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Description Of Ciprofloxacin Sensitivity On Bacteria Causing UTI In T2DM Patients

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ABSTRACT

Diabetes mellitus is a chronic metabolic disease characterized by a state of hyperglycemia due to a lack of insulin production by the pancreas or the body's inability to use the insulin produced or both. Uncontrolled hyperglycemia can suppress the immune system and making the body vulnerable to infection, especially urinary tract infections (UTIs). The main choice in UTI treatment is antibiotic therapy, one of the most frequently used is ciprofloxacin from the fluoroquinolone group.

The research design used was descriptive method with prevalence studies. The research was done using antibiotic sensitivity tests with agar diffusion methods. The number of samples were taken using total sampling method.

The results of ciprofloxacin sensitivity test were obtained as many as 22 isolates. *Escherichia coli* bacteria are sensitive to ciprofloxacin at 66.67%, intermediate and resistant 16.67% respectively. P*seudomonas aeruginosa* are 60% sensitive and 40% intermediate. *Enterobacter aerogenes* are 66,67% sensitive and 33,33% intermediate. *Shigella* spp. are 100% sensitive, and *Klebsiella* spp. 100% resistant.

The conclusion from the study showed that ciprofloxacin are an effective empirical therapy for UTI. Further research needs to be done on the description of antibiotic sensitivity as a therapy in UTIs with a wider and diverse population.

Keywords: Type 2 Diabetes Mellitus, UTI, Ciprofloxacin

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease that occurs the most in the world. This disease is characterized by a state of hyperglycemia due to lack of insulin production by the pancreas or the body's inability to use the insulin produced or both. The International Diabetes Federation (IDF) in 2015 stated that the number of adult DM sufferers in the world was 415 million. Southeast Asia ranks fifth in the world with a percentage of 8.5% in 2015. Indonesia ranks seventh with an estimated 10 million of sufferers (WHO, 2016). Based on the results of Riset Kesehatan Dasar (Riskesdas) in 2013, West Kalimantan had a percentage of DM sufferers diagnosed by doctors at 0.8% from the average of Indonesia at 1.5%. This percentage increased from 2007 which was at 0.6% from the

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Indonesian average of 0.7% (Riskesdas, 2008).

Uncontrolled hyperglycemia will become a factor in the emergence of DM vascular complications (Acharya et al, 2015; Fowler, 2014). Chronic hyperglycemia in DM is associated with progressive damage, dysfunction, failure of various organs in the body such as the eyes, genitourinary system, innervation, heart, and blood vessels. The state of hyperglycemia also suppresses the immune system by creating conditions that are tolerant of infection due to neutrophil dysfunction (Acharya et al, 2015). High urine glucose levels and suppression of the immune system are predisposing factors for infection, especially urinary tract infections (UTIs) (Brown et al, 2005). Various studies have shown that DM patients are more at risk of developing UTI than non-DM patient (Acharya et al, 2015; Al-Rubeean et al, 2013; Black & Hawks, 2009). Symptoms of UTI in diabetic patients are generally asymptomatic but can develop to be symptomatic and increase the risk of hospital admission with bacteremia to bilateral pyelonephritis (Sudoyo et al, 2009; Saleem & Daniel, 2011).

Antibiotic therapy is the primary choice in the treatment of UTI. The selection of antibiotics must be based on appropriate indications by determining the dose, method of administration, duration of administration, and evaluation of the effects of antibiotics. The correct choice of antibiotics given is very im-portant in the development of pathogenic microorganisms because each antibiotic needs a certain time to reach the target cell so the microorganisms within infected tissue are eliminated so that therapeutic goals can be achieved (Katzung, 2012). Antibiotics which widely used in hospitals generally have a broad spectrum such as cephalosporins and fluoroquinolones (Triono & Purwoko, 2012).

