ANTIBIOGRAM STUDY AND ANTIBIOTIC USE EVALUATION USING GYSSEN METHOD IN PATIENTS WITH DIABETIC FOOT

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ABSTRAK

Latar belakang. Infeksi kaki adalah masalah umum dan serius pada orang dengan diabetes, yang memerlukan pengelolaan tepat (pendekatan diagnostik dan terapetik) agar dapat disembuhkan. Regimen antibiotika empiris harus didasarkan pada data klinis dan pola kuman yang tersedia, tetapi terapi definitif harus didasarkan pada hasil kultur jaringan yang terinfeksi. Kesulitan untuk pemilihan antibiotika pada terapi awal dan penggunaan yang kurang bijak menjadi masalah tersendiri dan beresiko pada munculnya resistensi antibiotika. Perlu adanya evaluasi penggunaan antibiotika untuk mendorong penggunaan yang lebih bijak. Tujuan. Menganalisis pola kuman pada kaki diabetik dan uji sensitifitasnya terhadap antibiotika, menganalisis antibiotika empiris yang dapat direkomendasikan, dan menganalisis penggunaan antibiotika dengan metode Gyssen. Metode. Penelitian ini adalah studi analisis observasional (deskriptif non-eksperimental), retrospektif dan prospektif pada pasien infeksi kaki diabetik yang memenuhi kriteria inklusi. Data tetrospektif digunakan untuk mengenalisis pola kuman dan uji sensitifitas terhadap antibiotika dan data prospektif digunakan untuk mengevaluasi penggunaan antibiotika berdasarkan pola kuman yang ada, selama periode akhir Maret-awal Agustus 2015 di RSUD Mardi Waluyo Kota Blitar. Evaluasi dilakukan dengan metode Gyssen. Hasil, sampel data retrospektif diperoleh 30 temuan kuman infecting selama bulan Agustus 2014-Maret 2015. Prevalensi kuman gram negatif sebanyak 53,33% dengan jenis kuman terbanyak E.coli dan Klebsiella oxytoca (13,33%), dan gram positif sebanyak 46,67% dengan kuman terbanyak Staphylococcus spp. dan Streptococcus spp. Dari data prospektif yang memenuhi kriteria inklusi sebanyak 13 pasien dengan prevalensi kuman terbanyak gram negatif adalah Klebsiella oxytoca (28,57%), dan terbanyak gram positif adalah Staphylococcus auerus (35,71%). Sementara analisis kualitatif penggunaan antibiotika dilakukan terhadap 50 jenis pemberian antibiotika. Hasil analisis kualitatif menggunakan metode Gyssens didapatkan penggunaan kategori sebanyak 62%, penggunaan kategori sebanyak 2%, kategori sebanyak 14%; kategori 2B sebanyak 26%; kategori 3A sebanyak 10%; kategori 4A sebanyak 52%, kategori 4B sebanyak 6%; kategori 4C sebanyak 8% dan tidak ada penggunaan antibiotika yang masuk kategori V dan kategori VI. Simpulan. Dari analisis gyssen ini dapat diperoleh data bahwa penggunaan antibiotika pada pasien kaki diabetik di RSUD Maerdi Waluyo Kota Blitar didominasi oleh ketidak tepatan dalam pemilihan antibiotika, dan ketidaktepatan dalam interval pemberian antibiotika. **(FMI 2016;52:198-208)**

Kata kunci: pola kuman, antibiotik, infeksi kaki diabetik, metode Gyssen

ABSTRACT

Foot infection is a common and serious problem in people with diabetes, which require proper management (diagnostic and therapeutic approaches) that can be cured. Empiric antibiotic regimen should be based on clinical data and bacteria pattern that are available, but definitive therapy should be based on the results of the infected tissue culture. The selection of initial antibiotic therapy was difficult and unwise use can lead to antibiotic-resistant. Evaluation is needed for using antibiotics to benefit wisely. The aim of this research is to analyzed the pattern of bacteria in diabetic foot and to its sensitivity test to antibiotics, analyze empiric antibiotics that can be recommended, and analyzed the use of antibiotics by Gyssen method. Data was analyzed with observational studies (descriptive non-experimental), retrospectively and prospectively in patients diabetic foot infection that met inclusion criteria. Retrospective data are used to analyzed bacteria pattern and its sensitivity test, while prospective data are used to evaluated the use of antibiotics based on bacteria pattern, during the period of late March-early August 2015 at Mardi Waluyo Hospital. Evaluation was conducted by Gyssen method. The results, retrospective data samples obtained 30 infection bacteria during August 2014-March 2015. The prevalence of gram-negative bacteria as 53.33% with most types of bacteria E.coli and Klebsiella oxytoca (13.33%), and gram-positive bacteria as 46.67% with the highest bacteria are Staphylococcus spp. and Streptococcus spp. From the prospective data in inclusion criteria, 13 patients with the highest prevalence of gram-negative bacteria are Klebsiella oxytoca (28.57%), and most gram-positive Staphylococcus auerus (35.71%). While the qualitative analysis of antibiotic use was conducted on 50 types of antibiotics. The results of the qualitative analysis using Gyssens method obtained category as 62%, 2%, 14%, 2B category as 26%, 3A category as 10%, 4A category 52%, 4B category as 6%, 4C category as 8% and there are no use of antibiotics in the category V and VI. Conclusions, Gyessen method can show that the use of antibiotics in diabetic foot patients in Mardi Waluyo hospital is dominated by inaccuracy in choice of antibiotic, and inaccuracies in the interval antibiotics. **(FMI 2016;52:198-208)**

