therapy in VAP. The initial selection of antibiotic is very important to determine outcome in VAP patients, as well as a main factor that plays a role in the development of antibiotic resistance. Availability of bacterial pattern and bacterial sensitivity pattern is very important to make consideration on empirical antibiotic treatment in VAP patients. The purpose is to identify bacterial pattern, bacterial sensitivity pattern and to analyze antibiotic therapy in VAP patients. An observational prospective analysis was carried out in the ICU Dr. Soetomo Hospital. Data was collected from January to March 2013. Patients who met the inclusion criteria were observed prospectively. Bacterial pattern and bacterial sensitivity pattern were identified based on the results of culture test and sensitivity test. Quality of antibiotic usage could be assessed with Gyssen's flowchart. From 158 patients with ventilator, nine patients met the inclusion criteria with thirty specimens (13 sputum, 17 blood). *Pseudomonas aeruginosa* was the common bacteria found in the sputum. Blood culture, revealed that *Staphylococcus coagulase-negative* was the common bacteria. Antibiotics that are still sensitive against *Pseudomonas aeruginosa* are Piperacillin-tazobactam, Cefoperazone-sulbactam, Meropenem, Tobramycin, Levofloxacin. *Pseudomonas aeruginosa* is the common cause of pneumonia in adult patient who used ventilator that susceptible with various antibiotic spectrums. (FMI 2013;49:168-172)

Keyword : ventilator-associated, pneumonia, antibiotic, Gyssen's flowchart, bacterial, pattern, sensitivity, bacterial, pattern,

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1. **American Thoracic Society, (2005)**. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. - : Am J Respir Crit Care Med
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ANALYSIS OF ANTIBIOTIC USE IN VAP (VENTILATOR-ASSOCIATION PNEUMONIA) PATIENTS

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ABSTRAK

VAP adalah infeksi nosokomial yang paling sering terjadi di ICU. VAP meningkatkan morbiditas, mortalitas, biaya pengobatan dan rawat inap di ICU. Antibiotik adalah terapi utama dalam VAP. Pemilihan awal antibiotik sangat penting untuk menentukan hasil, serta faktor utama yang berperan dalam pengembangan resistensi antibiotik pada pasien VAP. Ketersediaan pola bakteri dan pola kepekaan bakteri sangat penting untuk membuat pertimbangan pengobatan antibiotik empiris pada pasien VAP. Tujuannya adalah untuk mengidentifikasi pola bakteri, pola sensitivitas bakteri dan menganalisis terapi antibiotik pada pasien VAP. Sebuah analisis prospektif observasional dilakukan di ICU Rumah Sakit Dr Soetomo. Data dikumpulkan dari Januari sampai Maret 2013. Pasien yang memenuhi kriteria inklusi diamati secara prospektif. Pola bakteri dan pola kepekaan bakteri diidentifikasi berdasarkan hasil tes kultur dan uji sensitivitas. Kualitas penggunaan antibiotik dapat dinilai dengan flowchart Gyssen. Dari 158 pasien dengan ventilator, sembilan pasien yang memenuhi kriteria inklusi dengan tiga puluh spesimen (13 sputum, darah 17). *Pseudomonas aeruginosa* adalah bakteri yang umum ditemukan dalam dahak. Kultur darah, mengungkapkan bahwa *Staphylococcus koagulase-negatif* adalah bakteri umum. Antibiotik yang masih sensitif terhadap *Pseudomonas aeruginosa* adalah Piperacillin-tazobaktam, Cefoperazon-sulbaktam, Meropenem, tobramisin, levofloxacin. *Pseudomonas aeruginosa* adalah penyebab umum pneumonia pada pasien dewasa yang menggunakan ventilator yang rentan dengan berbagai spektrum antibiotik. (FMI 2013;49:168-172)

Kata kunci: ventilator-associated pneumonia, antibiotik, gyssen flowchart, pola bakteri, sensitivitas pola bakteri

