Evaluasi Penggunaan Antibiotik pada Pasien Gagal Ginjal Kronis di RSUP Dr. Soeradji Tirtonegoro Klaten Periode 2014

Evaluation of the Use of Antibiotics in Chronic Renal Failure Patients in RSUP Dr. Soeradji Tirtonegoro Klaten Period 2014

Gita Ayu Pradina and Zakky Cholisoh
Fakultas Farmasi, Universitas Muhammadiyah Surakarta
Jl. Ahmad Yani Tromol Pos I, Pabelan Kartasura Surakarta 57102
e-mail: gitayu14@gmail.com

Abstrak

Antibiotik merupakan salah satu obat yang paling banyak digunakan dalam menyembuhkan berbagai macam penyakit infeksi. Penggunaan antibiotik khususnya pada gagal ginjal kronis perlu diperhatikan karena dapat menyebabkan nefrotoksisitas pada ginjal. Tujuan penelitian ini untuk mengevaluasi kerasionalan penggunaan antibiotika di RSUP Dr. Soeradji Tirtonegoro pada kasus gagal ginjal kronis tahun 2014. Evaluasi meliputi tepat indikasi, tepat obat, tepat pasien, dan tepat dosis. Penelitian ini merupakan penelitian yang dilakukan dengan cara retrospektif yang didasarkan pada penulusuran rekam medik milik pasien gagal ginjal kronis pada instalasi rawat inap RSUP Dr. Soeradji Tirtonegoro Klaten tahun 2014. Hasil penelusuran rekam medik didapat hasil penggunaan antibiotik yang tepat indikasi sebanyak 20 kasus (55,56%), pasien gagal ginjal kronis yang memenuhi kriteria tepat pasien berjumlah 39 kasus (97,7%), penggunaan antibiotik yang tepat obat ada 13 kasus (29,5%), dan untuk penggunaan antibiotik yang tepat dosis sebanyak 21 kasus (47,7%). Status kepulangan pasien dengan jumlah total 36 kasus (100%) pulang dalam keadaan membaik. Dari hasil angka hitung leukositnya terdapat 33 kasus (91,67%) angka leukositnya yang turun kekeadaan normal.

Kata kunci: Antibiotik, Gagal Ginjal Kronis, Rawat Inap, RSUP Dr. Soeradji Tirtonegoro Klaten

Abstract

Antibiotics are one of the most widely used drugs in curing various kinds of infectious diseases. The use of antibiotics, especially in chronic renal failure, need to be considered because it can cause nephrotoxicity in kidneys. The purpose of this study was to evaluate the rational use of antibiotics in RSUP Dr. Soeradji Tirtonegoro in cases of chronic renal failure in 2014. The evaluation includes the right indication, the right drug, right patient, and proper dosage. This research is conducted in a manner that is based on a retrospective medical record belongs to chronic renal failure patients on inpatient RSUP Dr. Tirtonegoro Klaten 2014. The search results obtained from medical records and evaluation results indicated the use of appropriate antibiotics as many as 20 cases (55.56%), patients with chronic renal failure who meet the appropriate criteria are 39 cases (97.7%), use of the right type of antibiotics drugs there were 13 cases (29,5%), and to use appropriate antibiotics doses were 21 cases (47.7%). Discharge status of patients with a total of 36 cases (100%) with result of the patient's health improved. From the result of arithmetic leukocytes figure, there are 33 cases (91.67 %) with leukocytes count back to normal.

Keywords: Antibiotics, Chronic renal failures, Inpatient, RSUP Dr. Soeradji Tirtonegoro Klaten

Introduction

The damage of the kidney that has been happened for three months by the symptoms of pathological disorder or kidney failure like proteinuria called as chronic renal failure If there was no symptom of pathological disorder, the diagnosis will be based on the flow of glomerulus filtration $<60mL/minute/1,73m^2$ in >3 months with or without kidney failure (Chonchol, 2009).