Keywords: bacteria patterns, antibiotics, diabetic foot infections, Gyssens method

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INTRODUCTION

Foot infection is a common and serious problem in people with diabetes. Diabetic foot infections or Diabetic Foot Infection (DFI) usually starts with injuries, most often neuropathic ulceration. While all wounds are colonies of microorganisms, the presence of infection is defined by the findings of inflammation or pus. Infections and classified into mild (superficial and limited in size and depth), moderate (deeper or wider), or severe (accompanied by signs of systemic or metabolic disorders). This classification system, along with vascular assessment, help determine which patients need to be hospitalized, which may require special imaging procedure or surgical intervention, and requiring amputation (Lipsky 2012).

The prevalence of diabetic ulcers in Indonesia amounted to 15% of patients with DM. Most diabetes care is always associated with diabetic ulcers. Mortality and amputation remains high, and the fate of post-amputation in diabetic patient is still very bad, as many as 14.3% will die within a year of post-amputation and 37% will die of 3 years post-amputation (Waspadji 2006). Meanwhile, according to Riyanto, amputation figure reached 30%, 32% mortality rate, and diabetic ulcers is because the majority of hospital treatment by 80% in the case of diabetes mellitus (Riyanto 2007).

Mardi Waluyo Hospital Kota Blitar, of Profile Installation Medical Record of 2013 data showed that cases of hospitalization for diabetes mellitus ranks third after a stroke and a heart big, that some 495 cases or 3.51% of all cases of hospitalization. Of that number 66 cases (13.33%) were diabetic foot infections. In 2014 increased to 524 cases (3.8%), ranks second after stroke. 82 (15.65%) cases were DM patients with diabetic foot infections. From these data seen an increase in the number of cases. While the treatment of patients with diabetic foot infections the use of antibiotics has been no recommendation related to the pattern of the infecting organism (Profil Mardi Waluyo Hospital Medical Records Kota Blitar 2013-2014).

Most diabetic foot infections are polymicrobial, with gram-positive cocci, especially staphylococci which is the most common causative organism. Gram-negative rods often copathogen in chronic infection or the antibiotic treatment, and obligate anaerobes may copathogen on ischemic or necrotic wounds (Frier 2006). Wound infection without evidence of soft tissue or bone does not require antibiotic therapy. Empirical antibiotic therapy can be targeted narrowly at GPC (gram positive cocci) in many patients with acute infection, but those who are at risk for infection or chronic antibiotic resistant organisms, or severe infection usually requires a broader spectrum of drugs (Lipsky 2012).

Evaluation of the use of antibiotics in general can be performed quantitatively and qualitatively. To evaluate the quality of antibiotics there are many parameters that are used as dose accuracy, precision interval of administration, route of administration, and others. Qualitative assessment allows us to know whether antibiotics were given was appropriate, conducted by in-depth analysis of the medical records, also known as practical audit. Qualitative assessment is rarely done because of the lack of standardization, the methodology is difficult, and requires human resources (Cusini 2010). Nevertheless qualitative discussion of antibiotics can encourage clinicians to be more prudent in the use of antibiotics. Gyssen groove is one of the algorithms used for the qualitative evaluation of the use of antibiotics (Habib 2014).