ABSTRACT

VAP is a nosocomial infection that most often occurs in the ICU. VAP increases morbidity, mortality, treatment costs and hospitalization time in the ICU. Antibiotic is primary therapy in VAP. The initial selection of antibiotic is very important to determind outcome in VAP patients, as well as a main factor that plays a role in the development of antibiotic resistance. Availability of bacterial pattern and bacterial sensitivity pattern is very important to make consideration on empirical antibiotic treatment in VAP patients. The purpose is to identify bacterial pattern, bacterial sensitivity pattern and to analyze antibiotic therapy in VAP patients. An observational prospective analysis was carried out in the ICU Dr. Soetomo Hospital. Data was collected from January to March 2013. Patients who met the inclusion criteria were observed prospectively. Bacterial pattern and bacterial sensitivity pattern were identified based on the results of culture test and sensitivity test. Quality of antibiotic usage could be assessed with Gyssen's flowchart. From 158 patients with ventilator, nine patients met the inclusion criteria with thirty specimens (13 sputum, 17 blood). *Pseudomonas aeruginosa* was the common bacteria found in the sputum. Blood culture, revealed that *Staphylococcus coagulase-negative* was the common bacteria. Antibiotics that are still sensitive against *Pseudomonas aeruginosa* are Piperacillin-tazobaktam, Cefoperazon-sulbactam, Meropenem, Tobramycin, Levofloxacin. *Pseudomonas aeruginosa* is the common cause of pneumonia in adult patient who used ventilator that susceptible with various antibiotic spectrums. (FMI 2013;49:168-172)

Keywords: ventilator-associated pneumonia, antibiotic, gyssen flowchart, bacterial pattern, sensitivity bacterial pattern

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INTRODUCTION

Patients were treated in an intensive care unit (ICU) have a 5-10 times greater risk of experiencing nosocomial infection compared with other patients (Blot et al 2005, Safdar et al 2005, Warren et al 2003). In general, the most common infection in the ICU is pneumonia, followed by urinary tract infection and bacteremia (Geffers & Gastmeier 2011). The most common pneumonia occurred in the ICU is associated

with the use of a mechanical ventilator or Ventilator-Associated Pneumonia (VAP) (PAPDI 2006). The mortality rate of VAP ranges from 24-50% and can reach 75% in some circumstances or in pulmonary infections caused by high-risk pathogens (Chastre & Fagon 2002). Primary management of therapy in cases of VAP is antibiotics. Based on the 2005 American Thoracic Society guidelines, it is required adequate empirical antibiotic therapy and soon after found clinical signs suspected VAP. Inadequate antibiotics and

antibiotic treatment delays associated with poor outcomes and increased mortality in patients with VAP (American Thoracic Society 2005, Brusselaers et al 2011, Iregui et al 2002, Luna et al 2006).

The high resistance in the ICU increased awareness to be effective in the use of antibiotics, it is the selection of appropriate antibiotics. The selection of initial antibiotics is critical in determining outcome in patients with VAP, as well as a major factor contributing to the development of antibiotic resistance (American Thoracic Society 2005, Brusselaers et al 2011, Kollef 2001, Luna et al 2006). Availability of patterns of germs and bacteria to the antibiotic sensitivity pattern is very important as a consideration in the guidelines empirical antibiotic treatment of VAP in patients undergoing treatment in the ICU. Because of the sensitivity pattern of change in each particular periodic, then the data needs and data sensitivity pattern of bacteria antibiotics in intensive care units need to be held (Kollef 2006). Study about patterns of bacteria and bacterial sensitivity patterns in adult patients with VAP in ICU Dr. Soetomo Hospital have not been done before. The purpose of this study was to identify patterns of bacteria, bacterial sensitivity patterns and analyze antibiotic therapy in patients with VAP in ICU Dr. Soetomo Hospital.