Antibiotic was one of the mostly used medicines to cure many kinds of inflectional

disease. The use of antibiotics mainly in the chronic renal failure needs to be taken care seriously because it can cause nefrotoxicity to the kidney (Kenward & Tan, 2003). By the consideration of the kidney insufficiency, so the evaluation of the use of antibiotics for the kidney failure patients about the effectifity and the rationality of the dosage need to be considered (Kunin, *et al.*, 1959). The use of antibiotics needs to be considered because some antibiotics have the characteristics of toxic to the kidney (Chasani, 2008).

The evaluation of antibiotics for the patients with kidney failure had been done in RSUD Dr. Moewardi in 2007. The antibiotics that had not been adapted their dosage to the patients with kidney failure was as 16,1%, the antibiotics that were contraindicated to the patients with kidney disease was as 1,8%, appropriate indication with in appropriate medicine was as 10,9%, correct indication with correct medicine was as 81,8%. Based on the therapy of antibiotics medications, the result shows that there is 45,5% of good results (Yulianti, *et al.*, 2007). The hospital used for the research is RSUP Dr. Soeradji Tirtonegoro Klaten.

Research Methodology

Instruments: the instruments was used data collection sheet, Drug Prescribing in Renal Failure : Dosing Guidelines for Adults, British National Formulary 2009, Pharmacotherapy Handbook, Pedoman Umum Penggunaan Antibiotik dari Peraturan Menteri Kesehatan nomor: 2406/MENKES/PER/XII/2011 and Clinical Pharmacy book (Parfati, *et al.,* 2003*).*

Materials: the materials used the medical record data of the chronic kidney failure patients in RSUP Dr. Soeradji Tirtonegoro Klaten in 2014 that included in the inclusion criteria.

1. Population and Sample

The population and sample in this research are all of the chronic kidney failure patients who got infection and also used antibiotic in their medications in RSUP Dr. Soeradji Tirtonegoro Klaten in 2014. The total

patients who had been diagnosed with chronic kidney failure and also got infection and used antibiotics are 40 patients.

The calculation of the sample taken using Krejcie and Morgan table, (1970) ia as follow:

Table 1. Krejcie & Morgan Table (sample calculation)

N	S	N	S	N	S
10	10	220	140	1200	291
15	14	230	144	1300	297
20	19	240	148	1400	302
25	24	250	152	1500	306
30	38	260	155	1600	310
35	32	270	159	1700	313
40	36	280	162	1800	317
45	40	290	165	1900	320
50	44	300	169	2000	322
55	48	320	175	2200	327
60	52	340	181	2400	331
65	56	360	186	2600	335
70	59	380	191	2800	338
75	63	400	196	3000	341
80	66	420	201	3500	346
85	70	440	205	4000	351
90	73	460	210	4500	354
95	76	480	214	5000	357
100	80	500	217	6000	361
110	86	550	226	7000	364
120	92	600	234	8000	367
130	97	650	242	9000	368
140	103	700	248	10000	370
150	108	750	254	15000	37
160	113	800	260	20000	Y5
170	118	850	265	30000	377
180	123	900	269	40000	379
190	127	950	274	50000	380
200	132	1000	278	75000	381
210	136	1100	285	1000000	382
					384

N (the amount of population)
S (the amount of sample)

Based on the calculation there are some determination about Krejcie and Morgan table as follow:

a. The assumption of reliability level 95%, because it uses value of $X^2 = 3,841$ that means that it uses $\alpha = 0,05$ on degree of freedom

b. The assumption of population variety that is included in the calculation is $P(1-P)$, where $P = 0,5$

c. The assumption of estimated galat value 5% (d= 0,05)
d. The available amount of the sample population is as 40 samples, so the amount of the sample taken is based on the calculation using Krejcia and Morgan table as 36 samples.

Research Location: The research was done in RSUP Dr. Soeradji Tirtonegoro Klaten.

