THE USE OF ANTIBIOTICS IN PATIENTS WITH URINARY TRACT INFECTION

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ABSTRAK

Tingginya frekuensi multiple resistent di ICU meningkatkan kewaspadaan untuk lebih efektif dalam penggunaan antibiotic. Salah satu pendekatan yang dapat dilakukan adalah dengan pembuatan pola kuman, pola sensitifitas serta evaluasi kualitatif antibiotik pada pasien ISK di unit ICU RSUD Dr. Soetomo. Penelitian dilakukan melalui studi observasional dengan design cohort retrospektif dan prospektif. Data dianalisa pada terapi empiris dan definitif pada pasien ISK, regimentasi obat (rute pemberian, dosis, frekuensi dan durasi pemberian antimikroba), pembuatan antibiogram dan peta resistensi kuman dan evaluasi penggunaan antibiotik melalui pertanyaan terstruktur (metode Gyssens). Jenis kuman yang paling banyak ditemukan pada spesimen urin gram positif adalah Staphylococcus Coa Negatif sebesar 8,20% sedangkan gram negatif diduduki oleh kuman Escherichia coli (22,95%), Acinetobacter spp (14,75%), Enterobacter spp (13,11%), Pseudomonas aeruginosa (11,48%), Klebsiella pneumonia (8,20%). Dari hasil antibiogram (pola kuman terbanyak), antibiotik dengan sensitifitas direkomendasikan (> 60%) untuk kuman Escherichia coli adalah antibiotik amikasin, gentamisin, meropenem, imipenem, ertapenem, ciprofloxacin nitrofurantonin, dan cefoperazone sulbactam. Evaluasi penggunaan antibiotik dengan menggunakan metode Gyssens terbagi menjadi 7 kategori dengan sebelas peresepan antibiotik dari 7 pasien yang tersaji. Diperoleh hasil 5 peresepan antibiotik (54,55%) yang termasuk kategori IV A-IV B,sedangkan 6 antibiorik sisanya termasuk kategori 0 (45,45%) yang juga diartikan peresepan antibiotik rasional. Banyak peluang terjadinya permasalahan terkait pemberian obat antibiotic sehingga perlu adanya pengendalian resistensi antibiotik agar tercapai outcome yang optimal. ***(FMI 2014;50:204-210)***

Kata kunci*: analisa antibiotik, ICU RSUD Dr. Soetomo*

ABSTRACT

The high frequency of multiple resistant in ICU raises awareness for the more effectiveness in using the antibiotics. The approach is to do with germs pattern making, sensitivity and qualitative evaluation of antibiotics in patients with UTI in ICU of Dr. Soetomo Hospital. The study was conducted through an observational study with retrospective and prospective cohort design. The data were analyzed on empirical and definitive therapy in patients with UTI regimentation of the drug (route of administration dose frequency and duration of antimicrobial administration). The manufacture of antibiogram and resistance map germs and evaluation of the use of antibiotics through questions structured (Gyssens method). Type of bacteria most commonly found in gram-positive urine specimens were negative for Staphylococcus Coa 8.20% while occupied by gram-negative bacteria Escherichia coli (22.95%). Acinetobacter spp (14.75%). Enterobacter spp (13.11%). Pseudomonas aeruginosa (11.48%). Klebsiella pneumoniae (8.20%). From the results of antibiogram (most germs pattern). The recommended antibiotic sensitivity (> 60%) for the bacteria Escherichia coli are antibiotic amikacin, gentamicin, meropenem, imipenem. ertapenem. ciprofloxacin nitrofurantonin and cefoperazone sulbactam. Evaluation of the use of antibiotics by using Gyssens divided into 7 categories with eleven prescribing antibiotics of 7 patients who presented. Antibiotic prescribing 5 obtained results (54.55%) which includes category IV A-IV B while the remaining 6 antibiotics category 0 (45.45%) were also interpreted the rational antibiotic prescribing. Many problems related to the possibility of antibiotic medication that is necessary to control antibiotic resistance in order to achieve optimal outcomes. ***(FMI 2014;50:204-210)***

Keywords*: analysis of antibiotics, ICU of Dr. Soetomo Hospital*

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INTRODUCTION

Nosocomial infections occur throughout the world with the highest incidence in poor countries and developing countries due to infectious diseases which still be a major factor. A study conducted by WHO showed that the highest frequency of reported nosocomial infection is the most numerous in the Middle East region and Southeast Asia respectively as much as 11.8% and 10.0%. This issue is important for the study to be able to decrease that number (Ducel et al 2002). The results of the research in the Department of Internal Medicine IRNA Dr. Soetomo hospital shows of 135 patients with urinary tract infections was found that the prevalence of

urinary tract infection which can be categorized as nosocomial infections was 16.3% with the germs that cause the majority of nosocomial urinary tract infection is the bacteria *Escherichia coli* (Mirozha 2009).

