

A Review: Rational Drug Use of Antibiotics in Patients With Urinary Tract Infection At Hospitals In Indonesia

Sintiya Regimulya¹, Sri Oktavia^{1*}, Widya Kardela¹

¹(Department of Pharmacology and Clinical Pharmacy, School of Pharmaceutical Science (STIFARM) Padang, Raya Siteba street, Kurao Pagang, Padang, Indonesia, 25147)

Received 29 January 2021; Accepted 13 February 2021

Abstract:

Background: The rational drug use of antibiotics will provide antibiotic therapy optimization. The effectiveness of using antibiotics will play an important role in the treatment of Urinary Tract Infections (UTIs). Antibiotics used for UTI therapy include cephalosporin and quinylone antibiotics. The purpose of this literature study is to summarize the results of the research on the rational use of antibiotics in urinary tract infection (UTI) patients according to the research parameters as follows: the appropriate indications, drug selection, dose selection, patient, and duration of drug administration.

Results: Therefore, it can be concluded that the appropriate percentage of the indication from the eight articles is 99.35%. The percentage of appropriate drug selection from data from eight articles is 82.68%. The percentage of the appropriate dose administration data from the nine articles obtained is 67.78%. And the percentage of the appropriate duration of the administration of the five articles is 53.18%. From the results of this percentage, it can be seen that not all hospitals have determined the rational use of antibiotics.

Methods: Literature searches were carried out on computerized databases such as ScienceDirect, PubMed, Semantic Scholar and Google Scholar. The inclusion criteria for selected articles were prospective data, data regarding the rational drug use, and research that is conducted in Indonesia.

Keywords: Rational Use of Drug, Antibiotics, Urinary Tract Infection (UTI)

I. INTRODUCTION

Drug use is said to be rational if a patient receives a drug that suits his/her needs, for an adequate period of time and at the cheapest price for the patient and society [1]. Rational drug selection is the key to quality health services, especially in the use of antibiotics, irrational use of antibiotics will have a negative impact, one of which is the increasing incidence of bacterial resistance to antibiotics [2]. This is in accordance with the statement of the World Health Organization (WHO) Global Strategy, which stated that the rational use of antibiotics is the use of antibiotics that are cost effective with increasing clinical therapeutic effects, minimizing drug toxicity and minimizing the occurrence of resistance [3].

Antibiotics are chemical substances produced by fungi and bacteria that have deadly properties or inhibit the growth of germs, while their toxicity in humans is relatively small. The antibiotic that was first discovered by Alexander Fleming in 1929, penicillin, came from the *Penicillium notatum* fungus, penicillin is classified as a beta-lactam antibiotic because it is characterized by a beta-lactam ring in its chemical structure that plays an important role in the biological activity of this compound. Until now it is still the most reliable drug in the handling of cases of infectious diseases [4]. When a type of antibiotic no longer has an effect on certain types of bacteria, the bacteria is said to be antibiotic resistant. Bacteria or germs will become resistant to the drug if the germs change some of the ways to protect themselves against the effects of the drug or make the drug become inactive (neutralize the action of the drug) [5].

Infectious disease is a health condition that is often found in every hospital and doctor's practice, especially in developing countries [6]. The most reliable drugs to overcome this problem are antimicrobials, including antibacterial / antibiotic, antifungal, antiviral, and antiprotozoal [7]. Antibiotics can be found in various preparations, and their use can be via topical, oral, or intravenous routes [8]. Some of the ideal properties of the antibiotics chosen for the treatment of urinary tract infections are that they are well absorbed, well tolerated by patients, and have a wide spectrum of known or suspected microbes [9]. Studying the patterns of antibiotic use is fundamental in the design of direct interventions both regionally and locally in the optimization of rational drug use [10].

Urinary Tract Infection (UTI) is defined as the presence of microorganisms in the urinary tract that result in contamination of the urinary tract. Organisms have the potential to invade the tissues of the urinary tract and adjacent structures [11]. According to Torpy, women are more prone to UTIs than men around 50-

60%, and 10% of postmenopausal women also experience UTIs with a frequency of once a year [12]. Imaniah also stated that women had a higher rate of UTI by 57.41% than men (42.59%) in Dr. Moewardi Hospital in 2014 [13]. The causes of UTI from Gram negative bacteria were *Escherichia coli* (48.44%), *Klebsiella pneumonia* (17.19%), *Acinetobacter baumannii* (14.07%), *Proteus mirabilis* (6.25%), *Stenotrophomonas maltophilia* (3.13%), and *Pseudomonas aeruginosa* (3.13%) while Gram positive bacteria were *Enterococcus faecalis* (4.69%), and *Staphylococcus haemolyticus* (3.13%) [14]. Chitrangingtyas also stated that the highest bacterial cause of UTI was *Escherichia coli* [15].