2. **The Inclusion and Exclusion Criteria**
   a. **Inclusion criteria:**
      1) Patients with chronic renal failure in RSUP Dr. Soeradji Tirtonegoro Klaten in 2014.
      2) The patients got antibiotics therapy for the medication of the infection.
      3) The complete data at least contain patients' data for example: the medical record number, age, body weight, sex, symptoms, diagnose, medicines, dosage, antibiotics duration, the date of giving, ureum, kidney function test (BUN and creatinin serum), leukocyte count number, and the last condition of the patients.
   b. **Exclusion criteria:**
      The patients died in medication.

3. **Analysis**
   The data were analyzed using descriptively by counting the percentage of the 4-appropriateness method, they are the appropriate indication, appropriate patient, appropriate medicine, and appropriate dosage.
   a. % appropriate indication =
   $$\frac{the\ number\ of\ appropriate\ indication\ case}{total\ case} \times 100\%$$

   b. % appropriate patient =
   $$\frac{the\ number\ of\ appropriate\ patient\ case}{total\ case} \times 100\%$$

   c. % appropriate medicine =
   $$\frac{the\ number\ of\ appropriate\ medicine\ case}{total\ case} \times 100\%$$

   d. % appropriate dosage =
   $$\frac{the\ number\ of\ appropriate\ dosage\ case}{total\ case} \times 100\%$$

Result And Discussion

This research was a retrospective study, the data obtained by investigation of medical record of the patients with chronic renal failure in RSUP Dr. Tirtonegoro Klaten in 2014. The number of patient case that is included in the inclusion criteria was as 40 patients, but based on the calculation of the sample taken is as 36 samples.

1. **General Characteristics of the Patients**
   The results showed that were 36 samples of patients with chronic kidney failure in RSUP Dr. Tirtonegoro Klaten that were included into inclusion criteria. The patient's demography data is based on the age and sex can be seen in Table 2.

Table 2. Patient's Demography Data based on sex and age

Data (age)	Data (sex)			
	Male	%	Female	%
25-34	5	13,9%	1	2,8%
35-44	3	8,3%	2	5,6%
45-54	8	22,2%	6	16,6%
55-64	5	13,9%	-	-
65-74	1	2,8%	2	5,6%
>75	3	8,3%	-	-
Total	36	69,4%	11	30,6%

Based on table 2, for the male and female patients with chronic renal failure were mostly in the age of 45 – 54, there are eight male patients (22,2%) from all of the total case and there were 6 female patients (16,6%) from all of the total case. Based on KemenKes (ministry of health) in 2013, the number of patients with chronic renal failure was increased significantly in the age of >35 years old. This was because of the decreased of the kidney function, decreased of the muscle mass along with the age (BPOM, 2013).

2. Patient's Antibiotics Usage Data

From the investigation of the medical record, the patient's antibiotics usage data in the treatment installetion of RSUP Dr. Tirtonegoro Klaten (Table 3).

Table 3. The antibiotic usage data on the patients of chronic kidney failure in treatment installation

Data (antibiotic usage)				
		The amount of patient were given antibiotics	Patient number	
Trade Name	Generic name			
Ceftriaxon	Ceftriaxon	17		36,9%
Cefixim	Cefixim	12	3,5,6,8,	26,1%
Ceftazidim	Ceftazidim	1	2	2,2%
Cefat	Sefadroksil	2	4,12	4,3%
Amiksisilin	Amoksisilin	3	6,17,19	6,6%
		4		8,7%
Cefotaxime	Cefotaxime	4		8,7%
Clindamycin	Clindamycin	1	16	2,2%
tanpa antibiotik		2	18,27	4,3%
Jumlah		46		100%

The results showed the mostly was used of antibiotic for the patients with chronic renal failure was the group of sefalosporin. The antibiotic from the sefalosporin group that is mostly used is seftriakson with the number of patients with this kind of medication by seftriakson is as 17 patients (36,9%). Seftriakson is mostly used for the patients with chronic renal failure because it was considered as a safe medicine to be used for the patients with chronic renal failure especially for the patients with clirens creatinin >10mL/minute (Bayer,2012).