During Mardi Waluyo Hospital in Kota Blitar have never done research on patterns of bacteria in patients with diabetic foot and there is no information related to empiric antibiotics based on the pattern of germs. Therefore, with this study are expected to be obtained from the data pattern of the bacteria on a culture of microbiological sample of pus patients with diabetic foot and sensitivity test antibiotics against germs (retrospective data), which later became the basis of the selection of empiric antibiotics, and then carried out qualitative evaluation of the use of antibiotics prospectively using Gyssens groove. Evaluation of the use of antibiotics in general can be performed quantitatively and qualitatively. To evaluate the quality of antibiotics there are many parameters that are used as dose accuracy, precision interval of administration, route of administration, and others. Qualitative assessment allows us to know whether antibiotics were given was appropriate, conducted by in-depth analysis of the medical records, also known as practical audit. Qualitative assessment is rarely done because of the lack of standardization, the methodology is difficult, and requires human resources (Cusini 2010). Nevertheless qualitative discussion of antibiotics can encourage clinicians to be more prudent in the use of antibiotics. Gyssen groove is one of the algorithms used for the qualitative evaluation of the use of antibiotics (Habib 2014).

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foot and sensitivity test antibiotics against germs (retrospective data), which later became the basis of the selection of empiric antibiotics, and then carried out qualitative evaluation of the use of antibiotics prospect-vely using Gyssens groove.

MATERIALS AND METHODS

Making antibiogram done by connecting the data bacteria culture results and antibiotic sensitivity test in the form of a table. Based on antibiogram can be seen the percentage of antibiotic sensitivity and categories that can be recommended for empirical use. Descriptive analysis is used to assess the results of the evaluation of the quality of the use of antibiotics with Gyssen method, first, time use of antibiotics (category I); Second, the regimentation dose, interval, these antibiotics (category II A - II C); Thirdly, the duration of use of antibiotics (category III A - III B); Fourth, the choice of the form of clinical efficacy, toxicity, price and sprektrum antibiotic coverage (category IV A - IV D); and fifth, an indication of the use of antibiotics (category V - VI), which will then be given a percentage on each key subject of evaluation.

Analysis

The analysis is conducted qualitatively by methods Gyssen against the use of antibiotics by referring to the data patterns of bacteria and sensitivity to antibiotics.

RESULTS

Data Retrospective

From skitar 42 patients hospitalized with a diagnosis of diabetic foot infection in hospitals Mardi Waluyo there were 23 patients who met the inclusion criteria and pus obtained 28 cultures, 30 isolates of bacteria and 20 types of germs infecting.

Germs Profile in Patients with Diabetic Foot

Table 1 shows the types of bacteria that cause infections in the diabetic foot hospital inpatient Mardi Waluyo period August 2014 - March 2015. Of the 23 patients obtained 28 results hulkur pus which produces 30 isolates of bacteria with prevalence of gram-negative bacteria as much as 53.33% and gram-positive in 46.67%.

Sensitivity Profile Germs on the Diabetic Foot Infection Antibiotics

Table 2 displays the results of the research profile pussy isolates, the prevalence and antibiotic sensitivity test results. Percentage (%) of antibiotic sensitivity is obtained by calculating the number of antibiotic-sensitive test divided by the number of isolates germs multiplied by 100%.

Table 1. Type of germs that cause diabetic foot infection period from August to March, 2015

No	Type of Germs	N (%)	Gram + / -	% Gram -/+	Note
1	Escherichia coli	4(13,33)	-	53.33%	
2	Klebsiella oxsytoca	3(10,0)	-		Klebsiella spp (13.33%)
3	Klebsiella pneumoniae	1(3.33)	-		
4	Citrobacter freundii	2(6,67)	-		
5	Enterobacter sakazakii	1(3.33)	-		Enterobacter spp (6.67%)
6	Enterobacter agglomerans	1(3.33)	-		
7	Pseudomonas aeruginosa	1(3.33)	-		Pseudomonas spp (10%)
8	Pseudomonas flourescens	1(3.33)	-		
9	Pseudomonas gladiolli (Burkholderia gladiolli)	1(3.33)	-		
10	Kluyvera ascorbata	1(3.33)	-		
11	Staphylococcus auerus	2(6,67)	+	46.67%	Staphylococcus spp (16.67%)
12	Staphylococcus haemolyticus	1(3.33)	+		
13	Staphylococcus sciuri	1(3.33)	+		
14	Staphylococcus schleiferi	1(3.33)	+		
15	Streptococcus agalactiae	3(10,0)	+		Streptococcus spp (16.67%)
16	Streptococcus pyogenes	1(3.33)	+		
17	Streptococcus porcinus	1(3.33)	+		
18	Kytococcus sedentarius	2(6,67)	+		
19	Kocuria kristiae	1(3.33)	+		
20	Kokus gram positif	1(3,33)	+		
	TOTAL	30(100)			