Ciprofloxacin is an antibiotic that belongs to the second generation fluoroquinolone group. Fluoroquinolone antibiotics are currently recommended as prophylactic and therapies for UTI because fluoro-quinolones have strong antibacterial properties against the bacteria that cause UTI. Ciprofloxacin is also the most widely used fluoroquinolone group. But lately, there have been many reports about the re-sistance of the fluoroquinolone group as prophylaxis or UTI therapy, especially ciprofloxacin, which ranges from 20% - 30% (Triono & Purwoko, 2012; Marwazi & Erkadius, 2014). Research conducted by Chowdhury and Ramendu (2015) states that *Escherichia coli* is resistant to ciprofloxacin and levofloxacin. Research conducted by Endriani et al. (2009) also found that *Escherichia coli* was resistant

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to ciprofloxacin (45.45%), *Pseudomonas* spp. (75%), *Klebsiella* spp. and *Enterococcus* spp. (80%). Cases of ciprofloxacin resistance as UTI therapy also been reported in several major cities in Indonesia, including Jakarta, Surakarta, Yogyakarta, and Pekanbaru. Until now, there has been no previous research or report that specifically examines this in Pontianak. On this basis, the research was conducted to determine the sensitivity of ciprofloxacin which is an empirical therapy of UTIs in patients with Type 2 Diabetes Mellitus (T2DM) in Sultan Syarif Mohamad Alkadrie Hospital Pontianak.

METHODS

This research uses a descriptive method with prevalence studies. The time allocation for this study began in July 2019-October 2019 and was carried out at the Microscopic Laboratory of the Faculty of Medicine, Tanjungpura University. The number of samples used were 22 isolates. The isolates were obtained from laboratory collection (isolates of bacteria that cause UTI in T2DM patients which have been isolated in previous studies). The ciprofloxacin antibiotic disc used had a concentration of 5µg.

RESULTS

Table 1. Ciprofloxacin Sensitivity Test Results

Num.	Isolate Code	Bacterial Name	Clear Zone Diameter (mm)	Interpretation
1.	6	*Escherichia coli*	31.50	Sensitive
2.	11	*Pseudomonas aeruginosa*	21.60	Intermediate
3.	38B	*Enterobacter aerogenes*	27.60	Sensitive
4.	42A	*Escherichia coli*	26.08	Sensitive
5.	45	*Escherichia coli*	27.15	Sensitive
6.	58A	*Escherichia coli*	29.36	Sensitive
7.	63A	*Shigella* sp	32.24	Sensitive
8.	63B	*Escherichia coli*	27.27	Sensitive
9.	67B	*Escherichia coli*	11.28	Resistant
10.	72A	*Pseudomonas aeruginosa*	32.18	Sensitive
11.	73A	*Eschericia coli*	25.66	Intermediate
12.	73B	*Enterobacter aerogenes*	31.78	Sensitive
13.	74B	*Pseudomonas aeruginosa*	24.32	Intermediate
14.	82	*Pseudomonas aeruginosa*	27.14	Sensitive
15.	88	*Klebsiella sp*	14.94	Resistant
16.	89A EMB	*Escherichia coli*	27.44	Sensitive
17.	95 EMB	*Escherichia coli*	23.31	Intermediate
18.	96 EMB	*Enterobacter aerogenes*	23.16	Intermediate
19.	99 EMB	*Escherichia coli*	28.29	Sensitive
20.	102A EMB	*Escherichia coli*	28.20	Sensitive

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21.	103A	*Pseudomonas aeruginosa*	27.68	Sensitive
22.	103B	*Escherichia coli*	16.16	Resistant

Enterobacteriaceae: Sensitive = ≥26 mm, Intermediate = 22-25 mm, Resistant = ≤21 mm; Pseudomonas: Sensitive = ≥25 mm, Intermediate = 19-24 mm, Resistant = ≤18 mm

