PATTERN OF ANTIBIOTICS USE IN ADULT PATIENTS WITH URINARY TRACT INFECTION (UTI)

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Abstract: Introduction: Urinary tract infection (UTI) is an infectious disease caused by the growth and proliferation of bacteria in the urinary tract, including infections in the bladder to the renal parenchyma with a certain number of bacteria in the urine*. The use of antibiotics is therapy that commonly used to treat infectious diseases caused by bacteria. Irrational use of antibiotics can lead to bacterial resistance and toxicity. Objective: To determine the rationality of using antibiotics in adult patients with a urinary tract infection (UTI) in the X Hospital Yogyakarta from January-December 2017.Methods: This study is a non-experimental study with a descriptive observational study design and retrospective data collection. The sample of this study was inpatients with a diagnosis of urinary tract infection (UTI) and was recorded in the Medical Record X Hospital Yogyakarta for the period January-December 2017 which was included in the inclusion criteria. Results: Medical records that were included in the inclusion criteria were 61. The single most widely used antibiotic was ceftriaxone in 25 cases (44.64%) and the most widely used combination antibiotic was ceftazidime + levofloxacin in 2 cases (40%). The use of antibiotics with the right indication was 61 patients (100%), the right type was 61 patients (100%), the correct duration was 54 patients (88.52%), the right dose was 61 patients (100%), the right interval was 60 patients (98.36%) and the right route of administration was 61 patients (100%).*

Keywords: *Urinary tract infection, antibiotic, rational*

INTRODUCTION

Urinary tract infection (UTI) is the second most common infectious disease after respiratory infection and it is reported that UTI occurs in 8.3 million cases per year.[1] UTI in society increases with age. Based on a survey in a United States hospital showed that the death caused by UTI is estimated to be more than 13,000 (2.3% mortality rate). Young people less than 40 years have a prevalence of 3.2%, while those over 65 years old are 20%.[2]

The prevalence of UTI in Indonesia is quite high. According to data from the Ministry of Health of the Republic of Indonesia in 2014 in Indonesia, it shows that the number of UTI sufferers reaches 90-100 cases per 100,000 population per year.[3] Antibiotic resistance to bacteria can have consequences that can be fatal. Infectious diseases caused by failure to respond to treatment can lead to prolonged illness, an increased risk of death and an extended length of stay.[4] Resistance with first-line antibiotics to treatment infectious diseases, second or third-line antibiotics must be used, which are more expensive and sometimes more toxic.[5]

The relatively high and unwise prescription of antibiotics in Indonesia has resulted in an increased incidence of resistance. Various studies have shown that there are already resistant microbes, including Methicillin Resistant *Staphylococcus Aureus* (MRSA), multi-drug resistance in tuberculosis (MDR TB) and others. The impact of antibiotic resistance is in the form of increased morbidity, mortality and health costs.[6]

The increased prevalence of UTIs and irrational use of antibiotics prompted to research on the evaluation of antibiotic use patterns in inpatient UTI in X Hospital Yogyakarta from January - December 2017.

RESEARCH METHOD

This is a non-experimental study with a descriptive observational study design and retrospective data collection without any intervention to the patient. This research was carried out at the X Hospital Yogyakarta Medical Record Installation in February-March 2019.

Sampling was done by using purposive sampling technique in inpatients suffering from UTI with aged criteria between 16-65 years, receiving antibiotic therapy, and having completed treatment.

RESULT AND DISCUSSION

Based on medical record, there were 107 patients diagnosed UTI, but just 61 patients fulfill the inclusion criteria. In this study, there were differences in the sex distribution of UTI patients, which showed that women had more UTI than men.

Table 1. Characteristics based on genders

Gender	Amount	Percentage (%)
Female	50	81,97
Male	11	18,03

The results of this study are in accordance to previous study that there are more female UTI patients than men. Women are five times more likely to suffer UTIs than men due to differences in the anatomical arrangement of the urinary tract between women and men.[7,8]

Based on the study sample, the age group 51-65 years is the age group most diagnosed with UTI, while the ages of 31-40 and 41-50 years are the age group diagnosed with UTI the least. The number and percentage can be seen in table 2.

Table 2. Characteristics by Age

Age (year)	Amount	Percentage (%)
16-30	21	34,43
31-40	8	13,11
41-50	8	13,11
51-65	24	39,34

The highest number of patients in group 51-65 years was 24 patients

(39.34%) and in the 16-30 year was 21 patients (34.43%), these results indicate that adults are at risk of suffering from UTI. This is in accordance with the research that UTI occur mostly in adulthood between 19-65 years.[10] This may be due to more active sexual relations and decreased function of the urinary tract organs at the age of more than 60 years.[11] Patients more than 50 years old, may be due to a process of deterioration in urinary tract function and an enlarged prostate in men.[12] The prevalence of UTI will increase in the elderly because increase in bacteriuria levels from 5-10% at the age of 70 years to 20% at the age of 80 years, this is due to a decrease in the body's immune system.[13]

The most common clinical manifestation of UTI was fever 37 (60.66%), followed by nausea 36 (59.02%) and vomiting 35 (57.38%), the patient's clinical symptoms can be seen in table 3.