Table 2. Sensitivity Profile germs to antibiotics period August 2014- March 2015

Class of Antibiotics	Antibiotics	% Antibiotics Sensitivity					
		Gram Negatif			Gram Positif		
		E. coli (n=4)	*Kleb. oxytoca* (n=3)	*Citro. freundii* (n=2)	*Strep. Agalactiae* (n=3)	*Staph. Aureus* (n=2)	*Kytococ. Sedent* (n=2)
Penisilin	Penisilin	-	-	-	0	0(1)	100
	Ampisilin	0	0	0	33,3	0(1)	100
	Amoksisilin	-	-	-	-	-	-
	Oksasilin	0	0	0	0	0(1)	50
	Amoks-klav	0	0/33,3i	50	-	0(1)	-
	Piperasilin	-	-	-	-	100(1)	-
	Metisilin	-	-	-	-	0(1)	-
Sefalosporin	Sefiksim	-	-	-	-	0(1)	-
	Sefadroksil	-	-	-	-	0(1)	-
	Sefotaksim	0	33,3	100	-	0(1)	-
	Sefazolin	0	33,3	0/50i	-	-	-
	Seftazidim	0/25i	33,3	100	-	100(1)	-
	Seftriakson	0	33,3	100	0(1)	-	0(1)
	Sefpirom	-	-	-	-	100(1)	-
Karbapenem	Imipenem	-	-	-	-	100(1)	-
	Meropenem	0/25i	0/66,7i	0(1)	-	100(1)	-
Monobaktam	Aztreonam	0	33,3	50s/50i	-	-	-
Glikopeptida	Vankomisin	100(1)	-	-	66,7	100(1)	50
Tetrasiklin	Tetrasiklin	0	33,3	0	0	0	100
Makrolida	Eritromisin	-	-	-	66,7	0(1)	100
	Fosfomisin	-	-	-	-	100(1)	-
Fenikol	Kloramfenikol	-	-	-	-	0(1)	-
Aminoglikosida	Amikasin	75	66,7s/33,3i	100	100	100	100
	Dibekasin	-	-	-	-	100(1)	-
	Gentamisin	75	33,3	100	66,7s/33,3i	0	100
	Streptomisin	-	-	-	-	-	-
	Tobramisin	50	33,3	50	100	100(1)	100
Folic inhibitor	TMP-SMZ	0	33,3	50	66,7	0	50
Quinolon	Siprofloksasin	0	33,3	50	66,7s/33,3i	50	100
	Levofloksasin	0	66,7	50	66,7s/33,3i	50	100
	Ofloksasin	-	-	-	-	100(1)	-
	Norfloksasin	-	-	-	-	100(1)	-

Information	
	Sensitivity>60% : recommended
	Sensitivity 30-60% : considered
	Sensitivity<30% : not recommended
(number)	Bacterial number in senstivity test
s/i	Sensitive/intermediary

Prospective Data

For prospective data of 13 patients obtained the inclusion of 28 patients with diabetic foot, with 14 cultures and 14 isolates germs infecting.

Patient demographics

Table 3 shows the demographic data of patients diabetic foot patients who met the inclusion criteria which include gender of the patient, age, severity of disease, and the patient's status. Number 8 female patients (61.54 %), and men's number 5 (34.46%). Patients age 50-60 years dominated as much 8orang (61.54%), while the rate of infection of patients are mostly severe infections

(10 cases; 76.93%). Status patients mostly BPJS (9; 69.23%).

Table 3. Profile of patients with a diagnosis of diabetic foot infection period late March-early August 2015

Demography of Patient	N	Percentage
Sex		
- Male	5	38.46%
- Female	8	61.54%
Age		
- < 50 years old	1(P)	7.69%
- 50 – 60 years old	8(3P,5L)	61.54%
- > 60 years	4(P)	30.77%
Infection Severity		
- Mild	-	0%
- Moderate	3	23.07%

- Severe	10	76.93%
Status of patient		
- BPJS	9	69.23%
- SPM	1	7.69%
- Others	3	23.08%

* Percentage is calculated based on the total number of patients that 13 patients

Profile Germs on Diabetic Foot Infection

Table 4 shows the types of bacteria that cause infections in the diabetic foot hospital inpatient Mardi Waluyo period end of March - beginning of August 2015. Of the 13 patients obtained 14 results hulkur pus which produces 14 isolates of bacteria with prevalence of gram-negative bacteria as much as 42.86% and gram-positive as much as 57.14%. Most gram-negative types are *Klebsiella oxsytoca* (28.57%), and most gram positive *Staphylococcus auerus* (35.71%).

