EVALUATION OF ANTIBIOTIC DOSE APPROPRIATENESS IN PATIENTS WITH CHRONIC RENAL FAILURE IN HAJI ADAM MALIK HOSPITAL MEDAN ON PERIOD JANUARY – JUNE 2014

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ABSTRACT

Antibiotic is a substance produced by microbes that can inhibit or eradicate other microbes. In patients with chronic renal failure, the adjustment dose of antibiotic based on creatinine clearance. As some antibiotics are mainly excreted through renal, therefore it is necesarry to adjust the dose. One important indicator to reach therapy is the accuracy in giving dose to inhibit the progression of renal disease and to maintain the patient's life quality. The aim of this study was to evaluation of antibiotic dose appropriateness in patients with chronic renal failure in Haji Adam Malik Hospital Medan on period January – June 2014. The method of dose adjustment in patients with renal failure is based on the drug clearance by Cockcroft-Gault equation. There are 82 medical records of patients with chronic renal failure which fits the inclusion criteria and used as a sample. The result showed that the majority of patients with chronic renal failure was at 39 – 48 years old (30,5%) and female (51.2%). Based on the stage, the majority of patients with chronic renal failure was stage 5 (72%), followed by stage 4 (18.3%), stage 3 (8.5%) and stage 2 (1.2%). The most widely antibiotic which used by patients with chronic renal failure was ceftriaxone (59.7%). The dose appropriateness of antibiotic was 93%. There was no difference of dose in patients with chronic renal failure in Haji Adam Malik Hospital Medan on period January – June 2014 based on characteristics of age, sex and stage chronic renal failure.

It can be concluded that the dose of antibiotic use in patients with chronic renal failure on period Januay – June 2014 was appropriated, in accordance with standard treatment recommended by Haji Adam Malik Hospital Medan.

Key words: Dose appropriateness, antibiotic, chronic renal failure

BACKGROUND

Chronic kidney disease is a pathophysiological process with diverse etiologies, can result in a progressive decline in renal function, and generally end up with kidney failure requiring renal replacement therapy which remains, in the form of dialysis or kidney transplantation (Suwitra, 2006). Chronic renal failure (CRF) is one disease that is not contagious and is a state of impaired renal function which is a chronic, progressive and irreversible underway (can not be returned to its original state) (Romauli, 2009).

Criteria for chronic renal disease is kidney damage (renal damage) that occurred more than three months, in the form of structural or functional abnormalities, with or without a decrease in glomerular filtration rate (GFR). Manifestations is pathology and there are signs of renal disorders including abnormalities in the composition of blood or urine or abnormalities in imaging tests (imaging tests) and glomerular filtration rate (GFR) of less than 60 ml / min / 1,73 m2 for 3 months, with or without damage Renal (Suwitra, 2006).

According to Aslam (2003), the signs and symptoms of disease with chronic renal failure (CRF) include nocturia, edema, anemia (iron-resistant, normochromic, normocytic), electrolyte disturbances, hypertension, bone disease (renal osteodystrophy), neurological changes (lethargia example, mental disorder), impaired muscle function (eg, muscle cramps, sore feet) and uraemia (eg, decreased appetite, nausea, vomiting, pruritus). Uraemia (urea in the blood), which illustrates the high levels of blood urea, is often used as another word for renal failure (acute and chronic).

Now, the prevalence of chronic renal failure (CRF) is increasing every year in developing countries. According to the research results Hallan, et al., 2006 states that the prevalence of chronic kidney disorders in the general population of Europe is equal to 10.2%, and

the prevalence of the United States in the amount of 11.5%. Based on data from the United State Renal Data System (USRDS) in 2013 estimated that more than 20 million (or more than 10%) of adults in the United States have chronic kidney disease per year. Cases of kidney disease in the world per year increased by more than 50%. Based on the survey results of Perhimpunan Nefrologi Indonesia (PERNEFRI) showed 12.5% (approximately 25 million people) of the population in Indonesia decreased kidney function (PERNEFRI, 2009). In recent years, patients with kidney failure in Indonesia is relatively high, reaching 300,000 people but not all patients can be treated by the medical staff, the new estimated 25,000 patients who can be treated, meaning that there are more than 80 percent of patients who have not received treatment (Susalit, 2012).

Antibiotics are a group of drugs most commonly used today. Excessive use of antibiotics and is not appropriate in some cases, cause problems antimicrobial resistance. The use of more than one antibiotic for treatment of infection is still a controversial issue today (Aslam, 2003). Antibiotics are substances produced by microbes that may inhibit or eradicate microbes other types. Drugs used to kill microbes, cause infection in humans, must have selective toxicity properties as high as possible. This means that the drug must be very toxic to microbes, but relatively non-toxic to its hospes (Abidin, 2010).