MATERIALS AND METHODS

The type of the study is an observational study on data descriptive of the use of antibiotics in patients with VAP in the ICU Dr. Soetomo Hospital, during the period January to March 2013. Inclusion criteria for this study were patients with diagnosis of VAP during care in the ICU, the data contained microbiological culture results and antibiotic sensitivity, and received antibiotic therapy for VAP during ICU treatment. The primary data obtained from patient medical records, nursing notes and records pharmacist. The data recorded includes patient demographics, clinical patient characteristics data, laboratory data supporting infection, data on antibiotic therapy, as well as the culture of data. Antibiotics were evaluated using Gyssens Classification.

RESULTS

During the study period, found the number of patients in the ICU Dr. Soetomo Hospital that as many as 158 patients on a ventilator. Of the 158 patients, who met the inclusion criteria were 9 patients. Based on the profile of patient characteristics (Table 1), it was found that late-onset VAP is more common in ICU Dr. Soetomo Hospital. The high frequency of late-onset

VAP in accordance with the pattern of the majority of bacteria found in this study, they are *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

The incidence of VAP in ICU Dr. Soetomo Hospital in the January and March 2013 can be calculated by: (Number of VAP patients)/(Total long days in the ICU ventilator installation) \times 1000. During the study period from January to March 2013 obtained 9 VAP patients and 158 patients on a ventilator with a total installation of the old days is 686 days. So we get the incidence of VAP in ICU Dr. Soetomo Hospital in January-March 2013 as follows: $9/(686) \times 1000 = 13,12$ ventilator day

Table 1. Profile Characteristics of Patients with VAP, Ventilator Mounting Period, Onset VAP

Patients Characteristics	Number of Patients (n=9) (%)
Gender	
Male	5 (55.6)
Female	4 (44.5)
Age (years)	
≤ 20	1 (11.1)
21-40	3 (33.3)
41-60	4 (44.5)
≥ 60	1 (11.1)
Main Diagnostic	
a. Nerve Disease	
GBS	3 (33.3)
Stroke	2 (22.2)
Meningioma	1 (11.1)
b. Malignance	
Ca Thyroid	1 (11.1)
c. Pregnancy Disorders	
Heavy Pre-eclampsia	1 (11.1)
d. Trauma	
Mild Brain Injury	1 (11.1)
Ventilator Mounting Period (days)	
≤ 10	3 (33.3)
11-20	3 (33.3)
21-30	0 (0.0)
31-40	1 (11.1)
41-50	1 (11.1)
>50	1 (11.1)
Onset VAP	
Early (≤ 4 days after mechanical ventilation)	2 (22.2)
Advanced (> 4 days after mechanical ventilation)	7 (77.8)

The results of bacterial culture of the patient and the patient's profile can be seen in Table 2 and Table 3. The bacteria most commonly found in sputum specimens of VAP in ICU patients Dr. Soetomo Hospital is *Pseudomonas aeruginosa* of 30.8%. While the blood specimens, obtained bacteria were *Staphylococcus coagulase negative* majority of 75% (Table 3).

Table 2. Results Patients Experiencing Culture VAP in January-March 2013

Specimen Types	Number	Percentage (%)	Positive Result	Negative Result
Sputum	13	43,3	13	0
Blood	17	56,7	8	9
Total	30	100	21	9

Table 3. Profile Bacteria from Sputum Specimens and Blood in Patients Who Have VAP in January-March 2013

Bacteria	Sputum		Blood	
	N	%	N	(%)
Aerob Gram Negative				
<i>Pseudomonas aeruginosa</i>	4	30.8	-	-
<i>Acinetobacter Baumannii</i>	2	15.4	-	-
<i>Klebsiella pneumoniae</i>	1	7.7	-	-
<i>Pseudomonas Spp</i>	1	7.7	-	-
<i>Acinetobacter spp</i>	1	7.7	-	-
<i>Enterobacter Aerogenes</i>	1	7.7	-	-
<i>Burkholderia Cepacia</i>	1	7.7	-	-
<i>Enterococcus Faecium</i>	-	-	1	12.5
<i>Brevibacterium Spp</i>	-	-	1	12.5
Aerob Gram Positive				
<i>Staphylococcus Aureus</i>	1	7.7	-	-
<i>Staphylococcus Coagulase Negative</i>	1	7.7	6	75.0
Total	13	100	8	100

The bacteria responsible for VAP in general are aerobic gram-negative bacteria. From the test results of culture and sensitivity test in the study during the period from January to March 2013 can be made a pattern of sensitivity for each bacterium. From the pattern of sensitivity, can be created categories based on percentage of antibiotic sensitivity of the bacteria most potential, as shown in Table 4. Percent of potential antibiotics obtained through the calculation of the number of antibiotic sensitive test trials divided number of antibiotic-sensitive and resistant multiplied by 100%.

