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Pharmacist counseling intervention to improve patient antibiotic compliance

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ABSTRACT

Background and purpose: Reported microbial resistance to antibiotics is increasing. One of the main factors is patient non-compliance in use of antibiotics. The purpose of this study was to determine the effectiveness of pharmaceutical counseling in a pharmacy setting to increase compliance with antibiotic use.

Methods: A randomized controlled trial was conducted on 104 adult patients aged 18 years and over who purchased antibiotics by prescription at a pharmacy in Denpasar City, Bali Province. Subjects were divided into intervention and control groups using block randomization method. The intervention group was provided with pharmaceutical counseling by a pharmacist, while the control group was provided drug information according to the pharmacy service standard. Subject compliance was measured by telephone interview using the Morisky Medication Adherence Scale-8 questionnaire within 3-5 days after purchasing the medication. Statistical analysis with the Mann Whitney U Test was performed to determine the difference in mean rank of compliance scores. Logistic regression analysis was conducted to determine the adjusted compliance ratio.

Results: The number of subjects analyzed was 98, as five subjects could not be contacted by telephone and one subject was hospitalized. The mean rank of compliance scores in the intervention group (61.05) was significantly higher ($p<0.01$) than the comparison group (37.95). The proportion of compliance in the intervention group was 65.3% and the control group was 18.4%, with the proportion ratio (PR) of 3.56 (95%CI: 1.90-6.64). Logistic regression analysis showed that variables which significantly increased compliance with antibiotic use were pharmacist counseling (APR=9.33; 95%CI: 3.24-26.87), frequency of taking medication (APR=6.94; 95%CI: 2.01-23.92) and method of payment (APR=4.30; 95%CI: 1.18-15.66).

Conclusion: Pharmaceutical counseling at a pharmacy setting was found to increase compliance of antibiotic use. Compliance of antibiotic use is also influenced by the frequency of taking medication and the method of payment. Pharmacist counseling when accessing medication at a pharmacy is crucial for improving patient compliance of antibiotic use.

Keywords: Pharmacist counseling, compliance, antibiotic use

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INTRODUCTION

Antimicrobial resistance has become a global concern with an incidence that tends to increase in various countries.[1] Estimated number of deaths due to antimicrobial resistance is around 10 million per year with a projected cumulative economic loss of USD 100 billion in 2050.[1] Surveillance of antibiotic resistance carried out in Indonesia in 2010 and 2012 showed an increased prevalence of extended-spectrum B-lactamase (ESBL) infections from 22% to 53% and methicillin-resistant S.aureus (MRSA) from 18% to 24%.[2]

One of the factors that influences the occurrence of antimicrobial resistance is the non-compliance of patients in the use of antibiotics.[3-5] Non-compliance was reported to occur more in those who self-medicated.[3-5] A study in Portugal showed that the prevalence of non-compliance with antibiotic therapy in adults was 57.7% and was related to delays and failures in taking prescribed medicine.[6] A study in Indonesia showed that the rate of compliance with short-term antibiotic use in children undergoing treatment at Cipto Mangunkusumo Hospital was 75.6% and it was reported that forgetfulness and preoccupation were factors that influenced the compliance.[7]

Pharmaceutical counseling is one of the services that must be carried out by a pharmacist to provide quality services, interact directly with patients and be responsible for drugs delivered to patients so that they can understand the use of the drugs.[8] Several studies showed that pharmaceutical counseling is proven to be effective in increasing compliance with the use of several types of drugs, including medicines for hypertension, diabetes and other chronic diseases,[9-14] but the effectiveness of pharmaceutical counseling in pharmacies on compliance with antibiotic use has not been widely published.

A study in Jakarta indicated that the provision of drug information at pharmacies to consumers

remains inadequate, with 98.5% of pharmacies do not meet the standards of communication, information and education for patients.[15] Preliminary observations conducted by researchers of this study indicate that the provision of information on medications in the pharmacy was too brief with only about 2 to 3 minutes, unstructured and carried out at the cashier area at the time of drug delivery, while pharmaceutical counseling that involves longer interaction between pharmacists and patients is rarely carried out. This study aims to determine the effectiveness of pharmaceutical counseling in a pharmacy setting to increase antibiotic use compliance.

METHODS

A randomized controlled trial (RCT) was conducted with 104 adult patients aged 18 years and above who were recruited when purchasing antibiotics at a pharmacy in Denpasar City, Bali Province in February-March 2018. This pharmacy was chosen because it has a one stop health care concept which include 10 specialists, pre-primary clinic, optics, physiotherapy and clinical laboratories, with around 500 prescriptions per day and 100 of them are mainly for antibiotic requests.