Table 4. Type of germs infecting End of period March 2015 - Beginning August 2015

No	Type og Germs	N(%)	Gram + / -	Note
1	*Klebsiella oxsytoca*	4(28.57)	-	Gram (-)
2	*Providencia stuartii*	1(7.14)	-	42.86%
3	*Morganella morganii*	1(7.14)	-	
4	*Staphylococcus auerus*	5(35.71)	+	Gram (+)
5	*Staphylococcus saccharolyticus*	1(7.14)	+	57.14 %
6	*Streptococcus agalactiae*	1(7.14)	+	
7	*Streptococcus haemolyticus*	1(7.14)	+	
	Total	14(100)		100%

Sensitivity Profile Germs on the Diabetic Foot Infection Antibiotics

Table 5. Sensitivity Profile germs to antibiotics Period End of March - Beginning August 2015

Class of Antibiotics	Antibiotics	% Antibiotics Sensitivity					
		Gram Negative			Gram Positive		
		Kleb. oxytoca (n=4)	*Provid. Stuartii (n=1)*	*Morg. morganii (n=1)*	*Strtococc. spp (n=2)*	*Staph. Aureus (n=5)*	*S.saccharo lyticus (n=1)*
Penisilin	Penisilin	-	-	-	0(1)	40	0
	Ampisilin	0	100	0	100(1)	20	0
	Amoksisilin	-	-	-		-	-
	Oksasilin	0	0	0	0(1)	0	0
	Amoks-klav	25s/50i	100	0	100(1)	-	-
	Piperasilin	-	-	-	100(1)	-	-
	Metisilin	-	-	-	-	-	-
Sefalosporin	Sefiksim	-	-	-	100(1)	-	-
	Sefadroksil	-	-	-	0(1)	-	-
	Sefotaksim	75	100	100	100(1)	-	-
	Sefazolin	50	-	0	-	-	-
	Seftazidim	75	i	100	100(1)	-	-
	Seftriakson	75	100	100	-	-	-
	Sefpirom	-	-	-	100(1)	-	-
Karbapenem	Imipenem	-	-	-	100(1)	-	-
	Meropenem	50s/50i	100	I		-	-
Monobaktam	Aztreonam	75	100	100		-	-
Glikopeptida	Vankomisin	-	-	-	100(1)	100	100
Tetrasiklin	Tetrasiklin	25i	0	0	50	40	0
Makrolida	Eritromisin	-	-	-	100(1)	60s/20i	0
	Fosfomisin	-	-	-	100(1)	-	-
Linkosamid	Klindamisin	-	-	-	0(1)	-	-
Fenikol	Kloramfenikol	-	-	-	100(1)	-	-
Aminoglikosida	Amikasin	100	100	100	50s/50i	80	0
	Dibekasin	-	-	-	100(1)	-	-
	Gentamisin	75	100	100	50	100	0
	Streptomisin	-	-	-	0(1)	-	-
	Tobramisin	75s/25i	100	i	i	80	0
Folic inhibitor	TMP-SMZ	25	100	0	50	100	0
Quinolon	Siprofloksasin	25s/25i	100	100	50s/50i	60s/20i	0
	Levofloksasin	50	100	100	100	80	0
	Ofloksasin	-	-	-	100(1)	-	-
	Norfloksasin	-	-	-	100(1)	-	-

	Sensitivity>60% : recommended	
	Sensitivity 30-60% : considered	
	Sensitivity<30% : not recommended	
(number)	Bacterial number in sensitivity tyest	
s/i	Sensitive/intermediary	

Use of Antibiotics Profile in Patients with Diabetic Foot and the Qualitative Analysis

The number of antibiotic therapy in 13 patients are as many as 14 kinds of antibiotics, where the patient can get more than one kind of regimentation of antibiotics with different doses and intervals. Originally a single administration of antibiotics can then for some reason there are additions or replacements both in terms of type, dose and administration interval so that the total number is 50 Award. Table 6 shows the suitability of dose and interval of antibiotics for the treatment of diabetic foot infection between guides guideline with reality given to the patient (by type). Rate the quality of the use of antibiotics in diabetic foot patients by

category Gyssens performed in hospitals Mardi Waluyo Blitar City during the period of late March - early August 2015 having previously performed a retrospective data collection period August 2014 - March 2015 who received antibiotic therapy, both empirical and definitive. The quality of antibiotic use were analyzed using flow Gyssens are divided into categories 0 to VI. From the analysis of the use of antibiotics with the highest use of antibiotics Gyssens method is more effective in 52% (category IV A); not appropriate intervals as much as 26% (category II B); teepat no dose by 14% (category IIA). Complete data analysis results with the use of antibiotics Gyssen method can be seen in Table 7.