This review article aims to summarize the results of the research on the rationality of using antibiotics in urinary tract infection (UTI) patients according to the research parameters as follows: the appropriate indications, drug selection, dose selection, patient, and duration of drug administration.

Methods

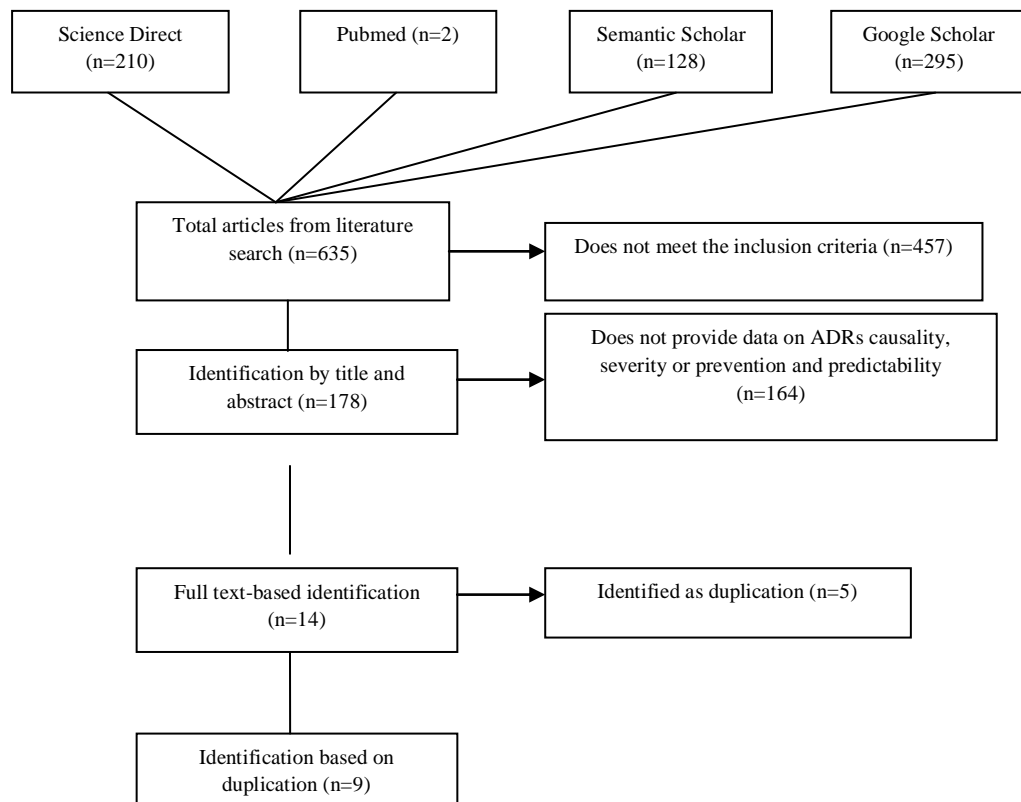
In compiling this review article, the technique used was the literature study method. Also, in making this review article the data used were searched via online media with the keywords as follows: "Rationality of Drug Use" "Antibiotics" "Urinary Tract Infection (UTI)". The main references used in this review article were searched through trusted websites such as Science Direct, PubMed, Semantic Scholar, Google Scholar, and other trusted journals. The literature used as material for scientific data was articles with a publication span of years from 2010-2020. Data extraction was carried out in October-December 2020.

The inclusion criteria for the selected articles were research articles containing the keywords used, articles that assessed drug rationality with research parameters as follows: the appropriate indications, drug selection, dose selection, patient, and duration of drug administration from prospective data. Research that discussed the use of antibiotics in Urinary Tract Infection (UTI) patients and articles published in the last ten years. The data collected in the article that discussed the rationality of this drug are in the form of sociodemographic data and rationality.

II. RESULT

The initial search returned 635 articles in both national and international searches (Fig. 1). After identifying the title and abstract, it was found that 457 articles did not meet the intended criteria. The remaining 178 articles were identified by studying the full text and it was found that 164 articles did not meet the required criteria, namely not presenting rationality data with research parameters as follows: the appropriate indications, drug selection, dose selection, patient, and duration of drug administration. 14 articles that met the inclusion criteria, but 5 of them were the same article. Finally, 9 articles were included in the literature study.