The high frequency of multiple resistant in the ICU increased vigilance to be effective in the use of antibiotics, namely the selection of the appropriate antibiotic. This can save the patient and prevent the spread of antibiotic resistance in the intensive care unit. Because of the sensitivity pattern of change in each particular periodic, then the data needs and data pattern sensitivity of bacteria to antibiotics in intensive care units need to be held (Japoni et al 2009).

The approach that can be done to control the use of antibiotics is the germ pattern making, pattern sensitivity and qualitative evaluation of antibiotics that can assist the clinician in determining appropriate empiric antibiotic therapy. The specific objective of this study was to identify patterns of germs, as well as qualitative analysis of the pattern of antibiotic sensitivity in patients who experience a UTI in the ICU Dr. Soetomo Hospital. The results of this study are expected to be the evaluation of the use of antibiotics in intensive care units of hospitals Dr. Soetomo Hospital as well be made an initial data pattern sensitivity of germs, which can then be used to determine the effective governance in the use of empirical antibiotics.

MATERIALS AND METHODS

This research was conducted in the ICU of Dr. Soetomo Hospital this is an observational study cohort analytic design retrospective and prospective. The sample used for the manufacture of table antibiogram divided into two patients with the diagnosis of urinary tract infection with positive urine culture in periods 1, 2012-February 28, 2013 (retrospective and prospective) and the period of May 1, 2012-December 31 2012 (retrospective), while sample used to evaluate the use of a method that is modified Gyssens met the patient inclusion criteria in the period of January 1-February 28, 2013 (prospective). As the criteria for inclusion in the study sample to evaluate the use of antibiotics is a modified method Gyssens patients with a diagnosis of urinary tract infection during care in the ICU, the patient men and women aged > 18 years, length of stay in the ICU > 48 hours, has been carried out sampling and microbiological culture antimicrobial sensitivity before the start of observation research, and antibiotic therapy for urinary tract infections during treatment in ICU. Instruments used during the study were: patient collection sheet to record the observation of anti-microbial therapy, clinical-laboratory conditions of infection from patient medical records, nursing notes, pharmacy records and by direct observation of the patient's condition.

All ICU patients were diagnosed with urinary tract infections that met the inclusion criteria, then performed the primary data obtained from patient medical records, nursing notes, and notes pharmacists, including patient demographic data (weight and gender), patient clinical data (date MRS/KRS and diagnosis before and while in the ICU, temperature, pulse and complications of diseases), laboratory data of patients (leukocytes, neutrophils, CRP, ESR, urinalysis), antimicrobial therapy (type, dose, route, frequency and duration of antimicrobial administration), and equipped with a urine culture examination date microbial culture and sensitivity to antimicrobials.

From the data obtained was then conducted the presentation in the form of tabulations and then grouped by category. Analysis of the data that will be made include patient demographics (gender, age, and risk factors in patients with UTI), the analysis of patients receiving antimicrobial therapy, including the manufacture of antibiogram and resistance maps UTI bacteria in patients in intensive care units through the data pattern sensitivity of germs and bacteria against certain antimicrobials, grouping the potential sensitivity of most UTI antibiotics on bacteria, antibiotic appropriateness of patient profiles with culture results and evaluation of the use of antibiotics through a structured questionnaire evaluation of five key features of antibiotics (Gyssens method).

RESULTS

In the study period from May to February, 2013, 61 isolates from urine, all of which showed positive results of bacterial growth which consisted of 14 (22.95%) aerobic gram-positive bacteria and 47 (77.05%) aerobic gram-negative bacteria. The bacteria most commonly found in the urine of patients UTI isolates in ICU Dr. Soetomo Hospital is a positive for gram negative *Staphylococcus Coa* was 8.20% while occupied by the gram-negative *Escherichia coli* bacteria by 22.95%.