The inclusion criteria were adult patients who presented at the pharmacy with a prescription to buy one or more types of oral antibiotic and were willing to participate in the study. The exclusion criteria were patients who worked as doctors, nurses, midwives and other health workers. The minimum number of 104 subjects was determined with a confidence level of 95% and a power of 90% with the effect size of 20%. The subjects were divided into two groups namely 52 subjects in the intervention group and 52 subjects in the control group using the block randomization method. The intervention group was provided a pharmaceutical counseling by a pharmacist at the time of delivery of the drug at the pharmacy. Before the intervention was conducted, training by researchers on the study procedures, materials and counseling techniques was carried out. Counseling content referred to the Pharmaceutical Services Counseling Guidelines in Health Facilities in 2007 which consisted of medication history, antibiotic regimens, methods of use, side effects, use of medication and the addressing of medical problems.[8] The counseling room was prepared in a special area separated from the patients waiting room, equipped with tables and chairs to ensure face to face interaction. Counseling for the intervention group was conducted for 15 minutes while the control group was given information at the counter of drug delivery for 1-2 minutes according to the standard of the pharmacy service which consisted of the name of the drug, dosage and frequency of taking medication.

Baseline data collected through interviews during enrollment consisted of age, gender, education, occupation, number of drugs, frequency of taking medication, duration of drug use, number of types of drugs in prescription, method of payment, and patient perception on drug prices. Compliance with antibiotic use was measured by telephone interview to patients using the Morisky Medication Adherence Scale-8 questionnaire[16] within 3-5 days after purchasing the medication.

Data were analyzed using STATA SE 12.1. The median difference in adherence scores was determined using the Mann Whitney-U Test and the proportion of compliance ratio (PR) calculated to measure the effectiveness of pharmaceutical counseling. Multivariate analysis was performed using logistic regression to determine the factors that influence compliance in antibiotic use. This study has been approved by the Ethics Committee of the Faculty of Medicine, Udayana University/ Sanglah General Hospital in Denpasar on January 22, 2018.

RESULTS

Of the 104 subjects who were recruited, six people were lost to follow-up, three people in the intervention group and three people in the control group. The reasons of loss to follow up were telephone number was not active, could not be contacted due to incorrect telephone number recorded in the data baseline and patients were hospitalized during the period of data collection. Subjects included in the analysis consisted of 49 subjects in the intervention group and 49 subjects in the control group (Figure 1).

Table 1 shows the characteristics of the intervention and control groups based on social demographic variables, patient perceptions of drug prices, method of payment, number of tablets prescribed, number of drug types and frequency of taking medication. The subject characteristics were not significantly different based on age ($p=0.08$), gender ($p=0.31$), education ($p=0.12$), occupation ($p=0.89$), patient perceptions of drug prices ($p=0.60$), the number of prescribed antibiotic tablets ($p=0.09$), frequency of taking antibiotic ($p=0.98$) and number of prescribed drug types ($p=0.05$). However, there are significant differences based on the method of payment ($p<0.01$) and duration of antibiotic use ($p<0.01$).

Table 2 presents the proportion and score of antibiotic use compliance in the intervention and

Table 1 Characteristics of subjects in the intervention and control groups

Characteristics of subjects	Intervention		Control		p
	n	%	n	%	
Age (years)					
45	30	61.2	38	77.6	0.08
45	19	38.8	11	22.4	
Gender					
Male	27	55.1	22	44.9	0.31
Female	22	44.9	27	55.1	
Education					
Elementary	4	8.2	0	0.0	0.12
Junior high school	22	44.9	25	51.0	
Senior high school	23	46.9	24	49.0	
Occupation					
Student	3	6.1	3	6.1	0.89
Employee	30	61.2	29	59.2	
Housewife	6	12.2	9	18.4	
Private business	5	10.2	5	10.2	
Retired	5	10.2	3	6.1	
Payment Methods					
Out of pocket	16	32.7	5	10.2	<0.01
Insurance	33	67.3	44	89.8	
Patient's perception of drug prices					
Expensive	3	6.1	3	6.1	0.60
Fair	46	93.9	45	91.8	
Cheap	0	0.0	1	2.0	
Number of prescribed antibiotic tablets					
3	3	6.1	3	6.1	0.09
6	14	28.6	23	46.9	
8	0	0.0	2	4.1	
9+	32	65.3	21	42.9	
Frequency of taking antibiotic (daily)					
Once	3	6.1	3	6.1	0.98
Twice	28	57.1	29	59.2	
Three times	18	36.7	17	34.7	
Length of antibiotic use (days)					
3	29	59.2	42	85.7	<0.01
4	1	2.0	2	4.1	
5	19	38.8	5	10.2	
Number of drug types					
1	3	6.1	0	0.0	0.05
2	24	49.0	16	32.7	
3	18	36.7	23	46.9	
4	4	8.2	10	20.4	
Total	49	50.0	49	50.0	