Figure 1. Flow chart of the literature search



The nine articles analyzed a prospective observational studies. These nine articles discussed the rationale for using antibiotics in Urinary Tract Infections (UTIs). These nine articles stated that women have a higher rate of UTIs than men. Of the 57 data studied, 17 patients (29.8%) were male and 40 patients (70.2%) were female [16]. Of the 87 cases treated at Samarinda Medika Citra Hospital (SMC) as many as 20.69% or 18 cases were experienced by male patients and 79.31% or 69 cases experienced by female patients [17]. Of the 60 cases of patients treated at the Klaten Hospital in the January-March period there were 49 female patients and 11 male patients [18]. Of the 62 cases studied 41 (66.2%) were female patients and 21 (33.8%) male patients [19]. Of the 47 cases in the inpatient installation of Prof. dr. RD Kandou Manado Hospital for the period July 2013 - June 2014, it was known that there were 10 (21.3%) male sufferers while 37 (78.7%) female sufferers. Female patients were more than male patients with a total percentage for female patients of 65.27, and male patients were 34.72 [20]. The incidence of urinary tract infections in this study occurred mostly in female patients, as many as 24 patients (60%) [21]. Statistics showed that 20-30% of women will experience recurrent urinary tract infections at some time in their life, whereas in men it often occurs after the age of 50 years and over [24].

Table 1. Summary of articles reviewed

Reference	Number of Patients M / F	Age (Years)	Study Rationality (%)				Appropriate Patients
			Appropriate Indication	Appropriate Drug	Appropriate Dosage	Appropriate Duration of Administration	
16	57	Male 18-31: 7 32-45: 5 46-60: 5 Female 18-44: 29 45-60: 11 Total 17 male and 40 female	96.5%	66.7%	53%	49.4%	-
17	87	-	100%	95.4%	100%	94.25%	-
18	60	-	98.3%	68.33%	85%	-	100%
19	62	-	100%	79%	67.7%	-	100%
20	42	18-25: 6 26-35: 10 36-45: 10 46-55: 18 56-59: 3	-	-	89.4%	27.7%	-
21	195	-	100%	98.97%	86.15%	83.08 %%	-
22	72	18-25: 11 26- 35: 11 36-45: 16 46-55: 19 56-64: 15	100%	96.5%	27.63%	-	100%
23	40	Male 19-64: 12 ≥ 65: 4 Female 19-64: 20 ≥ 65: 4	100%	90%	17.5%	-	100%
24	78	-	100%	66.6%	83.3%	11.5%	100%

From several articles reviewed, it was explained that the most commonly prescribed antibiotic is ceftriaxone [16,17,19,21,22,24]. Ceftriaxone is a group of 3rd generation cephalosporin antibiotics that have a broad spectrum [22]. The most widely used class of antibiotics was the second-generation fluoroquinolone (ciprofloxacin) with 32 patients (80%) and the 3rd generation cephalosporin (ceftriaxone) in 12 patients (30%) [23]. Cephalosporins are widely used in the treatment of urinary tract infections because they are the drug of choice for urinary tract infections [11].

III. DISCUSSION

Drug use is said to be rational if it meets the following criteria: Appropriate diagnosis, that is, drug use must be based on establishing a proper diagnosis. Appropriate indication, that is, the patient is given the drug with the appropriate indication according to the doctor's diagnosis. Each drug has a specific therapeutic spectrum. Appropriate drug, that is, based on the correct doctor's diagnosis, the appropriate drug selection must be made. Selection of the appropriate drug can be weighed from the accuracy of the class of therapy and the type of drug according to the diagnosis. Appropriate patient is the drug to be used by the patient considering the individual condition concerned. Appropriate dosage, namely the dose of the drug used must be within the range

of drug therapy. The appropriate method and duration of administration, namely the appropriate way of giving, must consider the safety and condition of the patient. This will also affect the dosage form and timing of drug administration. The appropriate price, namely the use of drugs without clear indications or for situations that do not require drug therapy at all is wasteful and very burdensome for patients, including expensive prescription drugs. Beware of side effects, namely being aware of the side effects of drug administration that have the potential to cause side effects, namely unwanted effects that arise when administering drugs at therapeutic doses. Drugs that must be given must be effective and safe. Appropriate information, namely information about drugs that must be taken or used by the patient will greatly affect patient adherence and the success of treatment. Appropriate follow-up is when deciding on therapy, patients should have considered the necessary procedures. Appropriate delivery of drugs (dispensing), namely rational drug use, also involves dispensers as drug providers and patients themselves as consumers [1].