Table 6. Interval Dose Antibiotic for Treatment Diabetic Foot (by type)

AntibiotiCS	Antibiotic doses (literature)	Dose in patients	Frequency*	Note
Seftriakson	1-2g /d, iv (Lipsky,2012)	2x1g/d,iv (empirical)	2	Appropriate
		2x1g/d,iv (definitive)	1	Appropriate
		2x2g/d,iv (empirical)	3	overdose
		2x2g/d,iv (definitive)	1	overdose
Sefoperazon	No data on guidelines of diabetic foot infection (usual dose:2-4g/d,iv- 2x / 12j)	2x1g/d,iv (empirical)	3	Appropriate usual dose
		3x1g/d,iv (empirical)	6	Appropriate usual dose, interval not appropriate
		2x1g/d,iv (definitive)	1	Appropriate usual dose
Sefotaksim	200mg/kg/d-iv-4-6hr Enterobacteriaceae (Bernard,2006)	3x1g/d,iv (empirical)	2	Not Appropriate dose &interval (underdose)
Metronidazol	3x500mg, iv/oral (Chahine, 2013)	3x500mg, iv(empirical)	5	Appropriate
		2x500mg, iv(empirical)	1	underdose
		2x500mg,iv(definitive)	1	underdose
Siprofloksasin	2x400mg,iv-each 12hr (Chahine,2013)	2x400mg,iv(empirical)	5	Appropriate
Levofloksasin	1x750mg/d, iv/oral (Chahine,2013) or 1x500mg/d iv/oral ±klindamisin	1x 500mg, iv (definitive)	4	Appropriate
Gentamisin	4mg/kg/d, each 24hr (combination)(Bernard,2006); conventional: 1-2,5mg/kg, each 8-12hr.	2x80mg,iv(empirical)	3	Appropriate dose, safer each 24 hr
		2x80mg,iv(definitive)	2	Appropriate dose, safer each 24 hr
Meropenem	3x1g, iv –each 8 hr (Chahine, 2013)	3x1g, iv (definitive)	2	Appropriate
Pelastin/imipenem - silastatin	1-2g/d,iv, 3-4x dose (500mg iv/6hr)	2x1g,iv (empirical)	1	Dose/d Appropriate, interval tdk Appropriate
		2x1g,iv (definitive)	1	Dose/d Appropriate, interval not appropriate
Amikasin	No data on guidelines of diabetic foot infection (usual dose: 5-7,5mg/kg/dose - each 8hr)	3x250mg,iv (definitive)	1	Appropriate
Tetrasiklin	No data on guidelines of diabetic foot infection (usual dose: dws 4x250-500mg oral)	3x500mg, oral (definitive)-discharge	1	Interval notAppropriate
		4x500mg, oral (definitive)-discharge	1	Appropriate
Ampisillin	Ampi-sulbaktam is suggested 3g,iv/6hr (ampisillin usual dose: 4x250-1000mg,iv/im each 6 hr	3x1g, iv (definitive)	1	Appropriate dose, interval Not Appropriate
Zibac/ Seftazidim	2g-iv, each 8-12hr (Chahine, 2013), DIH: 500mg-1gr, each 8 hr	3x1g,iv (empirical)	1	Appropriate

Vancep	30mg/kg,iv -2x/d (Bader, 2008) or 15-20mg/kg,iv - each 8-12hr(Chahine,2013)	4x500mg, syring pump (definitive)	1	Interval not appropriate

* Frequency indicates the number of patients using the drug with the dose, where one patient may receive more than one kind of dose, and the patient can also get more than one kind of antibiotic.

Table 7. Results of analysis of the use of antibiotics with Qualitative Methods

Categories	Evaluation	Total	Percentage
0	Antibiotic use appropriate/wise	31	62%
I	Antibiotic use not on time	1	2%
II A	Antibiotic use not appropriate in dose	7	14%
II B	Antibiotic use not appropriate in admnistration interval	13	26%
II C	Antibiotic use not appropriate in admnistration route	-	-
III A	Antibiotic use too long	5	10%
III B	Antibiotic use too short	-	-
IV A	Other more effective antibiotics are present	26	52%
IV B	Other less toxic/safer antibiotics are present	3	6%
IV C	Other less costly antibiotics are present	3	6%
IV D	Other narrower spectrum antibiotics are present	4	8%
V	No indication of antibiotic use	-	-
VI	Medical record data not complete dan not evaluable	-	-

*Each type of antibiotic someone has entered more than one category in a qualitative evaluation Gyssens.