Table 1. The types of bacterial UTI in patients at ICU Dr.Soetomo Hospital May 2012-February 2013.

Types of Germs	Sum	Percentage (%)
Gram Positive		
Enterococcus spp	3	4.92
Staphylococcus Coa Negative	5	8.20
Staphylococcus spp	3	4.92
Streptococcus non Haemolyticus	3	4.92
	14	22.95
Gram Negative		
Acinetobacterspp	9	14.75
Burcholdeniacepacea	1	1.64
Eschericia coli (6 ESBL positive)	14	22.95
Enterobacterspp	8	13.11
Klebsiella pneumonia (2 ESBL positive)	5	8.20
Pseudomonas aeruginosa	7	11.48
ProvidenciaRettigeri	1	1.64
Rountellaornithinolytica	1	1.64
Yersenia Pseudotuberculosis	1	1.64
	47	77.05
Total	61	100

Antibiogram pattern formed from the data on the antibiotic sensitivity of bacteria tested sensitive. Antibiogram was made of three parts, namely: antibiogram month of May 2012-February 2013 (Table 2) is used to create a picture of antibiogram intact, antibiogram months from May to December 2012 (Appendix 1) was used as a comparison evaluation of the use of antibiotics in January-February, 2013, while the antibiogram month January-February 2013 is used as a comparison antibiogram profiles change the month from May to December 2012 and January-February 2013.

Tabel 2. ICU patients' antibiogram in UTI Unit dr. Soetomo Hospital, May 2012-February 2013

Antibiogram		Gram Positive					Gram Negative							
		Ent sPP	Strep NHae	Stap Coag Neg	Stap Spp	AciSpp	Bur Cep	E Coli	Entb Spp	Kle Pneu	Pseu doA	Prov Rett	Rout Orni	Yer Pseudo
		3	3	5	3	9	1	14	8	5	7	1	1	1
		% S	% S	% S	% S	% S	% S	% S	% S	% S	% S	% S	% S	% S
Beta laktam	Ampicillin	33.33 (3)	-	0 (1)	0 (1)	-	-	0 (5)	0 (4)	0 (2)	-	-	0 (1)	0 (1)
	Penicillin	33.33 (3)	0 -(3)	0 (4)	0 (1)	-	-	-	-	-	--	-	-	-
	Oxacillin	-	-	25 (4)	100 (1)	-	-	-	-	-	-	-	-	-
	Ampicillin-Sulbactam	-	-	-	-	55.56 (9)	-	23.08 (13)	0 (7)	0 (4)	-	0 (1)	100 (1)	-
	Amoxiclav	-	-	-	-	-	-	25 (12)	12.5 (8)	0 (5)	-	0 (1)	0 (1)	100 (1)
	Piperacillin-Tazobactam	-	-	-	-	14.29 (7)	-	57.14 (14)	50 (8)	20 (5)	71.43 (7)	0 (1)	0 (1)	0 (1)
	Ticacillin	-	-	-	-	0 (2)	-	-	-	-	100 (2)	-	-	-
	Ticarcillin-Clavulanat	-	-	-	-	0 (3)	-	28.57 (7)	0 (2)	-	33.33 (6)	0 (1)	0 (1)	0 (1)
Cepholosporin	Cefazolin	-	--	-	-	-	-	0 (1)	0 (2)	-	-	-	-	-
	Cefalotin	-	-	-	-	-	-	0 (2)	0 (2)	-	-	0 (1)	0 (1)	-
	Cefuroxime	-	-	-	-	-	-	33.33 (3)	0 (2)	-	-	0 (1)	0 (1)	0 (1)
	Cefoperazone-sulbactam	-	-	-	-	-	-	66.67 (9)	42.86 (7)	0 (5)	71.43 (7)	0 (1)	100 (1)	0 (1)