The literature review results from 9 articles showed that the number of female urinary tract infection (UTI) patients was higher than that of males. This is in line with the literature which stated that urinary tract infections are more common in women than in men. If it often occurs in men, there is an underlying abnormality in the renal tract [25]. The cause of UTI often occurs in women because the female urethra is shorter so that it is easier for external microorganisms to reach the bladder which is located close to the perianal area [26]. If classified in terms of age, the largest incidence of UTIs was at the age of 17-45 years with female sex. This increase in incidence is associated with increased sexual activity in women of reproductive age [22]. Other literature stated that the prevalence of UTIs should be greater in postmenopausal women because the production of the hormone estrogen decreases which causes the pH of the vaginal fluid to rise, leading to an increase in the development of microorganisms in the vagina [16]. However, in some of these studies, the incidence of young women had a higher incidence because young age was often triggered by factors of intimate organ hygiene, sexual intercourse, and the use of contraception or spermicide gel could increase the risk of UTIs.

The use of antibiotics is the main choice in the treatment of urinary tract infections [17]. Antibiotic treatment is the most widely used treatment, in developing countries 30-80% of people with infections admitted to hospital receive antibiotics [18]. From this percentage, 20-65% of its use is considered inappropriate. Improper use of antibiotics can lead to resistance problems and undesirable drug effects [27]. The most widely used antibiotics for the treatment of UTIs in adult patients are broad spectrum antibiotics including the cephalosporins and quinolones [19].

From the literature review, 9 antibiotic classes and 18 antibiotics were prescribed. The profile of the type and class of antibiotics given during therapy was divided into 535 cases of single antibiotic use (**Table II**), 28 cases of combined antibiotic use (**Table III**).

Table II. Antibiotics Monotherapy

Antibiotics		Number	Percentage
Drug Class	Monotherapy		
Cephalosporin	Ceftriaxone	229	42%
	Cefoperazon	14	2.6%
	Cefotaxime	28	5.3%
	Cefadroxil	8	1.5%
	Cefixime	23	4.3%
	Tricefin	1	0.2%
Quinolones	Ciprofloxacin	158	30%
	Levofloxacin	52	9.7%
Penicillin	Ampicillin	4	0.74%
	Amoxicillin	6	1.3%
Aminoglycosides	Gentamicin	1	0.2%
	Amikacin	2	0.4%
	Kanamycin	1	0.2%
	Clindamycin	1	0.2%
Sulfonamide	Cotrimoxazole	6	1.3%
	Total	535	100%

Table III. Combined Antibiotics

Antibiotics		Total	Percentage of
Drug Class	Types of		
Combination of Cephalosporin and Penicillin	Cefoperazone-Sulbactam	7	25%
B-lactam and as. Clavulanate	Co-amoxiclav	1	3.6%
Penicillin and B-lactam	Pycin	2	7.2%
	Vicillin SX	13	46.4%

Cephalosporin and B-lactam Inhibitor	Cefoperazone + Sulbactam	5	17.9%
	Total	28	100%

Antibiotic monotherapy was predominantly used in 9 review articles, the cephalosporin group was ceftriaxone in 229 (42%) cases, then the quinolone group, namely ciprofloxacin, in 158 (30%) cases. Ciprofloxacin is a fluoroquinolone class of antibiotics which works by inhibiting the action of *DNA gyrase* during the growth and reproduction process of bacteria [27]. The most dominant combination antibiotics used were the penicillin and B-lactam groups, namely *Vicillin SX* in 13 (46.4%) cases.

The use of antibiotics in this review article is in accordance with the guidelines which explained that cephalosporin class antibiotics are the main alternative as a treatment for UTI [25]. Other literature suggested that UTIs can be treated most effectively with short-term (3 days) therapy using trimethoprim-sulfamethoxazole or fluoroquinolone antibiotics [1].

Evaluation of Rationality

1. Appropriate Indication

In the research of Aldy Wijaya *et al* in the inpatient installation of Undata Palu Hospital in 2012 with a total of 57 cases. The research data showed that 96.5% of patients received the appropriate therapy as indicated, and 3.5% received inappropriate therapy. As many as 3.5% of patients received drug therapy that was not properly indicated because they did not receive the antibiotics that should be given to patients with a diagnosis of bacterial infection [17]. Then it was found that 1 prescription with a percentage of 1.66% of the total 60 prescriptions was not properly indicated because the doctor's prescription was not suitable for patients in which the patient was not infected [18]. Other 6 studies stated that 100% of antibiotic use was given with the appropriate indication.

Each drug has a specific spectrum of therapy, for example, antibiotics. The use of drugs according to the indication must be in accordance with the existing symptoms and diagnosis. Antibiotics are indicated for bacterial infections; thus, the administration of this drug is only recommended for patients who have symptoms of a bacterial infection. Signs and symptoms of a bacterial infection in a patient can be seen by means of a laboratory examination with a urine sample, which could show leukosuria, hematuria, positive for nitrite and bacteria that would mean that the patient is infected with bacteria in the urinary tract area [17].