Table 3. Clinical Manifestation

Clinical manifestation	Amount	Percentage (%)
Fever	37	60,66
Headache	2	3,28
Nausea	36	59,02
Vomiting	35	57,38
Epigastric pain	20	32,79
Suprapubic pain	23	37,70
Back pain	6	9,84
Dizzy	23	37,70
Dysuria	10	16,39
Weak	14	22,95
Loss of consciousness	1	1,64
Cold sweat	4	6,56
Urinary retention	3	4,92
Shivering	1	1,64

Fever is the most frequent manifestation of UTI patients was fever followed by nausea, lower abdominal pain (suprapubic) and vomiting which specific symptom to a UTI. Upper UTI clinical symptoms usually back pain, nausea, vomiting and fever. Meanwhile, the clinical symptoms of lower UTI include lower abdominal pain, pain when urinating (dysuria) and frequent urination at night (nocturia).[10,14] Symptoms rarely found in this study were chills, decreased consciousness, headache, urinary retention and cold sweats.

Antibiotics used are from the fluoroquinolone / quinolone group (ciprofloxacin and levofloxacin), the aminoglycoside group (gentamicin), the second-generation cephalosporin group (cefuroxime), the third-generation cephalosporin (cefotaxime, ceftriaxone) and the cephalosporin group one patient). The single most widely used antibiotic therapy was ceftriaxone 25 (44.64%). The most widely used combination antibiotic therapy is ceftazidime + levofloxacin 2 (40%). The antibiotics used, both single and combined therapy can be seen in tables 4 and 5.

Table 4. Distribution of single therapeutic use of antibiotics

Antibiotic	Amount	Percentage (%)
Fluoroquinolone/quinolone		
Ciprofloxacin	9	16,07
Levofloxacin	4	7,14
Aminoglycoside		
Gentamicin	1	1,79
Second-generation cephalosporin		
Cefuroxime	1	1,79
Third-generation cephalosporin		
Cefotaxime	7	12,50
Ceftriaxone	25	44,64
Ceftazidime	8	14,29
Cefixime	1	1,79

Table 5. Distribution of combination therapeutic use of antibiotics

Antibiotic	Amount	Percentage (%)
Ceftazidime + levofloxacin	2	40
Ceftriaxone + clindamycin	1	20
Cefotaxime + levofloxacin	1	20
Levofloxacin + ceftriaxone	1	20

The use of antibiotics in all UTI patients in this study were from the fluoroquinolone / quinolone group (ciprofloxacin, levofloxacin and ofloxacin), the aminoglycoside group (gentamicin), the second-generation cephalosporin (cefuroxime), and the third-generation cephalosporin (cefazidaxone) group. cefixime) as initial empirical therapy in accordance with the recommendations of the 2015 Guidelines on Urological Infections of the European Association of Urology (EAU) and the 2015 Guideline for Management of Urinary Tract and Genitalia. However, in the condition of seriously ill patients, delaying antibiotic therapy can have a negative impact, the absence of symptoms is used to diagnose bacteria that cause UTI so that early empirical therapy must be carried out immediately.[15] In general, all samples in this study received initial empirical antibiotic therapy parenterally intravenously (IV). Based on the Summary of the UAA-AAUS Guidelines for Urinary Tract Infections from the 2018 International Journal of Urology, non-complicated acute pyelonephritis patients who have risk factors such as dehydration, anorexia and diabetes can be given parenteral initial empirical antibiotic therapy. In addition, according to the 2015 Guidelines on Urological Infections of the European Association of Urology (EAU) in patients with a diagnosis of severe pyelonephritis who cannot take medication orally because of systemic symptoms, namely nausea and vomiting, parenteral antibiotics can be treated, and if the patient's condition improves, can be replaced with oral antibiotic therapy.[18]

In this study, there were 5 patients who received antibiotic combination therapy. The use of single injection antibiotic combination therapy with oral antibiotics in cases of UTI can be given when the patient first arrives. In addition, antibiotic combination therapy is recommended to be given to patients with severe pyelonephritis or those accompanied by urosepsis, severe sepsis and septic shock.[14] In this study there were 3 patients who received replacement for antibiotic therapy, namely ceftriaxone IV (intravenous) (class III cephalosporins)

replaced with oral cefixime (class III cephalosporins), cefotaxime IV (generation III cephalosporins) replaced with levofloxacin IV (fluoroquinolones / groups). quinolones) and ceftriaxone IV (class III cephalosporins) were replaced with levofloxacin IV (fluoroquinolones / quinolones). Replacement of these antibiotics is in accordance with the recommendations of the 2015 Guidelines on Urological Infections from the European Association of Urology (EAU) and the 2015 Guideline for Management of Urinary Tract and Genitalia Infections. these antibiotics. This is in accordance with the research which shows that ceftriaxone has been resistant to *Escherichia Coli* (66.6%), *Pseudomonas sp* (100%) and *Enterococcus sp* (100%). The three bacteria enter into microorganisms most often as a cause of UTI. Ceftriaxone replacement may also be caused by side effects of antibiotics and hypersensitivity reactions to antibiotics.[1,7]