On impaired renal function, a dose of antibiotics adapted to creatinine clearance (creatinine clearance). Dose of medication is very important for a drug with toxic-therapeutic ratio is narrow, or who are suffering from kidney disease. In general with creatinine clearance 40-60 ml / min maintenance dose reduced by 50%. When the creatinine clearance 10-40 ml / min, other than maintenance dose reduced by 50% should also extend the provision doubling the distance and try to avoid drugs that are nephrotoxic. List of antibiotics with the main elimination through the kidneys and require dose adjustment among others: the majority of ß-lactams, aminoglycosides, TMP - SMX, monobactam, ciprofloxacin, levofloxacin, gatifloxacin, gemifloxacin, vancomycin, nitrofurantoin,

Phosphomycin, tetracycline, daptomycin, carbapenem, polymyxin B , colistin, and flucytosine (Ministry of Health, 2011).

In some studies related to the adjustment of drug doses in patients with chronic renal failure, there are several methods to estimate the exact dosage regime for patients with renal impairment. Dose adjustments in patients with renal impairment is based on the patient drug clearance. Two common approaches to pharmacokinetics dose adjustments include methods based on drug clearance and methods based on the elimination half-life (Hassan, et al., 2009).

Application of pharmacokinetics aims to improve the effectiveness of therapy or lowering the side effects and toxicity in patients. Dose adjustments in the form of a decrease in the total maintenance dose is often needed. Changes in dose are often encountered is lowering the dose of the drug or drug delivery interval prolongation, or a combination of both (Shargel and Yu, 1999).

According to Aslam (2003), to select and determine the drug dosage required knowledge of the physiological changes that occur in the elderly, (such as decreased renal function, with the consequent decrease in drug clearance) and the frequency of drug side effects is higher. Therefore, some antibiotics excreted primarily through the kidneys, a dose adjustment is necessary and monitoring of drug levels in serum against certain medications in the elderly. In general, the class of beta-lactam antibiotics have side effects that most rare and lightest.

Based on this background, it is necessary to study to look at the suitability dose of antibiotic use in patients with chronic renal failure are implemented in Haji Adam Malik Hospital.

METHOD
This research was conducted at the General Hospital Haji Adam Malik Medan is located at Jalan Bunga Lau number 17 in November 2014. As for the method, stage, flowcharts, operational definitions, data analysis, and the workings of this study. This study is non experimental and descriptive method design (design) cross-sectional study with

retrospective approach. The study was conducted in Haji Adam Malik Hospital with retrieval and data collection conducted in November 2014 with data collection for six months of observation, ie from January 2014 - June 2014.

Population and Sample
The population in this study were all patients with chronic kidney disease who received antibiotic therapy in Haji Adam Malik Hospital in the period January 2014 - June 2014.

Data Analysis
Data were collected from medical records checked and processed using the program Statistical Product and Service Solutions (SPSS) version 18.0, then presented in tabular form.

RESULTS AND DISCUSSION
This research has been conducted in Haji Adam Malik Hospital in November 2014. The data is taken from the medical records of patients hospitalized with a diagnosis of chronic kidney disease in the period January 2014 - June 2014. Based on the results of the research, found chronic renal failure patients is about 132 people and 82 patients from medical records of patients who met the inclusion criteria data to be used as research subjects.
Based on the characteristics of the age of the subjects of this study, the age range of patients according to the table below.

Table 1 Frequency Distribution Age Chronic Renal Failure Patients In Hospital Haji Adam Malik period January 2014 - June 2014.

Age (years old)	Frequency (Patients Number)	Percentage (%)
19 – 28	3	3,7
29 – 38	12	14,6
39 – 48	25	30,5
49 – 58	22	26,8
59 – 68	13	15,9
≥ 69	7	8,5
Total	82	100

In the above table shows that the age distribution in the age group 39-48 years

amounted to (30.5%) and the lowest age group were in the age group 19-28 years amounted to (3.7%). These results indicate that age group are more likely to suffer CRF at the age group he was around thirteen years younger that are in the age group 39-48 years.

Characteristics Stadium
Descriptions regarding patient demographics were also conducted to determine disease stage chronic renal failure suffered by the patient. Distribution characteristics of CRF stage suffered by the patient can be seen in the table below.

Table 3 Distribution Characteristics Stage Chronic Renal Failure Patients In Hospital Haji Adam Malik period January 2014 - June 2014.

Stadium	LFG (ml/min/1,73 m^2)	Frequency	Percentage (%)
I	>90	-	-
II	60 – 89	1	1,2
III	30 – 59	7	8,5
IV	15 – 29	15	18,3
V	<15	59	72
Total		82	100

Based on the results obtained from the characteristic table stage CRF suffered by patients in the period January 2014 - June 2014 showed that of 82 patients with CRF were using antibiotics, the majority were in stage 5 (72%). The small number of patients hospitalized in conditions of CRF stage 2 and the absence of CRF patients in stage 1 because the condition at an early stage the patient has not felt the complaint (asymptomatic) and the state of the glomerular filtration rate (GFR) was normal or even increased (Suwitra, 2006) , According Sjamsiah (2005), this is because in general the symptoms or clinical manifestations of the disease is the appearance of chronic renal failure is the sudden or gradual, even some that do not cause obvious symptoms early so that the decline in renal function are often not perceived even ignored by patients and only detected after his kidney condition worsened and the more severe clinical manifestations are usually on the condition of late-stage (stage 5).