2. Appropriate Patient

Appropriate patient is a drug delivery therapy that is not contraindicated and in accordance with the patient's condition [22]. In this review article, all patient data were appropriately obtained as all patients did not have hypersensitivity to the antibiotics given. Evaluation of patient accuracy also considers the patient's condition such as renal function, namely by looking at the value of *ClCr* and liver function by looking at the value of serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) [22].

The normal creatinine clearance value, calculated by the Jelliffe formula, is ≥ 90 ml / minute. This renal function test is useful in determining the accuracy of antibiotic administration in patients diagnosed with urinary tract infections [23].

3. Appropriate drug selection

Appropriate drug is a drug therapy given according to drug of choice in patients diagnosed with Urinary Tract Infection (UTI). Drug accuracy was evaluated based on the suitability of drug administration with reference to Clinical Practice Guidelines (PPK) and Guideline on Urological Infection [28].

In the research of Aldy Wijaya *et al* in the inpatient installation of Undata Hospital, Palu in 2012, with a total of 57 cases. The results showed that 66.7% of the choice of antibiotic type and class of antibiotics in UTI patients was appropriate and 33.3% had the inappropriate drug [16]. In the second study, the results were 95% or 83 cases, it was stated that the drug selection was appropriate and the drug selection was inappropriate in 4.60% or 4 cases. It is said to be inappropriate because in the 4 cases given ceftriaxone injection and stabactam injection which is a combination of sulbactam Na and cefoperazone Na, this is not in accordance with the guidelines used. [17]. Then in the next study, it was found that 19 prescriptions were 31.66% of the total 60 prescriptions said to be inappropriate in drug selection and 68.33% stated that the drug selection was appropriate [18]. It was known that as many as 13 prescriptions, namely 21% of the total 62 prescriptions, were considered inappropriate drugs [19]. In this study, there were 2 patients (1.03%) who did not receive therapy with the appropriate choice of antibiotics for urinary tract infections, and 193 patients (98.97) were declared the appropriate choice of antibiotics [21]. The next article found the accuracy of the drug was 96.05%, with the appropriate result of the drug being 3.95%. Drug inaccuracy occurs in the selection of definitive antibiotics,

where patients with *E. coli* and *Staphylococcus aureus* cultures received antibiotics that did not match their culture results [22]. The results of using antibiotics in urinary tract infection patients were 36 patients (90%) had the appropriate drug according to the drug of choice and 4 patients (10%) had the inappropriate drug because ceftriaxone was not the drug of choice in patients with lower urinary tract infections [23]. In the next article, we can see that as many as 66.66% of antibiotic prescriptions were appropriate for drugs and 33.34% of antibiotic prescriptions were not appropriate drugs for UTI patients in the inpatient installation of "X" Klaten Hospital during 2012 [24].

From this journal review, it was found that the overall accuracy of the drug was 82.68% with the most widely used type of antibiotic, ceftriaxon with 229 (42%) cases. Ceftriaxone is a group of 3rd generation cephalosporin antibiotics that have a broad spectrum [22].

In the review, it is known that one of the reasons for the inaccuracy of the drug is the use of vicillin SX for adult patients, the indication and the dose given to UTI patients were not listed in the literature thus they could not be compared [19]. Then the UTI patients at X Klaten Hospital, it was found that the inaccuracy of the drug was due to the selection of definitive antibiotics, where the patients were cultured with *E. Coli.* and *Staphylococcus aureus* bacteria received antibiotics that were incompatible with culture results [22]. The drug of choice for *E. Coli* bacteria is the fluoroquinolone and *Staphylococcus aureus* bacteria is trimethoprim-sulfamethoxazole [28] whereas in patients infected with *E. coli* and *Staphylococcus aureus* bacteria received the antibiotic ceftriaxone and thus became an inappropriate drug [22].

4. Appropriate dosage

Giving too small a dose will not achieve the expected therapeutic effect, while giving an excessive dose will have a high risk of side effects. From the research data, it was found that the appropriate dose was 53% and the inappropriate dose was 47% [16]. It was known that as many as 9 prescriptions of 15% were declared inappropriate doses [18]. It was then discovered that as many as 20 prescriptions, 32.3% of them were declared inappropriate doses [19]. The dose accuracy given to patients with urinary tract infections was 89.4%, while the inappropriate dose was 10.6%. Inappropriate dosage is a dose that can reach the MIC (Minimum Inhibitory Concentration) in blood or body fluids [20]. Based on the next article, it was shown that the inappropriate antibiotic dose was 13.85% and the appropriate antibiotic dose was 86.15% [21]. Subsequent articles showed that the number of drugs that did not meet the accuracy of the dose was 72.36% and the number of antibiotics that met the accuracy of the dose was 27.63% [22].