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Table 2 Compliance of antibiotics use in the intervention and control groups

	Intervention n (%)	Control n (%)	Compliance ratio	95%CI	p
Compliance					
Compliant	32 (65.30)	9 (18.40)	3.56	1.90-6.64	<0.01
Non-compliant	17 (34.70)	40 (81.60)			
Compliance score					
Mean rank	61.05	37.95			<0.01

Table 3 Antibiotic use compliance based on several variables

	Compliant		Non-compliant				
Variables	**n**	**%**	**n**	**%**	**PR**	**95%CI**	**p**
Age (years)							
<45	27	39.7	41	60.3	0.85	0.53-1.38	0.51
45+	14	46.7	16	53.3			
Gender							
Male	22	44.9	27	55.1	1.16	0.73-1.85	0.54
Female	19	38.8	30	61.2			
Education							
Elementary	4	100.0	0	0.0	-	-	1.00
Junior high	18	38.3	29	61.7	1.09	0.48-2.50	0.83
Senior high	19	41.8	28	59.2			
Frequencyof taking antibiotic (time/day)							
1-2	32	50.8	31	49.2	1.98	1.07-3.65	0.02
3-4	9	25.7	26	74.3			
Length of antibiotic use (days)							
3	25		14				0.09
4	2		10				
5	14		14				
Payment methods							
Out of pocket	14	66.7	7	33.3	1.90	1.24-2.92	<0.01
Insurance	27	35.1	50	64.9			

control groups. Mean rank of compliance scores was found to be significantly (p<0.01) higher in the intervention group (61.05) than in the control group (37.95). The proportion of compliance in the intervention group (65.3%) was also found to be significantly higher than in the control group (18.4%) with a compliance ratio (PR)=3.56 (95%CI: 1.90-6.64; p<0.01).

Table 3 shows compliance with antibiotic use based on social demographic variables, frequency of medication, duration of use and method of payment. Compliance was found to be significantly associated with the frequency of taking medication (PR=1.98; 95%CI: 1.07-3.65; p=0.02) and method of payment (PR=1.90; 95%CI: 1.24-2.92; p<0.01).

Table 4 shows the PR of antibiotics use compliance based on the frequency of taking medication and the method of payment. It was found that the proportion of compliance among subjects with taking medicine frequency of 1-2 times was significantly higher in the intervention group than in the control group (PR=2.64; 95%CI: 1.46-4.77; p<0.01). The proportion of compliance among subjects who took the antibiotics 3-4 times was also higher in the intervention group, however the ratio could not be calculated because there was a zero value. In addition, there was a significant difference of compliance in the group of payment by insurance with PR=3.17 (95%CI: 1.59-6.33), but there was no significant difference in the group of payment by out of pocket with PR=4.06 (95%CI: 0.69-23.82).

Table 5 presents the results of logistic regression and it appeared that the proportion of antibiotic use compliance was significantly higher among

Table 4 Specific compliance ratios in the intervention and control groups

Variables	Compliant		Non-compliant		PR	95%CI	p
	n	%	n	%			
Frequency of taking antibiotic (1-2 times/day)							
With counseling	23	74.2	8	25.8	2.64	1.46-4.77	<0.01
Without counseling	9	28.1	23	71.9			
Frequency of taking antibiotic (3-4 times/day)							
With counseling	9	50.0	9	50.0	-	-	<0.01
Without counseling	0	0.0	17	100.0			
Payment by out of pocket							
With counseling	13	81.2	3	18.8	4.06	0.69-23.82	0.03
Without counseling	1	20.0	4	80.0			
Payment by insurance							
With counseling	19	57.6	14	42.4	3.17	1.59-6.33	<0.01
Without counseling	8	18.2	37	81.8			

Table 5 Adjusted proportion ratios (APR) of pharmacist counseling, frequency of taking antibiotic and methods of payment

Variables	APR	95% CI	p
Pharmacist counseling			
With counseling	9.33	3.24-26.86	<0.01
Without counseling	1.00		
Frequency of taking antibiotic			
1-2 times/day	6.94	2.01-23.93	<0.01
3-4 times/day	1.00		
Method of payment			
Out of pocket	4.30	1.18-15.65	0.03
Insurance	1.00		