Use of Antibiotics

Based on the results of the study, of 129 antibiotic use in patients with CRF in Haji Adam Malik Hospital Medan period January 2014 - June 2014, the most widely used antibiotic was ceftriaxone (59.7%), followed by ciprofloxacin (29.5%), meropenem (5.4%), and metronidazole (3.9%). Data details can be found in Table 3.4 below.

Tabel 4 Distribution Use of Antibiotics in Patients with Chronic Renal Failure In Haji Adam Malik Hospital period January 2014 - June 2014.

No	Anibiotic	Frequency	Percentage (%)	P value
1	Cefotaxime	1	0,8	
2	Ceftazidime	1	0,8	
3	Ceftriaxone	77	59,7	
4	Ciprofloxacin	38	29,5	0,000
5	Meropenem	7	5,4	
6	Metronidazole	5	3,9	
	Total	129	100	

Appropriate Dose Antibiotic in Patients with CRF Results dispensing appropriate of antibiotic dosage in patients with CRF can be seen in Table below.

Table 5 appropriate Dose of Antibiotic in Patients with Chronic Renal Failure in Haji Adam Malik Hospital Medan period January 2014 - June 2014.

\appropriate Dose of Antibiotic	Frequeny	Percentage (%)
Appropriate	120	93
Not appropriate	9	7
Total	129	100

In this study showed dose conformity percentage of antibiotic use that from 129 the amount of antibiotics used in patients with CRF in Haji Adam Malik Hospital Medan period January 2014 - June 2014, acquired 120 number of antibiotics (93%) that their use complies with the standards on the treatment recommendations CRF patients, while 9 number of other antibiotics (7%) its use does not comply with the recommended standards.

Results of the dose dispensing appropriate of antibiotic use in patients with CRF based on the characteristics of age, sex, and stage of CRF can be seen in the table below.

Table 6 Appropriate Dispensing Antibiotic Dose in Patients with Chronic Renal Failure in Haji Adam Malik Hospital Medan period January 2014 - June 2014 Based on Characteristics of Age, Gender, And Stadium CRF.

Characteristic		Appropriate Dosage		P Value
		Appropriate (Number of Patients)	Not Appropriate (Number of Patients)	
Age	19 – 28	3	0	
	29 – 38	11	1	
	Group 39 – 48	24	1	0,806
	(Years Old) 49 – 58	19	3	
	59 – 68	11	2	
	69 – 79	6	1	
Sex	Female	36	6	0,157
	Male	38	2	
Stadium	II	1	0	
	III	7	0	0,327
	IV	15	0	
	V	51	8	

Based on the research that has been written in the table above can be seen that the characteristics of age, almost every age group there is a dose of antibiotics is not appropriate where the largest number were in the age group 49-58 years (3 people), then in the age group 59 - 68 years (2), at any other age group only one person, and only in the age group 19-28 years who did not have dosing of antibiotics are not appropriate.

On the characteristics of gender shows that female gender who have suffered the greatest number of nonconformities dose antibiotic use as many as six people. Then on the characteristics of the patient's CRF stage, it can be seen that only on stage 5, which has a discrepancy dose antibiotic use as many as 8 people. Stage 5 is the stage with the state of renal function has worsened and the patient began to experience symptoms severe enough because the kidneys are no longer able to maintain fluid and electrolyte homeostasis in the body, and therefore are expected to pay more attention to the dosing of antibiotics and also drug- Other medicines will be given so as not to worsen the patient's condition.

In Table 6 shows that there are 8 people CRF patients who experienced a number of mismatches dose of antibiotic use in accordance with the recommended dose, while in table 3.5, there are 9 number of antibiotics whose use is not in accordance with the recommended dose. The difference is because

there is a discrepancy figures panggunaan doses of antibiotics for 2 number of antibiotics that are given to a patient. In the seven other patients who had mismatches dose, each patient experienced a dose discrepancy antibiotic use antibiotics only for one number so that when added together it will remain there nine the number of antibiotics whose use is not in accordance with the recommended dose.

CONCLUSIONS

The percentage of the most widely used antibiotics in patients with chronic renal failure is ceftriaxone (59.7%), followed by ciprofloxacin (29.5%) and meropenem (5.4%). Analysis of the data showed that there are significant differences in the types of antibiotics that are used in patients with chronic renal failure in Haji Adam Malik Hospital Medan period January 2014 - June 2014. The level of dose conformity in the use of antibiotics are used in patients with chronic renal failure in Haji Adam Malik Hospital Medan the period January 2014 - June 2014 has been good, a total of 120 the number of antibiotics (93%) dose use has been in accordance with the recommended standard treatment guidelines based on the analysis of data and there is no difference suitability dose use of antibiotics in patients with chronic renal failure in Haji Adam Malik Hospital Medan the period January 2014 - June 2014 based on the characteristics of age, sex and stage of chronic renal failure.

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