In table 6 below, we can see the distribution of the accuracy of the duration or duration of antibiotic administration which has been adjusted to the Guidelines on Urological Infections of the European Association of Urology (EAU) 2015.[17]

Table 6. Distribution of the accuracy of antibiotics duration

Antibiotics duration	Amount	Percentage (%)
Shorter duration	5	8,20
Right duration	54	88,52
Longer duration	2	3,28

In this study, the shortest antibiotic therapy used was 1 day and the longest was 29 days. The administration of antibiotics with the right duration was 54 (88.52%), the shorter duration was 5 (8.20%) and the longer duration was 2 (3.28%). The length of hospitalization for UTI patients in this study was at most 3 to 4 days. Based on the 2015 Guidelines on Urological Infections from the European Association of Urology (EAU) and the 2015 Guideline for the Management of Urinary Tract and Genitalia, the duration is only for therapy in non-complicated acute cystitis, which is between 3-5 days, whereas in some patients with clinical manifestations including mild, moderate and severe non-complicated acute pyelonephritis as well as complicated UTI required therapy between 7-14 days to 21 days. So, in this study the evaluation of antibiotic administration was carried out by considering the suitability of the duration between the antibiotics obtained during hospitalization and the antibiotics that were taken home.

The evaluation of the accuracy of antibiotic doses in this study was adjusted to the 2015 Guidelines on Urological Infections from the European Association of Urology (EAU) and the reference dose for adult patients with a diagnosis of UTI as well as the general dosage in the Drug Information Handbook 22nd. In switching to antibiotics, the dose evaluated is a single therapeutic dose of each antibiotic.[18,19]

Table 7. Distribution of the accuracy Antibiotics dose

Antibiotics Duration	Amount	Percentage (%)
Shorter duration	5	8,20
Right duration	54	88,52
Longer duration	2	3,28

In this study all antibiotics given to patients were given the correct dosage, which was 61 (100%). The success of antibiotic therapy depends on 2 patterns, time dependent killing when the blood antibiotic level is maintained long enough to be above the minimum inhibitory concentration (MIC) and concentration dependent killing to kill bacteria if the antibiotic concentration is above the bacterial MIC. Antibiotic levels must be adequate and the dose given must be appropriate that reaches the MIC in blood or body fluids and able to reach the source of infection to effectively eradicate the invading microorganisms.[19, 20, 21]

The effect of therapy is depending on the dose of antibiotics was given. Giving too high dose can increase the risk of side effects, while an inadequate dose of antibiotics cannot guarantee the achievement of the expected therapeutic levels.[6]

Antibiotic administration needs to be monitored to see whether the antibiotics used have reached therapeutic levels or not during the treatment process.[23]

Evaluation of the accuracy of the antibiotic administration interval based on the 2015 Guidelines on Urological Infections from the European Association of Urology (EAU) and the Drug Information Handbook 22nd (APhA, 2013). The distribution of the accuracy of the antibiotic administration interval can be seen in Table 8.

Table 8. Distribution of accuracy antibiotic interval

Interval	Amount	Percentage (%)
Less	0	0
Right	60	98,36
More	1	1,64

Administration of antibiotics at inappropriate intervals can interfere with the pharmacodynamics of antibiotics and can cause an increased risk of antibiotic resistance.6 This needs to be considered to prevent fewer antibiotic levels in the blood than therapeutic levels, which can cause bacteria to regenerate and become resistant to antibiotic therapy used.[24]

Evaluation of the accuracy of the route of antibiotic administration in this study was adjusted to the reference to the Guidelines on Urological Infections from the European Association of Urology (EAU) 2015 and Drug Information Handbook 22nd (APhA, 2013). In this study, the route of antibiotic administration was 100% correct.

According to references in the Drug Information Handbook 22nd (APhA, 2013), antibiotics of the type of ciprofloxacin, levofloxacin, cefuroxime, clindamycin and azithromycin can be given intravenously or orally. Antibiotics gentamicin, cefotaxime, ceftriaxone and ceftazidime are only given intravenously. While cefixime is given only orally.[18,25]

Oral antibiotics should be the first choice in infection therapy, but for moderate to severe or severe infections, parenteral administration of antibiotics can be considered. When the patient is allowed to go home, the parenteral antibiotics given are replaced by oral ones because the patient's condition allows them to be given orally.[6]

CONCLUSSION

The use of antibiotics with the right indication was 61 patients (100%), the right type was 61 patients (100%), the correct duration of administration was 54 patients (88.52%), the right dose was 61 patients (100%), the right interval of administration was 60 patients (98.36%) and the right route of administration were 61 patients (100%). Based on the pattern of antibiotic use, the rational use of antibiotics has been made to help prevent antibiotic use resistance.

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