The accuracy of antibiotic drugs in upper urinary tract infection patients with the appropriate dose was 7 patients (17.5%), the duration was less than 11 patients (27.5%), the duration was more than 4 patients, the use of antibiotics with the PO route was 18 patients (45%).) while using the iv route was in 4 patients (10%) [23]. For the use of antibiotics in patients diagnosed with lower urinary tract infections did not have the appropriate dose, the inaccuracy of the dose was included in the category of over magnitude for as many as 14 patients (35%), over frequency for 14 patients (35%), over duration for 14 patients (35%), the use of antibiotics using the po route was in 14 patients (35%) and none with the iv route, based on the data obtained that patients diagnosed with lower urinary tract infections did not get the appropriate dose [23]. Administration of the appropriate antibiotic dose was 83.33% of 78 cases [24].

The accuracy of the dose is the administration of antibiotics in terms of the usual dose, i.e. the dose that can achieve a therapeutic effect is adjusted to the standard treatment of UTI [27]. Giving an inadequate dose will result in the ineffectiveness of the antibiotic because it cannot reach the MIC (Minimum Inhibitory Concentration) in body fluids, the lack of a dose can result in bacterial resistance remaining in the body, but if the dose is more it will result in the risk of unwanted side effects in patients [25].

Evaluation of the use of antibiotics against the dose accuracy variable was carried out by comparing the number of doses given to patients with several therapeutic standards used as a reference for dose calculation [30].

Table IV. Data on comparison of standard doses, and doses given by doctors

No	Antibiotic	Total R /	Dose R /	Standard Dose
1.	Ceftriaxone	229	500 mg (adults)	500-750 mg
2.	Cefoperazon	14	2 grams (adults)	2-4 g (adults)
4.	Cefotaxime	28	1 g (adults) 300 mg (children)	2 g (adult) / day 150 mg / kg BW
5.	Cefadroxil	8	1 g (adults) 50 mg / kg BW (children)	1-2 g (adults) 100 mg / kg BW (children)
6.	Cefixime	23	200mg	400mg
7.	Tricefin	1	1g (adults)	1-2 g (adults)
8.	Ciprofloxacin	158	500 mg (adults)	500-750 mg
9.	Levofloxacin	52	500 mg (adults)	500-750 mg
10.	Amoxicillin	6	3 g (adults)	250-500 mg

11.	Amikacin	2	30 mg	15 mg
12.	Cotrimoxazole	6	800 mg (adults) 200 mg (children)	960 mg / day 240 mg (children)

5. Appropriate duration of administration

Appropriate duration of antibiotics for UTI patients, that each antibiotic has a pharmacokinetic profile and the ability to inhibit or kill bacteria are different but in essence all antibiotics must pay attention to levels in plasma or urine fluid remain above the MIC of bacteria to a long time and quite [22]. The accuracy of the duration of antibiotics in the first study was 49.4% and the inaccurate duration was 50.6% [16]. And in the next article, it was shown that 94.25% accuracy in the duration of antibiotics and 5.75% [17]. Then in the next article, the results obtained were very low, namely the duration of drug administration in accordance with the duration of administration of 13 patients with a percentage of 27.7% while the duration of drug administration that did not match the duration of administration was 34 patients with a percentage of 72.3% [20].

Inappropriate duration refers to the time of administration that is too fast so that the therapy is too short, and the duration of administration that is too long. In the review article, the duration of antibiotic administration was too fast in 28 patients (83.08%), and the duration of antibiotic administration was too long in 5 patients (15.2%) [21]. It was known that the accuracy of the duration of antibiotic use is only 11.54%, while 88.46% of the duration of use of antibiotics was not appropriate [24]. The use of antibiotics with less duration is one of the factors that bacteria become resistant to antibiotics [26]. Too short administration can occur because the patient's condition has improved or the patient's family asks to go home. Too long administration can occur because the patient has other complications that require the patient to be hospitalized for a long time so that antibiotic therapy is required while the patient is treated [21].

The time interval for drug administration is seen from the suitability of the patient's interval in taking the drug at the first, second, and so on. Antibiotics that must be taken 3 times a day must mean that they must be taken at intervals of every 8 hours [1]. Data on antibiotic therapy in Urinary Tract Infections showed that the duration of antibiotics for 3 days is sufficient for mild Urinary Tract Infections and 7 to 14 days for severe Urinary Tract Infections. The duration of antibiotics is very important because if an antibiotic does not work according to the length of time it is used, it will result in tolerance for microorganisms that have not been completely destroyed so that they become resistant bacteria [20].