Table 4. Category Antibiotics based on the findings% Bacteria Most Potential in Patients Who Have a sputum specimen VAP in January-March 2013.

% Category of antibiotic potential	Most bacteria findings in Sputum Specimens	
	Gram Negative	
	<i>Pseudomonas aeruginosa</i> (n= 4)	<i>Acinetobacter baumannii</i> (n= 2)
< 30 % Usage not recommended	Ticarcillin-clavulanat	Cefotaxime
	Cefotaxim	Cefepim
	Ceftriaxone	Amikacin
	Cefepime	
	Astreonom	
	Gentamycin	
	Ceftazidime	Ampicillin-sulbactam
	Imipenem	Piperasilin-tazobaktam
	Amikacin	Ceftriaxone
	Ciprofloxacin	Imipenem
30-60 % Usage can be considered		Meropenem
		Tetracycline
		Tobramycin
		Cotrimoxazole
		Ciprofloxacin
		Levofloxacin
		Gentamicin (100%)
		Piperacillin-tazobactam (100%)
		Cefoperazon-Sulbactam(100%)
		Meropenem (66.67%)
>60 % usage recommended		Tobramycin (100%)
		Levofloxacin (100%)

From Table 4, it appears that the antibiotic that belongs to the category of potential > 60% against *Pseudomonas aeruginosa* is Piperacillin-tazobaktam (n = 3), Cefoperazon-sulbactam (n = 4), Meropenem (n = 3), Tobramycin (n = 1), levofloxacin (n = 2).

Table 5. Antibiotic Usage Profile in Patients Who Have VAP in January-March 2013

Empirical Antibiotics				Definitive Antibiotics			
Type of Antibiotics	Dose Used	Fre.	Duration (Day)	Type of Antibiotics	Dose Used	Fre.	Duration (Day)
Combination -Cefoperazon Sulbactam + Levofloxacin	3x1g + 1x750mg	1	5-8	Cephalosporin -Cefoperazon Sulbactam	3x1 G	3	5-12
Carbapenem -Meropenem	3x1 G	3	3-6	-Ceftriaxon	2x1 G	1	7
				Carbapenem -Meropenem	3x1 G	2	5-9
				Quinolon -Levofloxacin	1x750 Mg	1	7
				-Moxifloxacin	1x400 Mg	1	10
				Aminoglicosyde -Amikacin	1x1 G	1	9
				Macrolide -Azithromycin	1x500 Mg	1	5

Based on the sensitivity pattern in ICU Dr. Soetomo Hospital in July to December 2012, found that antibiotics were categorized as potential > 60% against *Pseudomonas aeruginosa* is Piperacillin-tazobaktam, Cefoperazon-sulbactam, Ceftazidim, Imipenem, and Gentamicin. Table 5 shows the profile of the use of antibiotics in patients with VAP in ICU Dr. Soetomo Hospital during the study period. The selection is based on the guidelines empirical antibiotic treatment of VAP by considering the local sensitivity patterns. In this study, there are 10 times the therapeutic uses of antibiotics definitive definitive antibiotic by 30% is the highest class of 3rd generation cephalosporins (Cefoperazon-sulbactam), and followed with carbapenem class (Meropenem) by 20%. From the table, it appears that the average length of empirical antibiotic therapy was 6.25 days and for definitive antibiotics was 7.57 days.