Appropriate Indications

The medicine given that was suitable with the indication it means that the medicine used has been appropriate with the symptoms and the diagnosis (Table 4).

Table 4. Antibiotic usage data based on the appropriate indication

Diagnosis	Antibiotic Usage		Appropriate Indication	
			Appropriate	Not
CKD, ISK	Yes	No		
	1,7,9,17,21		5	
CKD, Bronchitis				
	12,14		2	
CKD, Pneumonia				
	2,4,6,13,15,20,22,24,26		9	
		18,27		2
CKD, Prophylaxis				
	10,11		2	
CKD, Diarrhea				
	16,33		2	
CKD (Without infection)				
	3,5,8,19,23,25,28,29,30,31,32,34,35,36			14
Total	36		20	16

The result showed that there were some usage of the antibiotics that were not appropriated with the indication some of them were the given of antibiotics without indication as much as 14 cases (38,88%) and there is an indication but not given medicine in 2 cases (5,56%). The was used of antibiotics that does not have appropriate indications is 16 cases (44,44%) and for the usage of antibiotics that has appropriate indications was 20 cases (55,56%).

3. Appropriate Patient

The prescription of the medicine with the appropriate patient criteria was the accuracy in giving medicine based on the existence of the physiologies and pathologies condition of the patients that can hamper the giving of the medicine (contraindication) (Table 5).

The results showed that the patient with the chronic renal failure that fulfill the criteria of appropriate patient is 39 cases (97,7%) and for the inappropriate patient case was 1 (2,3%). This was because used of klindamisin antibiotic that was not suitable with the physiologies condition of the patient. Based on British National Formulary 2009, klindamisin has contraindication to the patient with diarrhea while the patient was taken clinical therapy of klindamisin has diarrhea.

Table 5. Patient data with the appropriate patient criteria.

Evaluation criteria	Antibiotic name	Data Patient number	Amount	
	Seftriakson			
Appropriate		1,2,7,8,10,12,13,14,16,20,21,24,28,29,30,32,33	17	
Inappropriate		-		0
	Sefiksim			
Appropriate		3,5,6,8,11,15,16,17,25,31,33,35	12	
Inappropriate		-		0
	Sefadroksil			
Appropriate		4,12	2	
Inappropriate		-		0
	Amoksisilin			
Appropriate		6,17,19	3	
Inappropriate		-		0
Appropriate		9,11,24,26	4	
Inappropriate		-		0
Appropriate		-	0	
Inappropriate		16		1
	Sefotaksim			
Appropriate		22,23,34,36	4	
Inappropriate		-		0
	Seftazidim			
Appropriate		2	1	
Inappropriate		-		0
Total			43	1
			44	

4. Appropriate Medicine

The medicine given of with the criteria of appropriate medicine in the use of antibiotics means that the accurateness of the drug choosing was based on the drug of choice for each inflectional disease that come along with the chronic renal failure patients in RSUP Dr. Soeradji Tirtonegoro Klaten. For the data of the accurateness in the giving off antibiotic there are 8 kinds of antibiotic usage (Table 6).

Table 6. Antibiotic usage appropriateness data in the infection cases of the patient with chronic kidney failure in treatment installation of RSUP Dr. Soeradji Tirtonegoro Klaten.

Antibiotic name	The amount of	Appropriate medicine	
Seftriakson	17	6	11
Seftazidim	1	0	1
Sefadroksil	2	0	2
	3	1	2
Sefotaksim	4	1	3
	4	1	3
	1	0	1
Sefiksim	12	4	8
Jumlah	44	13	31

From the data of the antibiotic usage appropriateness in the infectious patients with the chronic renal failure is 31 cases (70,5%) that is inappropriate medicine because the drug is not the drug of choice in the medication. For the use of antibiotic that is appropriate medicine is 13 cases (29,5%). The data has been compared with the appropriate of the usage of antibiotic from Dipiro, (2008); Guideline from Department of Surgical Education, (2001); journal from Gupta, et al., (2011); and Guideline Management of Community-Acquired Pneumonia in Adult.