VI. CONCLUSION

Our literature study on the rationality of antibiotic use in Urinary Tract Infection (UTI) showed that the use of antibiotics is not completely rational. From the nine data obtained, there is a difference in the percentage of rationality of drug use and the number of different cases. And not all data reaches 100%. This is due to many things, one of which is that not all patients get the therapy they should, prescriptions that are not in accordance with the diagnosis, and the inappropriate procedure of drug administration.

Therefore, it can be concluded that the appropriate percentage of the indication from the eight articles is 99.35%. The percentage of appropriate drug selection from data from eight articles is 82.68%. The percentage of the appropriate dose administration data from the nine articles obtained is 67.78%. And the percentage of the appropriate duration of the administration of the five articles is 53.18%. From the results of this percentage, it can be seen that not all hospitals have determined the rational use of antibiotics.

REFERENCES

- [1] Department of Health of the Republic of Indonesia. (2011). *Modul Penggunaan Obat Rasional*. Jakarta: Department of Health of the Republic of Indonesia.
- [2] Febiana, T. (2012). *Kajian Rasionalitas Penggunaan Antibiotik di Bangsal Anak RSUP Dr. Kariadi Semarang Periode Agustus-Desember 2011*. Scientific Paper. Semarang: Medical Faculty. University Diponegoro
- [3] World Health Organization. (2001). Antibiotic resistance : synthesis of recommendation by expert policy groups Alliance for the Prudent Use of Antibiotics
- [4] Woro, S. (2016). *Farmakologi*. Pusdik SDM Kesehatan. Jakarta: Health Minister of Republic Indonesia
- [5] Nasution, R. E. P. (2018). *Ebook Panduan Praktis Dosis Antibiotik untuk Dewasa, Anak, Ibu Hamil, dan Gangguan Ginjal*. WCH
- [6] Ghinorawa, T. (2015). *Penatalaksanaan Infeksi Saluran Kemih dan Genitalia Pria*. Surabaya: urologist bond.
- [7] Amin, L. Z. (2014). *Pemilihan Antibiotik yang Rasional*. Medical Review. Fakultas Kedokteran. University Indonesia. Jakarta: Vol. 27(3).