DISCUSSION

Of the 30 isolates germs infecting (retrospective data) obtained patterns of gram-negative bacteria dominated by as much as 53.33% 13.33% *E coli*, and *Klebsiella oxytoca* 13.33%, the rest is *Enterobacter spp*, *Citrobacter spp*, *Pseudomonas spp* well, and gram positive as much as 46.67% dominated by 16.67% of *Staphylococcus spp*, *Streptococcus spp* (16.67%). As for prospective data from 14 isolates of gram-negative bacteria gained as much as 42.86% and gram positive as much as 57.14%. Seen a shift in the percentage of gram negative and positive emerging, most types of gram-negative is *Klebsiella oxytoca* (28.57%), and most gram positive *Staphylococcus aureus* (35.71%). GPC especially Staphylococcus aureus and beta-hemolytic streptococci is the organism most often in patients with mild-moderate DFI, and patients who did not receive antibiotic therapy in the previous month. Patients with a history of chronic infection and have taken antibiotics tend to develop into a mixed infection between GPC and GNB with or without anaerobic organisms. The existence of obligate anaerobes associated with necrotic, gangrenous or ischemic tissue, and this is usually a chronic and severe infection (Chahine in 2013).

Antibiotic therapy can be as empirical and definitive treatment. The principle of election empiric antibiotics are: a) the spectrum of activity of antibiotics, b) the ability to penetrate the network good, c) take into account the patient (the severity of the infection, allergies, kidney disorders), d) the map data germs and patterns of antibiotic resistance local, and e) security and ease of administration to patients (Lipsky, 2007, Frykberg 2002, Cunha 2010). There are various recommendations on the use of empiric antibiotics in diabetic foot infections based on the level of infection, such as: a) mild-moderate infections; given the oral fluoroquinolones or aminopenisillin (amoksisillin-cla-vulanate, sulbactam ampisillin), with alternative clindamycin or Bactrim; b) moderate to severe infections, given the combination of clindamycin-ciprofloxacin intravenously; ceftazidime-metronidazole. Another recommendation for patients who have not been treated or cephalosporin antibiotics are aminopenisillin 2nd generation/3rd, to which had been treated antibioika: 3rd generation cephalosporin/4th, or fluoroquinolones + clindamycin; c) a life-threatening infection: class of carbapenem or aminoglycoside + clindamycin or a cephalosporin 3rd generation/4th + glycopeptide/ linezolid or fluoroquinolones + metronidazole (Lipsky 2007, Pranoto 2010).

Meanwhile, according to Chahine (2013), an antibiotic that can be recommended are: a) Mild infections: amoksisillin-clavulanate, cephalexin, clindamycin, dikloksasillin, levofloxacin, doxycycline and cotrimoxazole, given orally; b) moderate to severe infections: ampisillin sulbactam, sefoksitin, ceftriaxone, ciprofloxacin + clindamycin, ertapenem, imipenem-silastatin, levofloxacin + clindamycin, meropenem, moxifloxacin, tigesiklin, daptomisin, linezolid, and vancomycin; administered intravenously and each with regard to the nature of germs infecting (Table 2.15) (Chahine in 2013).

In this study, empirical antibiotic that is widely used is ceftriaxone, sefoperazon, cefotaxime, ciprofloxacin, metronidazole and gentamicin, either alone or in combination use. Based on the antibiogram, the data

sensitivity ceftriaxone and cefotaxime showed potentials > 60% (which means it can be recommended usage) only on bacteria Citrobacter freundii only, while for the bacteria *Klebsiella oxytoca* both have the potential between 30-60% (can be considered its use), but no data sensitivity to sefoperazon, while ciprofloxacin potentially deadly> 60% on Streptococcus agalactiae and Kytococcus sedentarius, and may be considered for the bacteria *Klebsiella oxytoca*, Citrobacter freundii, and Staphylococcus aureus (sensitivity between 30-60%). Gentamicin potentially deadly> 60% of bacteria *E. coli*, Citrobacter freundii, Stretococcus agalactiae and Kytococcus sedentarius, and can be considered the Klebsiella bacteria oxsitoca (sensitivity between 30-60%). For metronidazole more focused on anaerobic bacteria, which are often found in the condition of necrotic, gangrenous or ischemic tissue, and this is usually a chronic and severe infection. In this study, metronidazole is not determined its potential against anaerobic bacteria. Based on the research of diabetic foot wounds pus isolates (n = 120 isolates) in anaerobic test showed that metronidazole has a potential 99% against all anaerobic bacteria tested and have a low level of resistance compared with clindamycin (Syng et al, 2008).