5. Appropriate Dosage

The prescription with the criteria of appropriate dosage means that the amount of the medicine given to the patient was accurate, where the dosage given was in the therapy range that is recommended and agreed with the age and the condition of the patient. Because the evaluated subjects are the patients with the chronic renal failure, so it has the close relations with the value of clerins creatinins of the patients. It is known that the chronic renal failure patient in the treatment installation of RSUP Dr. Soeradji Tirtoneoro Klaten was mostly happened in stage IV with the amount of 15 patients (41,7%); stage V with 12 patients (33,3%); stage III with 8 patients (22,2%) and the lowest is the patient with kidney failure in stage II with 1 patient (2,8%).

The dosage agreement is calculated based on the value of clirens creatinins of the patients with the chronic renal failure was used formula from Parfati et al., (2003):

$$Do\ (GL) = \frac{Do\ (N)Do\ (N)}{Cl\ (N)\ Cl\ (N)} \times Cl(GL)$$

Information:
Do (N) = Dosage in normal kidney
Do (GL) = Dosage in kidney failure
Cl (N) = Clirens in normal kidney
Cl (GL) = Clirens in kidney failure

Besides that, for the dosage accurateness was used Drug Prescribing in Renal Failure: Dosing Guidelines for Adults, British National Formulary 2009 for some dosage of the given antibiotics. The result of the antibiotic usage that was appropriated in the dosage obtained as 21 cases (47,7%) and the used of antibiotic that was inappropriated in the dosage is 23 cases (52,3%) from total 44 of antibiotic usage.

6. Patient Restitution Status

The result showed the patient restitution status with the total number of 36 cases (100%) in returning home in good condition. The patients were not recorded to back home in recovered condition because chronic renal failure has the characteristic of irreversible or in other word, the condition of the kidney abnormal condition even with medication (Choncol, 2009). But if it is seen from the value of leukocyte amount that related with the success of the medication of antibiotic, the status of patients' restitution (Table 7).

Table 7. Patient's leukocyte counting number

Data (Leukocyte counting number)				
Patient Number	Leukocyte counting number			
	Come		Come Home	
	High	Low	High	Low
1,2,4,5,6, 9,10,11, 12,15,16, 17,20,21, 22,24,26, 27	18	-	-	18
13,18,7	3	-	3	-
3,8,14,19, 23,25,28, 29,30,31, 32,33,34, 35,36	-	15	-	15
Total	36		3	33

From the leukocyte counting number in table 10, there are 33 cases (91,67%) where the leukocyte number is decreasing to normal condition and 3 cases (8,33%) where the leukocyte number unvarying because they did not get antibiotic therapy.

7. Research Limitation

The data taken was based on the medical record data that the writing may be less understandable by the writer so the data obtained was evaluated based on the researcher's comprehension ability.

Conclusion

The antibiotic that is mostly used for the patient with chronic renal failure was sefriakson that was an antibiotic from the group of sefalosporin with the frequency of usage in 17 cases (36,9%). From the investigation of the medical record and the evaluation of the appropriate indication, appropriate patient, appropriate medicine, and appropriate dosage the result showed that the appropriate indication antibiotic usage was 20 cases (55,56%), the patient with chronic renal failure that included in the appropriate patient criteria was 39 cases (97,7%), the used of antibiotic that was in the criteria of appropriate medicine is 13 cases (29,5%), and for the usage of antibiotics that was in appropriate dosage was 23 cases (52,3%). The patient resuscitation status was 36 cases (100%) came home in better condition. From the result of the leukocyte counting number, there are 33 cases (91,67%) where the leukocyte number was decreased to normal condition.

Suggestions

Based on the research, the suggestion can be given are:

The carefulness of the doctors needs to be improved in making prescription for patients. The improving role of pharmacists for the improvement of the health care status related to the medicine usage for the patients. Improvement of the medic apparatus need to be done because in the writing of the medical record data, there are some parts that are difficult to understand.