- [8] Hospital Team Dr. Saiful Anwar Malang. (2016). Panduan Umum Penggunaan Antimikroba. Hospital Dr. Saiful Anwar Malang
- [9] Hashary, A. R. Manggau, M. Kasim, H. (2018). *Analisis Efektifitas dan Efek Samping Penggunaan Antibiotik pada Pasien Infeksi Saluran Kemih di Instalasi Rawat Inap RSUP dr. Wahidin Sudirohusodo Makasar*. Makasar: Pharmacology Pharmacy Magazine. Faculty of Pharmacy
- [10] World Health Organization (WHO). (2014). *Antimicrobial Resistance*. Global Report on Surveillance. World Health Organization.
- [11] Dipro, C. V. (2011). Urinary Tract Infections and Prostatitis. In B. G. Wells, J. T. Dipro, T. L. Schwinghammer, C. V. Dipro (Eds). *Pharmacotherapy Handbook* (8th ed) (pp.2048-2043). Washington, D. C: The McGraw-Hill Companies.
- [12] Torpy, J.M. (2012). Urinary Tract Infection. *The Journal of The American Association*. Vol. 307(17)
- [13] Imaniah, B.A. (2015). Peta Kuman dan Resistensinya terhadap Antibiotika pada Penderita Infeksi Saluran Kemih (ISK) di RSUD Dr. Moewardi Tahun 2014, Essay, Faculty of Pharmacy. University Muhammadiyah Surakarta.
- [14] Saudi, A.D.A. Rusdy. (2018). Uji Daya Hambat Antibiotika Terhadap Bakteri Penyebab Infeksi Saluran Kemih di Rumah Sakit Salewangang Maros. *Pharmaceutical Media*. Vol.XV(2).
- [15] Chitrangtyas D., Juliana C., Retno S. 2014. Profil Bakteri Penyebab Infeksi Saluran Kemih di Balai Besar Laboratorium Kesehatan Daerah. Surabaya.
- [16] Febrianto, A. W., Mukaddas, A., dan Faustine, I., (2013). Rasionalitas Penggunaan Antibiotik pada Pasien Infeksi Saluran Kemih (ISK) di Instalasi Rawat Inap RSUD Undata Palu Tahun 2012. *Online Journal of Natural Science*. 2(3): 20-29
- [17] Yusnita, R., Meylina, L., Ibrahim, A., dan Rijai, L. (2017). Kajian Efektivitas Penggunaan Antibiotik pada Pasien Infeksi Saluran Kemih (ISK) di Rumah Sakit Samarinda Medika Citra (SMC) Kota Samarinda. *Mulawarman Pharmaceuticals Conferences*.
- [18] Pambudi, A. S. (2017). Rasionalitas Penggunaan Antibiotik pada Pasien Infeksi Saluran Kemih di Instalasi Rawat Inap Rumah Sakit Islam Klaten Periode Januari-Maret Tahun 2017. Essay. Surakarta: Faculty of Pharmacy University Setia Budi.
- [19] Risdawati, R. (2018). Evaluasi Rasionalitas Penggunaan Antibiotik pada Pasien Rawat Inap Dengan Diagnosis Infeksi Saluran Kemih di Rumah Sakit Islam Klaten Tahun 2017. *Essay*. Surakarta: Faculty of Pharmacy University Setia Budi.
- [20] Mantu, F. N. K., Goenawi, L. R., dan Bodhi, W. (2015). Evaluasi Penggunaan Antibiotik pada Pasien Infeksi Saluran Kemih di Instalasi Rawat Inap Rsup. Prof. Dr. R. D. Kandou Manado Periode Juli 2013 - Juni 2014. *Pharmaceutical Scientific Journal*. 4(4).
- [21] Adriani, K.P. (2017). Evaluasi Rasionalitas Penggunaan Antibiotik Pasien Infeksi Saluran Kemih Dewasa di Instalasi Rawat Inap RS Bethesta Yogyakarta tahun 2015. *Essay*. Yogyakarta: Faculty of Pharmacy University Sanata Dharma
- [22] Nawatasari, N. Nugraheni, A. Y. (2019). *Evaluasi Penggunaan Antibiotik pada Pasien Infeksi Saluran Kemih di Instalasi Rawat Inap RSUP X di Klaten Tahun 2017*. *Indonesian Pharmacy Journal*. Vol. 16(1)
- [23] Puspitosari, E. (2015). *Evaluasi Penggunaan Antibiotik pada Infeksi Saluran Kemih di Instalasi RSPAU dr. S. Hardjolukito Yogyakarta Tahun 2014*. *Publication manuscript*. Surakarta: Faculty of Pharmacy University Muhammadiyah
- [24] Woelandary, W. (2014). *Evaluasi Penggunaan Antibiotik pada Penyakit Infeksi Saluran Kemih Pasien Rawat Inap di RS "X" Klaten Tahun 2012*. *Publication manuscript*. Surakarta: Faculty of Pharmacy University Muhammadiyah
- [25] BNF. (2018). *British National Formulary 74th Edition*. London: BMJ Publishing Group and The Royal Pharmaceutical Society.
- [26] Prabowo, F., Habib, I. (2012). *Identifikasi Pola Kepekaan dan Jenis Bakteri pada Pasien Infeksi Saluran Kemih di Rumah Sakit PKU Muhammadiyah Yogyakarta*. Research Articles. Medical Education Study Program, Faculty of Medicine and Health Sciences, Muhammadiyah University: Yogyakarta.
- [27] Fatimawali, Nua R.A, Bodhi W. (2016). *Uji Kepekaan Bakteri Yang Diisolasi Dan Diidentifikasi Dari Urin Penderita Infeksi Saluran Kemih (Isk) Di Rsup Prof. Dr. R. D. Kandou Manado Terhadap Antibiotik Cefixime, Ciprofloxacin Dan Cotrimoksazole*. Manado : UNSRAT Pharmaceutical Scientific Journal.
- [28] Grabe, M. Bartoletti, R. Johansen, T. E. B. Cai, T. Cek, M. Koves, B. *et al.* (2015). *Guidelines on Urological Infections*. European Association of Urology.
- [29] BNF. (2016). *British National Formulary 71th Edition*. London: BMJ Publishing Group and The Royal Pharmaceutical Society.
-

- [30] Gupta, K. Hooton, T. M. Nuber, K. Wult, B. Colgan, R. Miller, R. Moran, G. Nicolle, L. Raz, R. Schaeffer, A. J. Soper, D. (2011). *International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases*. IDSA : Guidelines.

Sintiya Regimulya, et. al. "A Review: Rational Drug Use of Antibiotics in Patients With Urinary Tract Infection At Hospitals In Indonesia." *IOSR Journal of Pharmacy (IOSRPHR)*, 11(02), 2021, pp. 01-09.