Table 6. Profile Quality Use of Antibiotics Based on Category Gyssens in Patients Who Have VAP in January-March 2013

Gyssens Category	Percentage (%)
Category 0	78.6
Category I	0
Category IIA – IIC	14.3
Category III A – IIIB	0
Category IV A – IV D	7.1
Category V	0
Category VI	0
Total	100

Assessment of quality of antibiotic use in patients with VAP during the period January to March 2013 under the category Gyssens with reference to the guidelines used in the ICU Dr. Soetomo Hospital is the American Thoracic Society Guidelines, 2005. Table 6 shows the results of the analysis Gyssens, where the use of antibiotics that are included in the rational use of 78.6%; dosage/interval/improper route of administration of 14.3%, and there are other antibiotics that narrower spectrum/cheaper/less toxic/more effective at 7.1%.

DISCUSSION

The condition where from 158 patients there were 9 patients who met the criteria likely due in part to patients in the ICU on a ventilator in just a short amount of time, in addition to the presence of various VAP prevention efforts that have been implemented in the ICU Dr. Soetomo Hospital, including the culture of hand washing before action; replacement tubing set is done routinely every week; patient even though consciously cultivated using the ventilator and the patient is positioned semirecumbent (half sitting), and the release of the ventilator as soon as possible.

Differences onset VAP is also associated with patterns of microorganisms causing VAP. In early-onset VAP caused by *S. pneumoniae* mostly, *H. influenzae*, methicillin-sensitive *S. aureus* (MSSA), or Enterobacteriaceae. While the late-onset VAP caused by *P. aeruginosa*, *Acinetobacter* sp, methicillin-resistant *S. aureus* (MRSA) and multiresistant gram-negative bacteria (Richard et al 1999, Fridkin 2001, Chastre & Fagon 2002).

Rosenthal et al, Stated that the incidence of VAP incidence in developing countries vary widely, between 10.0 to 52.7 per 1000 ventilator days, with an overall average is 24.1 per 1000 ventilator days (Rosenthal et al 2006). A multicenter study in Turkey showed that the country ICU VAP incidence ranged from 12 to 45.8 per 1000 ventilator days (Leblebicioglu et al 2007). Erdem et al (2008) states that the incidence of VAP in the ICU of 22.6 per 1000 ventilator days. From the research, it was concluded that the incidence of VAP incidence in the ICU Dr. Soetomo Hospital is relatively small, this can be due to VAP prevention efforts that have been performing well in the ICU Dr. Soetomo Hospital.

Several studies have reported that more than 60% of VAP caused by this group of bacteria. Gram-negative bacteria are the major cause of VAP is *P. aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter* spp. While infections caused by gram positive bacteria such as *Staphylococcus aureus* also began to increase (Richards et al 1999, Fridkin 2001, Chastre & Fagon 2002). In this study, the bacteria were found in the sputum specimen is the most aerobic gram-negative bacteria, namely *Pseudomonas aeruginosa* (4 specimens), followed by *Acinetobacter baumannii* (2 specimens). It appears that the sensitivity pattern of *Pseudomonas aeruginosa* is similar between the study results with data from the Laboratory of Microbiology. Nevertheless, it appears that there is little shift in the pattern of sensitivity to multiple antibiotics. This suggests that the pattern of sensitivity of bacteria need to be updated periodically in order to follow the development pattern in the ICU Dr. Soetomo Hospital, so it will be useful in providing a guide empirical therapy.

CONCLUSION

Most bacteria are found in sputum specimens are gram-negative bacteria are *Pseudomonas aeruginosa*, while the majority of bacteria in blood specimens which are gram-positive coagulase-negative *Staphylococcus*. The pattern of antibiotic sensitivity in *Pseudomonas aeruginosa* is: Antibiotics are still sensitive (> 60%): Piperacillin-tazobaktam, Cefoperazon-sulbactam,

Meropenem, Tobramycin, Levofloxacin. From the results of the qualitative analysis of antibiotics by the method Gyssens found that antibiotics are correct 78.6%, 14.3% incorrect dosage, there are other, more effective antibiotics 7.1%.

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