Reference

Bayer, A., Erler, M., Gerlach, F.M., Haefeli, W.E., Petersen, J.J., Rath, T., Rochon, J., & Saal, K., 2012, *How to Improve Drug Dosing For Patients With Renal Impairment in Primary Care - a Clusterrandomized Controlled Trial,* Jerman, BMC Family Practice, 13:91.

BMJ, 2009, *British Formulari National*, GGP Media GmbH, Possneck, Germany.

BPOM., 2013, Lampiran 3: *Informatorium Obat Nasional Indonesia*, Jakarta, CV Sagung Seto.

Chasani, S., 2008, Antibiotik Nefrotoksik: Penggunaan pada Gangguan Fungsi Ginjal, *Laporan Penelitian,* Semarang: Fakultas Kedokteran, Universitas Diponegoro.

Chonchol, M. & Spiegel, D.M., 2009, *The Patient with Chronic renal failure*, *In*: Schrier, R.W., 6th ed, *Manual of Nephrology*, Philadelphia, Lippincott Williams and Wilkins.

Dipiro, T.J., Matzke, G.R., Posey, L.M., Talbert, R.L., Wells, B.G., & Yee, G.C., 2006, *Pharmacotherapy Handbook,* Sixty Edition, Mc. Graw Hill.

Feldman, C., Brink, A.J., Richard, G.A., Maartens, G., & Bteman, E.D., 2007, *Management of Community-Acquired Pneumonia in Adult,* Afrika, Working Group of the South African Thoracic Society, 97(12)

Gupta, K., Hooton, T.M., Naber, K.G., Wult, B., Colgan, R., Miller, L.G., Moran, G.J., Nicolle, L.E., Razz, R., Schaeffer, A.J., & Soper, D.E., 2011, *International Clinical Partical Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society for Microbiology and Infectious Disease,* Boston, Oxford University Press on behalf of the Infectious Diseases Society of America, 52(5):e103-e120.

Kenward, R. & Tan, C.K., 2003, Penggunaan Obat Pada Gangguan Gagal Ginjal, dalam Aslam Farmasi Klinis: *Menuju Pengobatan Rasional dan Penghargaan Pilihan Pasien 2003*, Jakarta, PT. Elex Media Komputindo Gramedia.

Krejcie, R.V. & Morgan, D.W., 1970, Determining Sample Size for Research Activities. *Educational and Psychological Measurement.*

Kunin, C.M., Glazko, A.J. & Finland, W., 1959, *Persistence Of Antibiotics in Blood of Patients With Acute Renal Failure. II. Chloramphenicol and Its Metabolic Products In The Blood Of Patients With Severe Renal Disease or Hepatic Cirrhosis,* Detroit, Mich, Thorndike Memorial Laboratory, Second and Fourth (Harvard) Medical Services, *Boston City Hospital, and the Department of Medicine, Harvard Medical School*, Boston, Mass., and from the Research Division, Parke, Davis and Company.

Parfati, Budisutio, F.H., & Tan, C.K., 2003, Farmakokinetik Klinis, dalam Aslam Farmasi Klinis: *Menuju Pengobatan Rasional dan Penghargaan Pilihan Pasien 2003*, Jakarta, PT. Elex Media Komputindo Gramedia.

Peraturan Menteri Kesehatan RI nomor: 2406/MENKES/PER/XII/2011, 2011, Pedoman Umum Penggunaan Antibiotik, Jakarta, Menteri Kesehatan Republik Indonesia.

Yulianti, T., Hakim, L. & Putranto, W., 2007, Evaluasi Penggunaan Antibiotik Pada Pasien Gagal Ginjal Kronik di RSUD Dr. Moewardi Surakarta Periode September-November 2007, *Tesis*, Yogyakarta: Fakultas Farmasi Pasca Sarjana,

http://etd.ugm.ac.id/index.php?mod=review&sub=Review&act=view&typ=html&buku_id=38187&obyek_id=4&unitid=1&jenis_id (diakses tanggal 20 September 2014)