DISCUSSION

Clear zone measurement results showed that the isolates of bacteria that cause UTI were sensitive to ciprofloxacin as many as 14 isolates (63.63%), intermediate 5 isolates (4.54%), and resistant as many as 2 isolates (9.09%). With details of distribution, *Escherichia coli* bacteria are sensitive at 66.67%, intermediate and resistant 16.67% respectively. *Pseudomonas aeruginosa* are 60% sensitive and 40% intermediate. *Enterobacter aerogenes* are 66,67% sensitive and 33,33% intermediate. *Shigella* spp. are 100% sensitive, lastly *Klebsiella* sp 100% resistant. Data obtained on the sensitivity of ciprofloxacin to *Escherichia coli* bacteria are following the results of Samirah's study (2006) which states that *Escherichia coli* are still sensitive to *ciprofloxacin* by 52%, and *Pseudomonas aeruginosa* by 75%. But different results were obtained from a study conducted by Pratiwi (2013), where according to the results of the study *Escherichia coli* bacteria was resistant to ciprofloxacin by 84.6%. Likewise, research conducted by Tandari (2016) stated that the *Escherichia coli* bacteria was resistant to ciprofloxacin by 66.6%, *Klebsiella* spp. by 50%, and *Enterobacter aerogenes* by 100%. In the "Guideline Penatalaksanaan Infeksi Saluran Kemih dan Genitalia Pria" compiled by the Indonesian Urologists Association in 2015 also conveyed the results of sensitivity tests carried out at RSUD Dr. Soetomo, where the results showed ciprofloxacin are less sensitive (sensitivity of 25.9% to all bacteria).

Ciprofloxacin, which is a fluoroquinolone has a mechanism of inhibiting topoisomerase II (DNA gyrase) and topoisomerase IV which have an important role in bacterial DNA replication. DNA gyrase works to reduce the strain on the DNA chain caused by the action of the DNA Helicase enzyme at the time of replication. With the inhibition of gyrase, the DNA chain will tangle due to supercoiling caused by DNA helicase activity. The intermediate and resistant results can be caused by two factors, namely intrinsic factor (bacterial) and extrinsic factor (environmental or individual). The intrinsic factor is the state of a natural mechanism formation for bacteria to survive. Bacteria that exposed to antibiotics over time can increase the ability to defend themselves from these familiar antibiotics. The adaptation of these bacteria induced by

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changes or mutations in the plasmid which then their genetic information can be transferred to other bacteria through conjugation. So finally the bacteria can survive antibiotic exposure. (Samirah et al, 2006; Kahuripan et al, 2009; Febrianto et al, 2013).

In *Escherichia coli*, one of the known causes of antibiotic resistance is due to a series of mutations that involve changes in the chromosomal target genes that encode DNA gyrase and topoisomerase IV which are the target of action of the fluoroquinolone antibiotic. This causes a reduced affinity of the drug against the *Escherichia coli* bacteria so that it becomes resistant. Also, resistance can occur due to the expression of plasmid-mediated quinolone resistance (PMQR) genes that protect DNA gyrase of *Escherichia coli* (Hooper & Jacoby, 2015)

The cause of antibiotic resistance to Klebsiella bacteria is usually caused by bacterial enzymatic modification of antibiotic drugs, modification of the target ribosome, decreased intracellular antibiotic accumulation through decreasing outer membrane permeability, as well as the active efflux of the bacteria itself. Active efflux in bacteria is initiated by an efflux protein in the form of a pump which removes the substrate that is considered toxic by the bacteria (Hooper & Jacoby, 2015; Liang et al, 2015)

As for the extrinsic factors, inappropriate use of antibiotics such as improper consumption of recommended time, giving a too low dose, improper selection of antibiotics, or incorrect diagnosis can be a supporting factor that causing resistance (Kahuripan et al, 2009; Febrianto et al, 2013).

CONCLUSIONS

Conclusions obtained from 22 bacterial isolates that cause UTIs in T2DM patients at Sultan Syarif Mohamad Alkadrie Hospital Pontianak is that ciprofloxacin antibiotics are still effective to treat UTIs in patients with 63.64% sensitive results, intermediate 22.72%, and resistant 13,64%. Further research needs to be done on the description of antibiotic sensitivity as a therapy in UTIs with a wider and diverse population from this study.

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