	Cefotaxime	-	-	-	-	0 (9)	-	23.08 (13)	42.86 (7)	0 (5)	25 (4)	0 (1)	0 (1)	-
	Ceftriaxon	-	-	-	-	10 (9)	-	38.42 (13)	37.5 (8)	0 (5)	16..67 (6)	0 (1)	0 (1)	0 (1)
	Ceftazidime	-	-	-	-	0 -(8)	-	23.08 (13)	42.86 (7)	0 (4)	33.33 (6)	0 (1)	0 (1)	0 (1)
	Cefepime	-	-	-	-	-	-		100 (1)	0 (1)	100 (1)	-	-	-
Carbapenem	Ertapenem	-	-	-	-	-	-	100 (1)	100 (2)	0 (1)	-	-	-	-
Carbapenem	Imipenem	-	-	-	-	66.67 (3)	-	100 (5)	75 (4)	100 (1)	100 (2)	100 (1)	100 (1)	100 (1)
Carbapenem	Meropenem	-	-	-	-	37.5 (8)	100 (1)	100 (14-)-	75 (8)	80 (5)	57.14 (7)		100 (1)	100 (1)
Glycopeptide	Vancomycin	-	100 (2)	-	-	-	-	-	-	-	-	-	-	-
Monobactam	Aztreonam	-	-	-	-	-	-	38.46 (13)	37.5 (8)	0 (5)	50 (6)	100 (1)	0 (1)	0 (1)
Other cell wall active agents	Fosfomycin	-	-	-	-	-	-	-	100 (1)	100 (1)	-	-	-	-
Tetracycline		0 (3)	-	0 (1)	100 (2)	0 (2)	-	0 (1)	0 (2)	0 (1)	-	-	-	-
Macrolides	Eryhtromycin	0 (2)	0 (3)	60 (5)	50 (2)	-	-	-	-	-	-	-	-	-
Lincosamides	Clindamycin		0 (3)	20 (5)	0 (1)	-	-	-	-	-	-	-	-	-
Chloramphenicol		50 (2)	50 (2)	25 (4)	0 (1)	-	100 (1)	41.67 (12)	0 (7)	50 (4)	16.67 (6)	0 (1)	100 (1)	0 (1)
Oxazolidinones	Linezolid	100 (2)	100 (2)	75 (4)	100 (3)	-	-	-	-	-	-	-	-	-
Aminoglicosides	Amikasin	-	-	-	-	33.33 (9)	-	78.57 (14)	57.14 (7)	100 (5)	71.43 (7)	100 (1)	100 (1)	100 (1)
Aminoglicosides	Gentamycin	-	-	50 (4)	33.33 (3)	12.5 (8)	-	64.29 (14)	37.5 (8)	20 (5)	60 (5)	100 (1)	0 (1)	0 (1)
Aminoglicosides	Tobramycin	-	-	-	-	0 (4)	-	40 (5)	66.67 (3)	0 (1)	100 (2)	100 (1)	0 (1)	0 (1)
Sulfametoxazol		-	-	75 (4)	50 (2)	37.5 (8)	100 (1)	16.67 (12)	28.57 (7)	0 (5)	14.29 (7)	0 (1)	0 (1)	0 (1)
Quinolones	Nalidix acid	-	-	-	-	-	-	28.57 (14)	37.5 (8)	0 (5)	0 (6)	0 (1)	0 (1)	-
Quinolones	Ciprofloxacin	-	-	-	-	0 (3)	-	60 (5)	50 (4)	-	100 (2)	0 (1)	0 (1)	100 (1)
Quinolones	Levofloxacin	100 (2)	0 (3)	60 (5)	100 (2)	14.29 (7)	100 (1)	41.67 (12)	83.33 (6)	0 (5)	66.67 (6)	0 (1)	0 (1)	100 (1)
Quinolones	Moxifloxacin	66.67 (3)	-	100 (2)	100 (1)	-	-	-	-	-	-	-	-	-
Quinolones	Gatifloxacin	66.67 (3)	-	50 (2)	100 (1)	0 (1)	-	-	-	-	-	-	-	-
Quinolones	Norfloxacin	66.67 (3)	-	-	-	-	-	-	-	-	-	-	-	-
Nitrofurantoin		100 (3)	-	-	-	-	-	85.71 (14)	28.57 (3)	20 (5)	-	0 (1)	100 (1)	-

Abbreviations of pathogenic germs:

EntSpp	*: Enterococci Spp*
StrepNHae	*: Streptococcus non Haemolyticus*
StapCoagNeg	*: Staphyllococcus Coagulase Negatif*
StapSpp	*: Staphyllococcus Spp*
AciSpp	*: Acinetobacter spp*
BurCep	*: Burcholdenia cepacea*
E Coli	*: Eschericia Coli*
EntbSpp	*: Enterobacter spp*
KlePneu	*: Klebsiella pneumoniae*
PseudoA	*: Pseudomonas aeruginosa*
ProvRett	*: Providencia Rettigeri*
RoutOrni	*: Rountella ornithinolytica*
YerPseudo	*: Yersenia Pseudotuberculosis*

: Not recommended
: Less recommended
: Recommended

The comparison of the number of male UTI patients outnumber female patients, the number of male patients by 6 patients (86%) and the number of female patients by 1 person (14%). From 7 patients in the ICU ISK January-February 2013, which is treated one patient treated with antibiotics definitive, three patients treated with antibiotics were not deescalated and three patients were not treated because of certain reasons. Further results can be seen on Table 3. From the 7 patients that evaluated the use of antibiotics UTI with Gyssens method obtained eleven antibiotic prescribing. Antibiotics are evaluated is empirical and definitive antibiotic. From the results of the evaluation of antibiotics, antibiotic obtained 5 (45.45%) were classified as category 0 and 6 antibiotics (54.55%) were classified as category IV. The complete data is shown in Table 4. Regimentation of antibiotic use (dose, frequency and route of administration of antibiotics) is compared with the literature Drug Information Handbook. The complete data is shown in Table 6.

Table 3. The distribution of primary diagnoses of UTI patient in Dr. Soetomo Hospital on January -February 2013.

Diagnosis Group	Primary Diagnose	Total	Percentage (%)
Nerve disease	GBS	2	29
	Stroke	1	14
	CIDP	1	14
	Brain Injury	2	29
Heart Disease	IMA	1	14
	Total	7	100

Table 4. Profile of patients with antibiotic suitability culture results

Name of Patient	Urine culture		Antibiotics Given	Notes
	Bacterial isolates	Antibiotics sensitive		
Mrs. Ma	*Enterococcus faecallis*	Amp, Levo, Moxi, Chloramp, Gati, Nitro, Norflox	Cefo Sulb	not escalated
Mr. Su	*Pseudomonas aeruginosa*	Amk, Genta, Piptaz, Cefta, Cefo, Ceftri, Cotri, Cefo sulb, Chloramp, Mero, Levo	Cefo Sulb	not escalated
	Burcholdeniacephacea	Levo, Chloramp, Mero, Nalidix, Ceftri, Cefo sulb, Tige, Cotri		
Mr. He	*Staphyococcusaureus*	Levo, Genta, Gati, Norflox, Nitro, Lnz, Oxa, Tetra	(untreated)	died
Mr. Ri	*KlebsiellaPneumoniae*	Nitro, Amk	(untreated)	Move to other room
Mr. Sl	*Enterobacter cloaceae*	Amk, Ampsl, Azt, Cefo, Ceftri, Cefta, Chloramp, Cipro, Levo, Genta, Imi, Mero, Piptaz, Tetra, Tobra	Levofloxacin	not escalated
Mr. Do	*Klebsiella pneumoniae*	Amk, Imi, Mero	Amikasin Meropenem	antibiotics definitive
Mr. Da	*Enterobacter cloaceae*	Amk, Levo, Imi, Mero, Piptaz, Cefo sulb	- (untreated)	move to other room

Tabel 5. Percentage of antibiotics use quality in Gyssens' cathegory

Category *Gyssens*	Sum	Percentage (%)
Category0	5	45,45
Category I	-	0
Category IIA – IIC	-	0
Category III A – IIIB	-	0
Category IV A – IV D	6	54,55
Category V	-	0
Category VI	-	0
Total	11	100

Tabel 6. Suitability regimentation of antibiotic use in Dr. Soetomo Hospital for UTI patients.