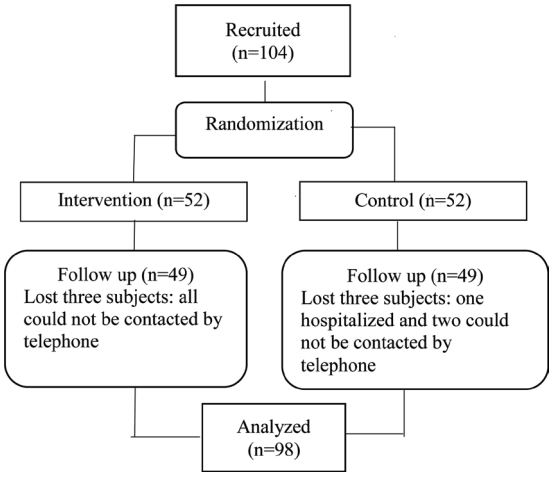

Figure 1 Subject selection

intervention group (with counseling) compared to control group (without counseling) with APR of 9.33 (95%CI: 3.24-26.86). Compliance was also significantly higher among subjects who provided with lower frequency of taking antibiotics with APR=6.94 (95%CI: 2.01-23.93) and payment by out of pocket (APR=4.30; 95%CI: 1.18-15.65).

DISCUSSION

This study shows that antibiotic use compliance was significantly higher in the group provided with pharmaceutical counseling (65.3%) than those who were only provided with information based on the pharmacy standards (18.4%). This study also shows that the proportion of antibiotic

use compliance was associated with the frequency of taking antibiotic and the method of payment. Subjects with a lower frequency of taking antibiotic (1-2 times/day) were found to be more compliant than those with a higher frequency (3-4 times/day). In addition, subjects who paid with out of pocket were found to be more compliant than those who paid with insurance. This is likely because patients who paid by out of pocket were using their personal funds to purchase the medication, therefore they tended to be more compliant in the antibiotic use.

The effectiveness of counseling on antibiotic use compliance was also reported in other studies. A study in Ireland showed that compliance and successful treatment of Helicobacter Pylori infection were significantly higher in patients with antipeptic and antibiotics treatment combined with counseling and follow-up by hospital pharmacists, compared to patients who were only provided with treatment without counseling and follow up.[3] Other published studies showed that counseling is proven to be effective in increasing compliance of medications other than antibiotics. Research in Mojokerto[10] conducted on hypertensive patients showed that the provision of counseling in the form of motivational interviewing was effective in increasing compliance of an anti-hypertension treatment when compared with the provision of leaflets. A study in Depok City, West Java[9] also showed that counseling was effective in increasing compliance in anti-hypertension treatment and reducing the patients' blood pressure, although the study showed no significant difference with the effectiveness of education through provision of leaflets.[9] Several studies in other countries aimed at determining the effectiveness of pharmaceutical counseling using an RCT design in patients with chronic diseases also found consistent results.[11-14]

The finding of our study on the association of compliance and frequency of taking antibiotics is consistent with an RCT study in patients with lower respiratory tract infections in the Netherlands which found that compliance in antibiotic use was higher in patients who received a one-time dose per day than those who received a three-time dose per day.[17] This current study finding is also consistent with a prospective observational study conducted in Spain from 2003 to 2008 in adult patients aged 18 years and over with respiratory tract infections, which showed that patient medication compliance decreased significantly with increasing frequency of antibiotic use and length of antibiotic therapy.[18] Another study in Portugal found an association between the duration of antibiotic treatment and patient compliance but did not assess treatment compliance based on the frequency of taking antibiotic per day.[6]

Other studies that aim to evaluate the association of medication compliance with payment methods remain very limited. A study in Portugal found that higher non-compliance in antibiotic treatment occurred in patients who had difficulty in purchasing medication, but did not investigate the payment methods used by patients.[6]

The limitation of this study is that the antibiotic use compliance was measured through interviews by telephone, so that the possibility of information bias may have occurred. Another limitation is the possibility of selection bias where in this study most of the subjects were middle and high school educated and only a small percentage were low educated. This study was only carried out at one pharmacy in the city of Denpasar so that generalization of the results to a wider population needs to be taken in caution.

CONCLUSION

Pharmaceutical counseling at a pharmacy setting was found to increase compliance of antibiotic use. Compliance in antibiotic use is also influenced by the frequency of taking antibiotic and the method of payment. Pharmacist counseling when accessing medication at a pharmacy should be enhanced to improve patients' compliance in the use of antibiotics, especially in patients given antibiotics with a frequency of 3-4 times/day and patients who use insurance as a payment method.

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