Based on the results of data processing retrospektik antibiogram, antibiotic potential is huge against gram negative and positive is amikacin (> 60%: against *E. coli*, Kelb. Oxytoca 75%, 100% against Citrobacter freundii), and between 33.3% against *Pseudomonas spp*; 100% of *Streptococcus spp*, *Staphylococcus spp*, and Kytococcus sedentarius; Gentamicin (> 60%: against *E. coli*, Kelb. Oxytoca 75%, 100% against Citrobacter freundii), and 33.3% against *Pseudomonas spp*; 66.7% against Streptoccus agalactiae, 100% of the Kytococcus sedentarius, and 40% against *Staphylococcus spp*.Terlihat also the potential of ciprofloxacin against gram-positive: 66.7% against Streptoccus agalactiae, 100% of the Kytococcus sedentarius and between 30-60% of the Kelb , Oxytoca and Citrobacter freundii. Levofloxacin looks more potent than ciprofloxacin in Klebsiella bacteria oxsitoca prevalence 13.33% in the diabetic foot. While vancomycin and tobramycin is more potent against gram-positive.

In the last 4 months period looked patterns germs little change related types of bacteria that appears, with the most prevalent gram-negative is *Klebsiella oxytoca* (28.57%), where sensitivity> 60% of the 3rd generation cephalosporins (75%) - the highest amikacin 100 %; between 30-60% of cefazolin, meropenem and levofloxacin; and most gram positive *Staphylococcus auerus* (35.71%), where sensitivity> 60% to vancomycin (100%), amikacin (80%), gentamicin (100%), tobramycin (80%), cotrimoxazole (100%), and levofloxacin (80%); antara30-60% sensitivity to tetracycline, erythromycin and ciprofloxacin.

Generally from antibiogram picture shows antibiotic may mengkafer gram negative and positive bacteria is amikacin, gentamicin, ciprofloxacin and levofloxacin. Generation cephalosporin astreonam 3And all the more potent against gram-negative, and vancomycin 100% potent against gram-positive. However, to be recommended as empiric antibiotics in diabetic foot patients would have to consider other factors. The age of patients for diabetic foot are mostly 50-60 year in which the function of organs, especially the kidneys have a tendency to 17 times higher chance of developing chronic renal failure than in healthy people, must be very careful in the use of aminoglycoside antibiotic class which has the side effect of nephrotoxic, neurotoxic, superinfection (C.difficile infection) on long-term use of gentamicin, and neuromuscular blockade or respiratory paralysis on amikacin (Lacy 2009). Besides the potential for higher antibiotic against bacteria in vitro infecting not necessarily effective in vivo. Conditions of acute injuries/chronic as well as the severity of the infection is also an important consideration. Based on these things, and refers to the guideline-guideline concerning empirical treatment of diabetic foot infection, we would recommend the use of ciprofloxacin or levofloxacin as empiric antibiotics in diabetic foot patients in hospitals Mardi Waluyo of Blitar. When should use aminoglycoside class, of course, it must be ensured also normal kidney function and do monitoring side effects. To mengkafer anaerobes, klidamisin oral/metronidazole iv/orally may be combined with ciprofloxacin or levofloxacin (Bader 2008, Lipsky 2012, Chahine in 2013).

The use of antibiotics in addition to considering the results of the culture, to note the patient's response to infection. If the lesion injuries to the patients improved and patients respond to empiric therapy, the replacement of antibiotics may not be necessary, although the results of antibiotic sensitivity test found infecting bacteria that are resistant to antibiotics that have been used empirically (Lipsky 1999). The use of broad-spectrum empiric antibiotics is required at the start of therapy (for information infecting bacteria is not known), when the results of culture and sensitivity test are known, should be done with the replacement of narrow-spectrum antibiotics. Due to the use of broad-spectrum empiric too long will lead to a selective process in which the pressure will increase the population of resistant bacteria and can alter the body's normal flora (Southwick 2007).

The results of the qualitative analysis using the method Gyssens obtained the use of antibiotics is appropriate

(category 0) as much as 62%, the use of atibiotika not timely (category 1) as much as 2%, not appropriate dose (category 2A) by 14%; not appropriate interval Award (category 2B) were 26%; antibiotics for too long (category 3A) as much as 10%; there are other antibiotics that are more effective (class 4A) in 52%, there are other safer antibiotics (category 4B) as 6%; there are other antibiotics that spectrum is narrower (category 4C) as much as 8% and no use of antibiotics in the category V and VI category.

CONCLUSION

From this analysis can gyssen data showed that the use of antibiotics in diabetic foot patients in hospitals Maerdi Waluyo Blitar City is dominated by inaccuracy in the selection of antibiotics (some are more effective), and the inappropriateness of antibiotics interval. It is therefore expected with this study is encouraging clinicians to further improve the quality of antibiotic use based on the pattern of germs.

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