Name of patients	Antibiotics	Dose			Frequency			Route of administration		
		Divining manual	Actual	Notes*	Divining manual	Actual	Notes*	Literature	Actual	Notes*
Mrs. Ma	Cefoperazone Sulbactam	1-2 g max 4 g/day	1 g	S	2-3x1	3x1	S	IV	IV	S
Mr. Su	Ceftriakson	1-2 g max 4 g/day	1 gr	S	2x1	2x1	S	IV	IV	S
	Cefoperazone Sulbactam	1-2 g max 4 g/day	1 g	S	2-3x1	3x1	S	IV	IV	S
Mr. He	Ampicillin Sulbactam	1,5-3 g max 4 g/day	1,5 g	S	3-4x1	3x1	S	IV	IV	S
Mr. Ri	Meropenem	1 g	1 g	S	3x1	3x1	S	IV	IV	S
Mr. Sl	Ceftriaxon	1-2 g max 4 g/day	1 g	S	2x1	2x1	S	IV	IV	S
	Levofloxacin	500-750 mg	750 mg	S	1x1	1x1	S	IV	IV	S
Mr. Do	Fosfomycin	2-3 g	2 g	S	1-2x1	2x2 g	S	IV	IV	S
	Amikacin	15 mg/KgBW /24 hour	1 g	S	1x1	1x1 g	S	IV	IV	S
	Meropenem	1 g	1 g	S	3x1	3x1	S	IV	IV	S
Mr. Da	Ampicillin Sulbactam	1,5-3 g max 4 g/day	1,5 gr	S	3-4x1	3x1	S	IV	IV	S

DISCUSSION

Antibiogram pattern formed from the data on the antibiotic sensitivity of the bacteria tested are sensitive, then the transactions are carried out with the data filtering CLSI (Clinical and Laboratory Standards Institute) to eliminate antibiotic that shows the results of the examination of bias in test cultures. In the antibiogram results, 61 urine isolates showed bacterial growth results consisting of 14 (22.95%) aerobic gram-positive bacteria and 47 (77.05%) aerobic gram-negative bacteria. The bacteria most commonly found in the urine of patients UTI isolates in ICU Hospital Dr. Soetomo Hospital is a positive for gram negative *Staphylococcus Coa* was 8.20% for occupied by gram-negative bacteria *Escherichia coli* (22.95%). The high number of bacteria (*Escherichia coli*) is caused by the normal intestinal flora and its distribution pattern

through the perineal region and colonized into the urethra or bladder (Christensen 2000). With the data show that the most germs infecting UTI is an infection of gram-negative. This is consistent with research that says Setiawan most pathogens are gram- negative ICU with details of *Enterobacter aerogenes* (34%), *Escherichia coli* (15%), *Pseudomonas aeruginosa* (10%), *Acinobacter spp* (8%) and the remaining sensitive to gram-positive bacteria (Setiawan 2010). Although the composition of gram-positive bacteria caused infections of the lowest UTI, it should be of concern because as an example of *Staphylococcus aureus* isolates can also reveal bacteremia infection in patients with UTI (Stamm 1995).

The number of patient sex in UTI men (86%) is bigger than women (14%) (Table 5). It is not appropriate description of the results of previous studies on the use of antibiotics in inpatient hospital room Dr. Soetomo Hospital that the female gender UTI patients more than men. This is reinforced by reason of the high risk factors female gender, influenced by anatomical factors of urinary tract (urethra) and excretion (anus) are adjacent, so it is more easily contaminated, in addition to the pH changes and the patterns of the normal flora bacteria also affect the menstrual cycle (Coyle & Prince 2005), these anomalies are not considered representative describe, probably due to the sample size is too small.Age distribution of patients UTI almost everything balanced in the various groups, the highest in the 30-39 year age group intervals (Table 5). Risk factors that trigger the occurrence of UTI in the age range including sexual activity and the presence of a comorbid risk factor for UTI such as renal impairment, diabetes mellitus (DM), and hypertension.

Based on the above, it is known that many opportunities for problems related to administration of antibiotics to patients UTI, both antibiotic regimens and associated antibiotic resistance, so the need for direct roles of the various parties involved in the administration of antibiotic therapy to patients as doctors, pharmacists, and nurses to improve treatment and control of antibiotic resistance in order to achieve optimal patient outcomes of therapy.

CONCLUSION

Antibiotics recommended for the bacteria *Escherichia coli*, which causes most UTIs cases are ertapenem, imipenem, meropenem, ciprofloxacin, sulbactam cefoperazon, nitrofurantonin, amikacin and gentamicin. As for the evaluation of the use of antibiotics by the method of prescribing antibiotics Gyssens generate the remaining 6 (54.55%), which can be said as appropriate.

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